Cancer Council Australia: Draft Clinical Practice Guidelines for keratinocyte cancer

Submission of the Australasian College of Dermatologists

About the Australasian College of Dermatologists

The Australasian College of Dermatologists (ACD) is the sole medical college accredited by the Australian Medical Council for the training and continuing professional development of medical practitioners in the specialty of dermatology. The College is the national peak membership organisation representing over 500 dermatologist Fellows (FACD) and 100 trainees.

The College is the leading authority in Australia for dermatology, providing information, advocacy and advice to individuals, communities, government and other health stakeholders on dermatological practice in Australia. The College's focus is to train and maintain highly qualified dermatologist specialists who work to improve outcomes in skin health of individuals and communities.

The ACD is the only medical college accredited by the Tertiary Education Quality Standards Agency (TEQSA) as a Higher Education Provider.

Executive Summary

About Mohs Micrographic Surgery

Mohs Micrographic Surgery (MMS) is a specialised technique for the treatment of skin cancers in which 100% of excised tissue margin is examined by frozen section, aiming to ensure complete tumour clearance while maximising normal tissue conservation and function. In contrast, with Wide Excision standard bread-loaf sectioning only 0.1 – 1% of the surgical margin may be subject to pathological examination. Mohs surgery is usually performed over the course of a day, under local anaesthetic, with defect repair on that same day. This cost-effective procedure has a small cost difference compared with Wide Excision, requiring specialised equipment and staff.

In Australia, the Australasian College of Dermatologists (ACD) is responsible for the training, site accreditation and ongoing professional development of MMS practitioners. The ACD maintains the Australian Mohs Register – the list of approved specialists who are eligible to claim MMS Medicare item numbers. The ACD also sets Appropriate Use Criteria for Mohs surgery and Clinical Benchmarks which have been adopted by Medicare.

Indications for Mohs surgery include:

- Poorly defined clinical tumour margins
- Recurrent or incompletely excised lesions
- Aggressive histopathological subtypes e.g. morphoeic, infiltrative, micro nodular, basosquamous
- Perineural and/or perivascular involvement
- Size > 2 cm
- Location: central face i.e. around eyes, nose, lips and ears
- When tissue sparing is of great importance

The literature comparing MMS with Wide Excision for the management of keratinocyte carcinoma supports the following statements:

- MMS is superior to Wide Excision in terms of cure rate for recurrent BCC of the face.
- MMS and Wide Excision show similar cure rates for primary BCC of the face.
    - Consideration should be given to MMS for primary BCCs within the H-zone or for those with aggressive histology where a higher cure rate may be achieved.
- MMS will produce a 38 – 48.6% decrease in defect area compared with Wide Excision for BCC which may allow simpler repair options.
- MMS and Wide Excision show similar cure rates for the management of SCC of the face.

The draft Guidelines: general comments

Five sections of the Guidelines contain content relating to MMS, some of which is reasonable and supported, and the plain English summary seems balanced. These sections include:

- Surgical Treatment
    - Optimal surgical technique for the treatment of basal cell carcinoma
    - Considerations when planning surgical treatment for cutaneous squamous cell carcinoma
    - Protocol to manage incompletely resected basal cell carcinoma
    - Criteria for choosing Mohs micrographic surgery in preference to other surgical techniques
- Economics of keratinocyte cancer

This submission outlines key comments for each section, with particular focus on 'Criteria for choosing MMS'. It is generally felt that the section lacks some cohesion and could be considerably improved. A number of studies of MMS in patients with SCC are not included in the evidence review; it is unclear whether they were excluded as a result of the search strategy or if this is an oversight. We present this high level evidence for consideration and strongly argue for its incorporation. In addition, the importance of smaller defect size with MMS for the management of primary BCC on the face – not only for clinical and aesthetic outcomes, but also for its economic implications – is not given due consideration. Finally, the place of MMS in the Australian health and policy setting, including training requirements and access to Medicare reimbursement, should be addressed.

Of some concern is the phrasing used when comparing treatments with similar clinical effectiveness or outcome. The authors use the approach of 'Treatment B has no advantage over Treatment A', which may be considered leading and lacking impartiality. We suggest wording to the effect of 'Treatment A and B show similar outcomes in this scenario' which will go some way to eliminate unintended bias and is considered a more even-handed approach.

Summary of comments on Recommendations and Practice Points

DRAFT CONTENT	SUGGESTED AMENDMENT
Surgical Treatment: Optimal surgical technique for the treatment of basal cell carcinoma	
EVIDENCE SUMMARY AND RECOMMENDATIONS There was no significant difference in recurrence rates between MMS and surgery	MMS is the treatment of choice for recurrent facial BCC. MMS and Wide Excision provide similar cure rates for primary BCC but consideration should be given to MMS for BCCs within the H-zone or those with aggressive histology where a higher cure rate may be achieved. In addition consideration should also be given to MMS over Wide Excision if a significantly smaller defect size could be of clinical benefit.
EVIDENCE-BASED RECOMMENDATION Patients with basal cell carcinomas with a high risk of recurrence (e.g. due to unfavourable histological type or anatomical site) should be offered wide surgical excision. Adequate follow-up should be provided.	Sufficient evidence for MMS to be included in the Evidence-based Recommendation. Consider wording suggested in Practice Point below.
PRACTICE POINT Patients with basal cell carcinomas with a high risk of recurrence (e.g. due to unfavourable histological type or anatomical site) should be offered wide surgical excision, where possible. Mohs micrographic surgery can be considered as an alternative. Adequate follow-up should be provided.	Patients with basal cell carcinomas with a high risk of recurrence (e.g. due to unfavourable histological type or anatomical site) should be offered surgical excision. Deciding between Wide Excision and MMS should take into account the "Criteria for choosing MMS in preference to other surgical techniques". (Link to chapter)
Surgical treatment: Considerations when planning surgical treatment for cutaneous squamous cell carcinoma	
EVIDENCE SUMMARY AND RECOMMENDATIONS Recurrence	MMS and Wide Excision of SCC on the face show similar cure rates at 5 year follow up.
Surgical treatment: Criteria for choosing Mohs micrographic surgery in preference to other surgical techniques	
PRACTICE POINT For patients with high-risk recurrent facial basal cell carcinomas, consider referral for assessment for Mohs micrographic surgery.	For patients with recurrent facial basal cell carcinomas, consider referral for MMS.
PRACTICE POINT Mohs micrographic surgery may be considered in the treatment of basal cell carcinomas with any of the following features: • poorly defined borders (particularly those of an aggressive histological subtype that are located in an anatomically sensitive area)	Mohs micrographic surgery may be considered in the treatment of primary basal cell carcinomas with any of the following features: • poorly defined clinical border • infiltrating or micro-nodular histology • residual following previous treatment • located in the H-zone of the face • large >10mm in diameter on the face

• recurrent or residual following previous treatment • high-risk at facial site • extensive	• by utilising MMS compared to Wide Excision the defect size reduction would be of clinical significance
	NEW PRACTICE POINT Mohs micrographic surgery should be considered in the management of SCC and utilised where 100% clearance of the surgical margin and tissue preservation offer clinical value
PRACTICE POINT Mohs micrographic surgery can be useful for histologically confirmed recurrent basal cell carcinomas of the face greater that are large (>10mm in diameter), show aggressive histological features, or are located on the H-zone of the face.	DELETE (SUGGEST MERGE WITH SECOND PRACTICE POINT IN THIS SECTION, AS SHOWN ABOVE)
	NEW PRACTICE POINT MMS practitioners should follow the Medicare Appropriate Use Criteria for MMS and clinical benchmarks developed by the Australasian College of Dermatologists.

SPECIFIC COMMENTS

Surgical Treatment: Optimal surgical technique for the treatment of basal cell carcinoma

Draft Clinical Practice Guidelines: wording	ACD Comments
Systematic review evidence	
What factors need to be considered when determining the optimal surgical technique for those with basal cell carcinoma?	Reported outcomes from identified studies in the systematic review included completeness of excision, recurrence rates and cure rates. We suggest that in addition to these outcomes, studies investigating defect size difference between MMS and Wide Excision should be included as this an important factor when determining optimal surgical technique. This important concept is also discussed in 'Criteria for choosing MMS in preference to other surgical techniques.' The ability of MMS to produce a smaller defect size compared to Wide Excision for any given tumour diameter has important clinical and economic considerations and is a major advantage of the technique. In short, the smaller the eventual defect the simpler the outcome for all. **What is the evidence that MMS for any given BCC will produce a smaller defect compared to wide excision?** Five papers have examined this area and include level 1b evidence. • In a study by Muller et al, nodular BCCs were randomized to MMS and Wide Excision in an adequately powered trial which reported a significantly smaller defect size after MMS compared to Wide Excision: 116.6 v 187.7mm2, P<.001, 38% reduction in surface area.[1] • Smeets et al (Reference 33 in the draft Guidelines) reported that defect sizes for BCCs that required two or more stages of MMS compared to those incompletely excised by Wide Excision were significantly smaller: 48.6 v 86.6mm2, P<0.001, 44% reduction in surface area.[2] • In a prospective study of 256 infiltrating BCCs on the head and scalp, van Kester et al noted a significant reduction in defect area following MMS compared to the calculated Wide Excision defect area: 154 v 298mm2, P<0.01, 46% reduction in surface area.[3] • In a retrospective study of facial and scalp BCCs, 54% primary and 46% recurrent, Gnaidecki et al measured the defect size after MMS and compared this to a calculated Wide Excision defect area using a 4mm or 6mm margin and showed a 40% reduction in defect size when MMS was used.[4] • Van der Eerden et al in a retrospective non-randomized cohort study of BCC and SCCs treated by MMS or Wide Excision showed statistically significant smaller defects with MMS (p<0.008). The authors comment that this may facilitate reconstruction.[5]

Draft Clinical Practice Guidelines: wording	ACD Comments
	The data available supports the argument that across a variety of clinical scenarios for BCC excision, MMS may reduce the defect area by 38 – 48.6% compared with Wide Excision. Taken together, these citations support the following statement: **MMS should be considered over Wide Excision for primary BCC where its tissue sparing properties would be clinically advantageous.**
Recurrence rates	
"Mohs micrographic surgery did not seem to have any advantage over standard surgery in most tumours.[1][2][3][6][7][11][12]"	We have reviewed the references cited above as follows: • References 1 and 2 are from the same Netherlands Group RCT. They report the 5 and 10 year results comparing MMS and Wide Excision for primary and recurrent facial BCC. Reference 2 is the most recent study and should be used. For primary facial BCC, 10-year recurrence rate was 4.4% with MMS vs 12.2% (p=0.100) with Wide Excision. For recurrent facial BCC, 10-year rates were 3.9% and 13.5% for MMS and Wide Excision respectively (p=0.023). • Reference 3 is a retrospective case series from Germany with 101 patients of whom 24 were treated with Mohs surgery, however the technique used was serial staged excision over a series of days and not comparable with Mohs surgery as defined by Medicare in Australia. The follow-up for recurrence is one year and no difference was observed. The authors note the small sample size and limited follow up period. This has limited weight if it is being used to support the 'no advantage' level 1 evidence seen by van Loo et al (Reference 2 in the draft Guidelines). • Reference 6 is an American prospective cohort study comparing multiple treatments for primary BCC and SCC. At 5 years no difference in recurrence was observed. However, sub-group analysis for tumours perceived to be high risk for recurrence showed a statistically significant recurrence rate at 5 years for SCCs and BCCs within the H-zone and those with an invasive histology. • Reference 7 is an American prospective non-randomized study of primary BCC and SCC judged appropriate for MMS which at 5 years showed no significant difference between Wide Excision and MMS. The authors noted that "In keratinocyte carcinomas judged appropriate for MMS, recurrence was less common after MMS than after other treatments". • Reference 11 is an American retrospective non-randomised study comparing MMS and WE in primary BCC and SCC. A total of 588 cases were assessed for recurrence at 3 years. No statistical difference between the two groups was seen. The authors called for randomised trials to compare the treatments over at least a 5-year period. • Reference 12 is a Dutch retrospective non-randomized cohort study of BCC and SCCs treated by a single facial plastic surgeon. 795 MMS cases were compared to 709 Wide Excision. Recurrence was assessed at 16 to 24 months

Draft Clinical Practice Guidelines: wording	ACD Comments
	without a statistical difference. However a statistically significant result (p<0.008) was shown for smaller defects after MMS. Of note, the study by Foroozan et al should be included. This systematic review and meta-analysis reported a significantly reduction in 5-year recurrence rate with MMS compared with standard excision for, recurrent high-risk facial BCC. The study was unable to make a conclusion for other types of BCC and SCC.[6] These citations support changing the 'no advantage' statement and indicate the following: • MMS provides the highest cure rate for recurrent facial BCC. • MMS and Wide Excision provide similar cure rates for primary BCC. • Consideration should be given to MMS for BCCs within the H-zone or those with aggressive histology where a higher cure rate may be achieved. • Consideration should also be given to MMS over Wide Excision if a significantly smaller defect size could be of clinical benefit.
Evidence Summary and Recommendations	
There was no significant difference in recurrence rates between MMS and surgery. II, III-2, III-3, IV [1], [2], [3], [6], [7], [11], [12]	As argued above this statement is not supported by the literature that it quotes. We suggest that it be replaced by: **MMS is the treatment of choice for recurrent facial BCC. MMS and Wide Excision provide similar cure rates for primary BCC but consideration should be given to MMS for BCC's within the H-zone or those with aggressive histology where a higher cure rate may be achieved. In addition consideration should also be given to MMS over Wide Excision if a significantly smaller defect size could be of clinical benefit. (Cancer Council References [2],[6],[7],[12] and [6]).**
Evidence-based recommendations	
Patients with basal cell carcinomas with a high risk of recurrence (e.g. due to unfavourable histological type or anatomical site) should be offered wide surgical excision. Adequate follow-up should be provided.	We argue that there is sufficient evidence to incorporate MMS into the Evidence-based recommendation. We also are of the view that the Practice Point is inadequate. We would suggest the following as an amended Evidence-based Recommendation: **Patients with basal cell carcinomas with a high risk of recurrence (e.g. due to unfavourable histological type or anatomical site) should be offered surgical excision. Deciding between Wide Excision and MMS should take into account the "Criteria for choosing MMS in preference to other surgical techniques". (Link to chapter)**
Practice point	
Patients with basal cell carcinomas with a high risk of recurrence (e.g. due to unfavourable histological type or anatomical site) should be offered wide surgical excision, where possible. Mohs micrographic surgery can be considered as an alternative. Adequate follow-up should be provided.	Please refer to comments above.

Surgical treatment: Considerations when planning surgical treatment for cutaneous squamous cell carcinoma

Draft Clinical Practice Guidelines: wording	ACD Comments
Systematic review evidence	
In patients undergoing surgical treatment for cutaneous squamous cell carcinoma, which surgery-related factors (margin width, depth of excision) or tumour-related factors (size, histological features, anatomical site) influence clinical outcomes (cure rate, local recurrence, regional lymph node involvement, metastasis)?	There are no RCTs comparing MMS and Wide Excision for the treatment of SCC to date. However, there is considerable lower-level evidence (2a and 2b) which supports the use of MMS for treatment of SCC. While we acknowledge that the systematic review has excluded level 2a, 2b evidence, we put forward that the following references should be closely reviewed. • A systematic review by Lansbury et al of observational studies assessed outcomes after MMS for SCC. The pooled average local recurrence rate was 3.0% (2.2% to 3.9%), which was non-significantly lower than the pooled average local recurrence of 5.4% (2.5% to 9.1%) after Wide Excision.[7] • A retrospective study in which high-risk SCCs were treated with MMS noted a recurrence rate of 1.2% after 4 years.[8] • A case series that followed primary or recurrent SCC for up to 5 years after MMS found recurrence rates of 3% and 6% respectively.[9] • An American prospective cohort study by Chren et al compared multiple treatments for primary BCC and SCC. At 5 years no difference in recurrence was observed. However, sub-group analysis for tumours perceived to be high risk for recurrence showed a statistically significant recurrence rate at 5 years for SCCs and BCCs within the H-zone and those with an invasive histology.[10] • An American prospective non-randomized study by Stuart et al of primary BCC and SCC judged appropriate for MMS at 5 years showed no significant difference between Wide Excision and MMS. The authors noted that 'In keratinocyte carcinomas judged appropriate for MMS, recurrence was less common after MMS than after other treatments.' The data regarding MMS and SCC is clearly presented for separate review from BCC.[11]
Evidence Summary and Recommendations	
RECURRENCE	This section lacks a section regarding the important area of surgical technique and recurrence rate. Using the references cited above support the following statement should be added: **MMS and Wide Excision of SCC on the face show similar cure rates at 5 year follow up.**

Surgical treatment: Protocol to manage incompletely resected basal cell carcinoma

Draft Clinical Practice Guidelines: wording	ACD Comments
Notes on the recommendations	
High-risk tumours in high risk sites warrant wider excision, if possible.	We suggest that the advice for wider excision could encompass MMS and wide excision.

Surgical treatment: Criteria for choosing Mohs micrographic surgery in preference to other surgical techniques

This section of the guidelines requires considerable amendment, as it fails to include much of the evidence cited and discussed in earlier sections of the submission (Optimal surgical technique for the treatment of basal cell carcinoma AND Considerations when planning surgical treatment for cutaneous squamous cell carcinoma). As such it does not adequately reflect the full criteria that should be considered in the decision-making pathway for selecting MMS or Wide Excision. Furthermore, we strongly urge that the Australian policy setting is represented, given that patient reimbursement through the Medical Benefits Schedule is offered only to practitioners listed on the Australian Mohs Register. It is critical that this be clarified to ensure that all practitioners are aware of and comply with Federal health policy.

Draft Clinical Practice Guidelines: wording	ACD Comments
Background	
Mohs micrographic surgery (MMS) is named after Frederick Mohs, who pioneered this technique. His original chemosurgery procedure has been modified to a fresh frozen tissue technique.	The background would be enhanced by giving some context of Mohs in Australia: "In Australia the ACD maintains the register of physicians who can claim the Mohs Medicare item number. The ACD is responsible for training accreditation and ongoing professional requirements to remain on the Mohs register. The ACD also sets Appropriate Use Criteria for the Mohs surgery and Clinical Benchmarks which have been adopted by Medicare."[12,13]
Following excision of the tumour, almost the entire peripheral and deep margins of the excised tissue are examined by frozen	This sentence could be improved by a greater degree of precision, for example: "Following excision of the tumour the specimen is processed so that 100% of the peripheral and deep margins of the excised tissue are examined by frozen section."
…section (much like a pie crust around a pie; specifically all the edges of the pie crust against the pie tin are inspected)	We would suggest deletion of this sentence. We would suggest that the analogy can be illustrated through the use of a simple Figure insertion. Many exist free to access on line: an example is Figure 1 of Tolkachjov et al.[14]
The MMS technique involves mapping and staining of the excised tissue and a specialised tissue sectioning	This sentence could be made clearer as follows: "The MMS technique through a combination of specialised tissue processing and mapping allows precise localisation of residual tumour."

Draft Clinical Practice Guidelines: wording	ACD Comments
procedure that enables precise localisation of any residual tumour.	
It aims to ensure complete tumour clearance while maximising normal tissue conservation and function.[8][9][10][11][12][13][14][15][16][17][18][19][20][21][3][22][23]	This sentence could be improved by moving to the above paragraph so it follows on from the description of unique methodology. Consider replacing it aims to by: "This aims to ……."
It is undertaken in several specialised centres in Australia [24][25][26][27][28][29][25][30] and is primarily used in a tertiary referral setting for difficult-to-treat tumours.	This sentence should be moved to the end of the first paragraph. It helps to explain the situation in Australia.
The key to this technique is careful marking of the specimen at surgical removal and then use of horizontal sections to perform topographic and microscopic analysis of the whole outer margin of tissue excised at the time of operation.	This paragraph is a repetition and we suggest that it could be deleted.
It is a time-consuming procedure, with each excision taking 5–30 minutes and the processing and reading of stained frozen sections taking from 15 minutes to several hours, depending on the size and complexity of the specimen.	We have concerns that this statement is subjective with the inclusion of 'time-consuming procedure'. We would suggest the following modification: "The procedure requires specialized equipment and staff. Each excision takes 5–30 minutes and the processing and reading of stained frozen sections takes from 15 minutes to one hour. The total procedure may take up to several hours depending on the size and complexity of the specimen. The procedure is capital intensive both in equipment and staff." Then follow directly on to cost analysis statement see comment below.
The procedure is capital intensive both in equipment and staff. The technique requires specific training and expertise, both for the MMS proceduralist and also for the assisting technicians.	This is subjective and perpetuates the idea that MMS is expensive and slow compared to Wide Excision. We suggest that the following sentence should be inserted: "In a prospective Australian cohort study a direct cost-analysis of MMS versus Wide Excision for BCC was carried out. This showed that MMS was more financially viable than previously appreciated. The absolute cost difference was that MMS cost $40.95 more than Wide Excision - a 6.6% increase. The authors concluded that as the cost between these interventions was small the difference in effectiveness between MMS and Wide Excision would be the major determinant in a formal cost-utility study".[15]
In addition, disconnected foci of tumour can result in a recurrence, and for certain tumours frozen section interpretation may be difficult, such as poorly	This sentence could be improved as follows and placed in the third paragraph before the final sentence: "The technique is based on the principle of contiguous tumour growth. Previous treatment by breaking up a tumour can limit its effectiveness. Furthermore the suitability of a tumour for frozen section analysis is an important part of case selection."

Draft Clinical Practice Guidelines: wording	ACD Comments
differentiated or spindle cell subtypes of cutaneous squamous cell carcinoma (cSCC).[7]	
It is a highly specialised technique required for only a very small number of tumours	Perhaps changing this to "a minority of tumours" would be of greater utility.
, the decision to offer MMS should be by a medical practitioner experienced in skin cancer diagnosis and management who has a clear understanding of the technique and its value.	The aim of this additional sentence is to provide a link from the introduction to the evidence, bearing in mind the chapter is to provide guidelines on when MMS should be used instead of Wide Excision and in what scenarios. We suggest the following addition after 'value': "If MMS offers a higher cure rate for a skin cancer compared to Wide Excision then it should be the treatment of choice for that skin cancer. The Australian Medical Benefit Schedule provides clear defect diameters (tumour diameter plus wide excision margin) for which it is acceptable to repair the defect with a flap or graft.[16] If MMS offers a similar cure rate for a skin cancer in a given location but produces a defect size significantly less than Wide Excision, then consideration should be given depending on the clinical scenario to its use. The ability to produce a smaller defect size that could be repaired primarily, rather than using a flap or graft, is not without consideration clinically and economically. If evidence exists for this then the case should be considered that for any given tumour diameter Wide Excision may require unnecessarily extensive reconstructive surgery compared with MMS.[17] The next section considers evidence regarding these two areas for MMS and Wide Excision: cure rate and tissue sparing."
Overview of evidence (non-systematic literature review)	
Overview of evidence (non-systematic literature review)	This non-systematic literature review should be orientated clearly around why Mohs should be chosen in certain scenarios over wide excision. At the moment the layout is unclear as to why these papers are collected together. Below the heading we would suggest the following: "The criteria for choosing Mohs over other techniques include scenarios where a clear advantage in tumour cure are present and or where the tissue sparing capacity of the technique would be significant. The papers in this non-systematic literature review are grouped under these two headings".
**Immediately under 'Overview of evidence (non-systematic literature review)	Suggest inserting sub-heading "**Evidence regarding differences in cure rate for Keratinocyte cancer between Mohs and Wide Excision.**"
A systematic review and meta-analysis reported a significantly reduction in 5-year recurrence rate with MMS compared with standard excision for recurrent high-risk facial basal cell carcinoma (BCC), but not for primary facial BCC.[32]	This reference is an abstract that has not been subsequently published although supporting the Dutch group's work. We do not agree with the statement at the end of this sentence '…but not for primary facial BCC' based on the published abstract. We would suggest altering this to: "…recurrent high -risk facial basal cell carcinoma (BCC). The study was unable to make a conclusion for other types of BCC and SCC." Please note the conclusion in the Abstract of this reference:

Draft Clinical Practice Guidelines: wording	ACD Comments
	"To the best of our knowledge, this is the most comprehensive systematic review on recurrence rates after MMS for BCC and SCC. Based on the current literature, only high-risk recurrent facial BCC had lower recurrence rate after MMS or similar surgical techniques with meticulous histologic evaluation of all margins. Because of the insufficient number of high-quality studies and heterogeneity of existing studies, we were unable to make a conclusion for other types of BCC and SCC. Our study illuminates the current status of literature on MMS and highlights the lack of high quality trials, particularly in SCC. Additional well-designed trials are needed. However, ethical concerns may prevent performing such studies."
To date there has only been one randomised clinical trial looking at surgical margins using recurrence of tumour as a study endpoint.[33] This study compared recurrence at 30 months following standard excision and Mohs' surgery. There was no significant difference in terms of recurrence between the two groups. *High-quality evidence supporting the use of MMS is mainly for recurrent facial BCC.[33]*	We disagree with these statements and argue that they should be updated to include the study of van Loo (2014). We suggest the following amendment: "A RCT conducted over 10 years in the Netherlands compared MMS with standard excision for primary and recurrent facial BCC. The final analysis showed a 10-year recurrence rate of 4.4% for facial primary BCC treated with MMS compared with 12.2% (p=0.100) following Wide Excision. For recurrent BCC the 10-year recurrence rates were 3.9% and 13.5% for MMS and Wide Excision respectively (p=0.023)."[18]
There are only a few retrospective studies assessing other skin cancers such as cSCC. *There is no proven benefit for Mohs surgery in the treatment of cSCC.*	We argue that these two spatially disparate sentences should be combined in the following new paragraph and include the following studies: "There are no RCTs comparing MMS and Wide Excision for the treatment of SCC to date. However there is significant lower level evidence (2a and 2b) which supports the use of MMS for treatment of SCC." Please refer to page 6 of this submission (*Surgical treatment: Considerations when planning surgical treatment for cutaneous squamous cell carcinoma - Systematic review evidence*) for a summary of these 5 studies[7-11] and discussion. We strongly argue that this evidence should be cited accordingly. Regarding the literature comparing MMS with Wide Excision for management of BCC and SCC the following statements are supported: • MMS is superior in terms of cure rate to Wide Excision for recurrent BCC of the face. • MMS and Wide Excision of the face show similar cure rates for primary BCC of the face. • MMS and Wide Excision of the face show similar cure rates for the management of SCC.
Despite high cure rates, MMS remains unnecessary for the vast majority of tumours. It has been estimated that MMS is appropriate for and is used in approximately about 1–2% of keratinocyte tumours in Australia (See Prognosis).	This statement should be deleted as it does not fall under the subheading for this section which is "Overview of evidence". It can be addressed in 'practice points'.

Draft Clinical Practice Guidelines: wording	ACD Comments
**Immediately beneath the abovementioned paragraph:	We suggest that a new heading should be inserted to add coherence to the presentation of evidence: "**Evidence regarding differences in defect size for skin cancer between Mohs and Wide Excision**." Five papers have examined this area and include level 1b evidence.[1-5] Please refer to Page 3 of this submission (*What is the evidence that MMS for any given BCC will produce a smaller defect compared to wide excision?*) for summary and discussion. It should be noted that there are no RCTs regarding MMS v Wide Excision in the scenario of incomplete excision of a BCC following Wide Excision. However a prospective study described the use of MMS for 100 incompletely excised BCCs. The aim of the study was to assess how often BCC was found during the MMS process (69% of cases) rather than to assess long term recurrence from this approach.[19]
Practice Point	
For patients with high-risk recurrent facial basal cell carcinomas, consider referral for assessment for Mohs micrographic surgery.	The insertion of the phrase 'high-risk' is not supported by the Level 1 evidence which shows high-risk recurrent facial and recurrent facial BCCs have a better outcome with MMS than Wide Excision: "For patients with recurrent facial basal cell carcinomas, consider referral for MMS".
Mohs micrographic surgery may be considered in the treatment of basal cell carcinomas with any of the following features: • *poorly defined borders (particularly those of an aggressive histological subtype that are located in an anatomically sensitive area)* • *recurrent or residual following previous treatment* • *high-risk at facial site* • *extensive*	For clarity this [basal] should be defined as primary. We are of the view that this list is somewhat repetitive and lacks definition. We would suggest the following: • poorly defined clinical border • infiltrating or micro-nodular histology • residual following previous treatment • located in the H-zone of the face • large >10mm in diameter on the face • by utilising MMS compared to Wide Excision the defect size reduction would be of clinical significance
Mohs micrographic surgery can be useful for histologically confirmed recurrent basal cell carcinomas of the face greater that are large (>10mm in diameter), show aggressive histological features, or are located on the H-zone of the face.	We suggest that this a repetition of the above statement and suggest it be replaced with the following: 'MMS practitioners should follow the Medicare Appropriate Use Criteria for MMS and clinical benchmarks developed by the Australasian College of Dermatologists.'
***Insert new practice point between second last and last practice point	'Mohs micrographic surgery should be considered in the management of SCC and utilised where 100% clearance of the surgical margin and tissue preservation offer clinical value.'

Economics of keratinocyte cancers

Draft Clinical Practice Guidelines: wording	ACD Comments
Overview of evidence (non-systematic literature review)	
	This section should cite the cost-analysis study within the Australian system comparing MMS with Wide Excision for KCC. In a prospective Australian cohort study, a direct cost-analysis of MMS versus Wide Excision for BCC was performed. This study showed that MMS was more financially viable than previously appreciated. The absolute cost difference between MMS and Wide Excision was $40.95, representing a 6.6% increase in cost for MMS. The authors concluded that as the cost between these interventions was small, the difference in effectiveness between MMS and Wide Excision would be the major determinant in a formal cost-utility study.[15]

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