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Nolan, GS, Kiely, AL, Totty, JP et al. (4 more authors) (2020) Incomplete surgical excision of keratinocyte skin cancers: a systematic review and meta-analysis. British Journal of Dermatology. ISSN 0007-0963

https://doi.org/10.1111/bjd.19660

Incomplete surgical excision of keratinocyte skin cancers: a systematic review and meta-analysis

Running head: Meta-analysis of non-melanoma skin cancer incomplete excision

Word count: 2853

Table count: 2

Figure count: 4

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Funding: None.

Conflict of interest: None declared.

Bulleted statements

What is already known about this topic?

- Keratinocyte or non-melanoma skin cancer is the commonest cancer worldwide and current guidelines underestimate incomplete excision rates. These are based on extrapolated data from Mohs micrographic surgery, rather than primary clinical studies.

What does this study add?

- The proportion of incomplete excision was 11·0% for BCCs and 9·4% for SCCs. When based on clinical data the rate is double the proportion suggested by national guidelines. This data suggests that excision by specialists may reduce treatment failure.

Summary

Background

Keratinocyte or non-melanoma skin cancer (NMSC) is the commonest malignancy worldwide. Usual treatment is surgical excision. Current guidelines underestimate incomplete excision rates.

Objectives

We aimed to determine the risk of incomplete excision of NMSCs through a systematic review and meta-analysis of primary clinical studies.

Methods

A PRISMA-compliant systematic review and meta-analysis was performed using methodology proposed by Cochrane. A comprehensive search strategy was applied to MEDLINE, Embase, Scopus, CINAHL, EMCare, Cochrane Library and the grey literature (January 2000–27th November 2019). All studies were included except studies on Mohs micrographic surgery, frozen section or biopsies. Abstract screening and data extraction were performed in duplicate. The risk of bias was assessed using a tool for prevalence/incidence studies. The primary outcome was the proportion of incomplete surgical excisions. A random effects model for pooling of binominal data was used. Differences between proportions were assessed by sub-group meta-analysis and meta regression which were presented as risk ratios. PROSPERO CRD42019157936.

Results

Searching identified 3477 records, with 110 studies included, comprising 53 796 patients with 106 832 basal cell carcinomas (BCC) and 21 569 squamous cell carcinomas (SCC). The proportion of incomplete excisions for BCC was 11·0% (95% CI 9·7-12·4%) and for SCC 9·4% (95% CI 7·6-11·4%). Incomplete excisions by specialty were: dermatology 6·2% BCCs, 4·7% SCCs; plastic surgery 9·4% BCCs, 8·2% SCCs; general practitioners 20·4% BCCs, 19·9% SCCs. The risk of incomplete excision for general practitioners was four times that of dermatologists for both BCC (RR 3·9 [95% CI 2·0-7·3]) and SCC (RR 4·8 [95% CI 1·0-22·8]). Studies were heterogenous (I^2=98%) and at high risk of bias.

Conclusions

The proportion of incomplete excisions is higher than previously reported. Excisions performed by specialists may lower the risk of incomplete excision.

Keywords

Skin neoplasia

Carcinoma, Basal Cell

Carcinoma, Squamous Cell

Keratinocyte cancer

Non-melanoma skin cancer

Margins of Excision

Systematic Review

Meta-analysis

Introduction

Keratinocyte or non-melanoma skin cancer (NMSC) is an umbrella term which includes basal cell carcinoma (BCC) and cutaneous squamous cell carcinoma (SCC) as the most prevalent subtypes. They are the commonest cancers worldwide and in the United Kingdom (UK) they account for 20% of all new malignancies.[1] The UK incidence is 124-148 per 100 000 person years,[2] and is projected to rise due to increased reporting and historic exposure to ultraviolet radiation. In 2020, skin cancer is estimated to cost the NHS over £180 million per annum.[3]

The mainstay of treatment is complete surgical excision. For BCC, the likelihood of recurrence has been well established to be directly related to the adequacy of excision; 1%[4, 5] of BCCs recur where margins are clear, compared to 31-41% recurrence where margins are involved.[6, 7] The same data for SCC is lacking, however given its metastatic potential which is reported at 5-47%,[8] complete excision is desirable. Incomplete excisions may require further surgery or increased surveillance which burdens patients and healthcare systems, increasing the costs and morbidity of skin cancer care.[3]

In the UK, skin cancer excisions are predominantly performed in secondary care.[9] The joint guidance from the National Institute for Health and Care Excellence (NICE) and the British Association of Dermatologists (BAD) includes recommendations regarding surgical margins.[10, 11] Their recommendations are based upon data from studies using Mohs micrographic surgery, which was extrapolated to estimate the expected proportion of

incomplete excision with different peripheral margins[12-15] (i.e. 4–5mm peripheral margin is suggested to confer clear margins in 95% of small, well-defined BCCs.)[11] This gave the quoted figure of 5% incomplete excision rate, however this is not based on clinical studies using surgical excision. Two large-scale national audits of BCC and SCC excisions by UK dermatologists have reported different proportions of incomplete excision of between 2.3% to 3%.[16, 17]

The objective of this study was to systematically evaluate observational studies that present the risk of incomplete surgical excision in adults with NMSC worldwide. Secondarily, we aimed to determine if other factors were associated with the risk of incomplete excision.

Materials and methods

Search strategy and selection criteria

This systematic review and meta-analysis was conducted in accordance with our peer-reviewed published protocol,[18] registered prospectively on PROSPERO (CRD42019157936) and reported in adherence to Cochrane and PRISMA standards.[19]

Any study reporting the proportion of incomplete excisions for BCCs and SCCs in adult patients (≥ 18 years old) was eligible, regardless of publication status, language or setting. We excluded reviews, case reports, and case series with fewer than 50 patients as these studies may be underpowered to detect incomplete excision rates, and including underpowered studies may reduce the reliability of the meta-analysis. Studies using Mohs micrographic surgery or with intra-operative frozen section were excluded as the margin assessment takes place immediately during these techniques, and wider excisions are performed at the same sitting if tumour extends to a margin. Consequently, the incomplete excision rate for Mohs micrographic and intra-operative frozen section is theoretically close to 0% and including these studies would bias our meta-analysis to a lower proportion of incomplete excision. Furthermore, Mohs micrographic surgery is considered a separate procedure to standard wide local excision by many surgeons and not comparable. Studies reporting lesions expected to have incomplete margins (incision, shave or punch biopsies) were also excluded. Studies reporting on metastatic SCCs, and those located on the perineum and external genitalia (e.g. anal, vulvar and penile SCC) were not included as these patients are often treated via a different pathway to cutaneous lesions and require different management.

In accordance with our published protocol,[18] a structured search of MEDLINE, Embase, Scopus, CINAHL, EMCare, and Cochrane Library was undertaken from January 2000 onwards. The search was performed on 27th November 2019 however several more recent publications were identified after the search through hand-searching of included references and included. We limited studies to those conducted post-2000 as skin cancer care has progressed over time and data more than 20 years old is unlikely to be representative of current clinical practice. Additionally, the grey literature was searched using Open Grey, dissertation databases (e.g. Open Access Theses and Dissertations) and clinical trial registries (e.g. World Health Organization International Clinical Trials Registry Platform). We hand-searched the reference lists of included studies, relevant reviews, national clinical practice guidelines, and other relevant documents to identify cited articles not captured by electronic searches. Two authors (GSN, ALK or JPT) independently dual screened all titles and abstracts and obtained full text for references potentially meeting the inclusion criteria in Rayyan.[20] Translations were obtained for non-English articles using Google translate. The final decision about inclusion was based on the full texts. Discrepancies between reviewers were resolved through discussion.

Data analysis

Data were independently extracted onto a bespoke electronic sheet by two authors (GSN, ALK or JPT). Data on study demographics and design, patient demographics, time period of study, and risk of bias were collected. The primary outcome was the proportion of incomplete excisions (defined as residual tumour at either the peripheral or deep margin on histological examination). 'Closely' or 'near to' excised lesions were considered as

completely excised. Secondary outcomes were other factors which might be related to the risk of incomplete excision such as the discipline of the operating surgeon, the location of lesions, the types of reconstruction performed (e.g. skin grafts and flaps), the histological components,[10, 21] the use of loupe magnification, and year of study publication. Eleven study authors were contacted about missing data and responses were received from seven.

The risk of bias was assessed twice and independently by three authors (GSN, ALK and JPT) using a risk of bias tool for studies of prevalence/incidence.[22] This comprises of signalling questions and a summary assessment, which assesses the external validity of the study (selection and non-response bias) and the internal validity (measurement bias and bias related to analysis). Responses for individual items were either high or low risk of bias, and if there was insufficient data to decide the default was high risk of bias. The summary assessment evaluates the overall risk of study bias and is based on the rater's subjective judgement, given responses to the preceding questions, which is in line with Cochrane approaches.[23, 24] Response options for the summary assessment were low, moderate, or high risk of bias.

The pooled proportion of incomplete surgical excision of BCCs and SCCs were estimated using the *metaprop* package[25] in Stata/MP v15 (StataCorp). Dersimonian and Laird random-effects were used given the clinical heterogeneity. The Freeman-Tukey arcsine transformation was used to stabilise the variance. 95% confidence intervals (CI) around the study-specific and pooled proportion were computed using the score-test statistic.[26] Variations in the logit of the proportion of incomplete excisions by operator, use of loupes, year of publication, study design and the overall risk of bias were further explored by

subgroup meta-analyses and meta-regression using the *metareg* procedure.[27] The results of the meta-regressions were back transformed and are presented as risk ratios (RR). To account for the inflated type 1 error rates associated with meta-regression in the presence of many covariates and heterogeneity, p-values were corrected using the Monte Carlo permutation test with 20,000 iterations.[28] Three sensitivity analysis were undertaken. Firstly, where studies judged to be at high risk of bias, secondly when conference abstracts were excluded (as the limited word count of this format prevents proper methodological assessment of the study) and finally if study design (prospective/retrospective) affected the risk of incomplete excision. Further subgroup analyses of pooled NMSC (all BCCs and SCCs) were undertaken to address the secondary objectives as reconstruction of a defect is not specific to a type of skin cancer and lesions with a preclinical diagnosis of BCC or SCC are often found to be histologically different. We explored the proportion of incomplete excision by the overall risk of bias (high, moderate or low), study design (prospective vs. retrospective), the method of reconstruction, the proportion of lesions on the head and neck, use of loupes and year of study publication. Statistical heterogeneity was assessed by I^2 which corresponds with the proportion of total variation due to inter-study heterogeneity and by p-values for inter-study heterogeneity and overall.[29] A z-test (and the corresponding p-values) assessed whether the observed proportion was different from zero percent.

In order to assess possible small-study effects (or publication bias across studies), we produced a funnel plot using *metafunnel*.

Differences from the protocol

To accurately estimate the proportion of incomplete excision, we used the Freeman-Tukey arcsine transformation, rather than logit transformation, to stabilise the variances of proportions close to zero.

Data on histological components could not be extracted due to only a subsection of criteria being reported or was not reported for the majority of studies.

Results

Of the 3477 citations identified by the search strategy, 110 studies[16, 30-138] met the inclusion criteria (Figure 1). The characteristics of included studies are summarised in Table 1 and detailed in Supplementary Table 2.

A total of 106 832 BCC and 21 569 SCC excisions were included. These were excised from 53 796 patients across all studies (25 studies did not report the number of patients, instead reporting the number of lesions only).[16, 17, 34, 49, 59, 60, 62, 68, 69, 71-74, 78, 82, 96, 104, 107, 109, 112, 115, 120, 133, 135, 136] The mean age of patients undergoing BCC excision was 67·4 years (SD 14.9) and for SCC excision was 70·9 years (SD 14·1). Most patients were male (BCC 55·7% and SCC 65·1%).

Serious bias was present in the data, especially selection bias which might have been due to the retrospective design of the majority (82%) of studies. Selection bias was primarily due to the exclusion of lesions at higher risk of incomplete excision (e.g. previously incomplete) and including only a subset of patients (e.g. using Mohs micrographic surgery for more challenging cases). A minority of studies included consecutive excisions. Many studies did not include sufficient information on why participants were excluded. A definition and/or statement that lesions were examined by a histopathologist were absent in 38% and 28% of studies, respectively although It is very unlikely that studies from the last 20 years are not reported by a histopathologist. Errors and inconsistencies were identified in 12% of studies in either the numerator, denominator or differing figures throughout the text. Studies which were reported as conference abstracts only were often judged to be at a higher risk of bias

than full papers. The risk of bias summary plot is shown in Figure 2. The individual risk of bias for each study is included in the Supplementary Figure 1.

The total proportion of incomplete excisions for BCCs was 11·0% (95% CI 9·7-12·4%) and for SCCs was 9·4% (7·6-11·4%). When analysed by the operating specialty, dermatology had the lowest proportion of incomplete excisions and general practitioners had the highest (Figure 3 and 4, study-level estimates in Supplementary Figures 2-7.) Meta-regression showed that general practitioners were more likely to incompletely excise BCCs than dermatologists (RR 3·9 [95% CI 2·0-7·3] p<0·001, permuted p=0·002) and plastic surgeons (RR 2·4 [95% CI 1·4-4·2] p=0·003, permuted p=<0·001). Similarly, general practitioners had a higher proportion of incomplete SCC excisions than dermatologists (RR 4·8 [95% CI 1·0-22·8] p=0·05, permuted p<0·001) and plastic surgeons (RR 2·2 [95% CI 1·2-8·5] p=0·021, permuted p=0·002). Dermatologists had a lower proportion of incomplete excisions than plastic surgeons for both BCCs (RR 0·4 [95% CI 0·2-0·7] p=0·003, permuted p<0·001) and SCC (RR 0·3 [95% CI 0·1-0·8] p=0·021, permuted p=0·002).

Table 2 shows that plastic surgeons performed more complex reconstructions (skin grafts and flaps) than dermatologist for all NMSC. Other surgeons, such as maxillofacial surgeons and ophthalmologists, performed a similar proportion of reconstructions. No studies on excisions by general practitioners reported how the defects were reconstructed. Plastic surgeons excised a larger proportion of lesions from the head and neck compared to dermatologists, who in turn excised a higher proportion than general practitioners.

Intraoperative use of loupes was not associated with a different incomplete excision risk for NMSC (RR 1.6 [95% CI 0·3-7·4] p=0·537; Supplementary Figure 8). Over 20 years, there was no change in the proportion of incomplete excision NMSC (p=0·904; Supplementary Figure 9).

There was substantial statistical heterogeneity both within and between groups.

Sensitivity analysis using studies at low overall risk of bias only yielded a very similar proportion of incomplete excision of NMSC (10·2% [95% CI 8·5-12·1]; Supplementary Figure 10). The proportion of incomplete excisions for NMSC was similar between full papers, abstractions or conference materials (RR 1·0 [95% CI 0·7-1·5] p=0.826). Prospective studies reported a lower proportion of incomplete excision than others (RR 0·6 [95% CI 0·4-0·9] p=0.034; Supplementary Figure 11).

A funnel plot for all studies showed that datapoints are widely dispersed and the scatter is asymmetrical (Supplementary Figure 12; Egger's regression co-efficient 2·26 [95% CI 2·04-2·48] p<0·001) which suggests the presence of small-study effects.

Discussion

On the basis of 110 clinical studies, we have shown that the proportion of incomplete excisions for BCCs is 11·0% and SCCs is 9·4%. There is substantial variation and heterogeneity in the observed proportion of incomplete excision, ranging from 4·7 – 20·4% by operator. Dermatologists had the lowest proportion of incomplete excisions (6·2% BCCs, 4·7% SCCs) and general practitioners had the highest proportion (20·4% BCCs, 19·9% SCCs). Plastic surgeons had a slightly higher proportion of incomplete excisions than dermatologists (9·4% BCCs, 8·2% SCCs) however a greater proportion of their lesions were located on the head and neck (92·7%), and they also performed more complex reconstructions such as skin grafts and flaps, which imply that the lesions were likely to be larger or the macroscopic margin was less well defined. The use of loupe magnification had no statistically significant effect on the risk of incomplete excisions. Our risk estimates for incomplete excision of NMSCs are the most comprehensive to-date and should be used to inform the design of future studies and in the consent process for patients worldwide.

This study is limited by the high risk of bias in the majority of studies. More than 1 in 10 studies excluded recurrent, previously incomplete and other high-risk lesions from their primary studies. Further selection bias through the differential use of Mohs micrographic surgery by specialty and country will remove lesions that are at the highest risk of incomplete excision. Finally, standard histology using 'bread-loaf' techniques only assesses between 0.19% - 2% of specimen margins[139-141] so consequently, the actual incomplete excision rate in the population is likely to be higher than our estimates suggest. Prospective

studies were found to be at a lower risk of incomplete excision than retrospective studies, which may be due to selection bias caused by stricter inclusion criteria of randomised controlled trials than retrospective studies. Evidence of publication bias was identified by asymmetry in the funnel plot which is another limitation. Whilst there was statistically significant heterogeneity amongst studies, the greatest strength of this study is the breadth of data synthesised and readers should consider whether this heterogeneity is clinically relevant. A recent systematic review of incomplete SCC excisions showed a similar finding to ours (13%)[142] but included metastatic disease and fewer cases.

Our forest plots and meta-regression identify large differences in the proportion of incomplete excisions by different operating groups (Figures 3 and 4). General practitioners are four times as likely to incompletely excise NMSC compared to dermatologists (BCC OR 3·9 [95% CI 2·0-7·3], SCC OR 4·8 [95% CI 1·0-22·8]). This finding cannot be explained by selection bias, as it seems unlikely that general practitioners are excising more complex lesions than those they refer to dermatologists. Our data supports the notion that excisions of NMSCs should not be undertaken by non-specialists, as they may lack sufficient training and support which translates into a higher rate of incomplete excision. Multiple studies have shown that general practitioners with a special interest in skin cancer were at a lower risk of incomplete excision than their colleagues,[78, 125] so we see no reason to restrict excisions to secondary care. It is worth noting that a low risk, truncal BCC in an elderly patient that has been incompletely excised may never clinically recur, and incomplete excision does not always necessitate further surgery. The low risk for dermatologists is likely multi-factorial. The prevalent use of Mohs micrographic surgery by dermatologists is effective at removing the highest risk lesions from their caseload, and accordingly they

typically excise a greater volume of smaller, lower risk lesions. The more complex lesions they encounter are referred to plastic surgeons (27-52%[101, 143, 144] of skin cancer referrals plastic surgeons receive are from dermatologists). In contrast plastic surgeons excised larger lesions, of more aggressive subtypes, with indistinct macroscopic borders, and this study accordingly found a higher proportion of incomplete excision of BCCs (9·4%) and SCCs (8·2%). This systematic review highlights that the current skin cancer pathways are effective, with dermatologists excising large numbers of low risk lesions whilst plastic, ophthalmological, and head & neck surgeons deal with more difficult lesions which may also require reconstruction.

Specific anatomical factors also likely play a large role in the risk of incomplete excision. Periocular lesions appeared to be at a greater risk as shown by the relatively high risk with ophthalmology and plastic surgery studies on this subset of patients.[67, 87] Additionally, high-risk histological lesions, such as morphoeic BCCs, have been shown to be at higher risk of incomplete excision. In this systematic review, due to a lack of reporting of some high-risk elements such as peri-neural invasion, it was not possible to extract data on histological factors. Two studies were solely on morphoeic BCCs and these reported very different proportions of incomplete excisions of 6%[120] and 32%.[65] Additionally other factors may impact the proportion of incomplete excision which were not explored by this systematic review, such as the grade of the operating surgeon, the margin of normal tissue taken and the apriori plan for reconstruction: if the surgeon plans to close directly then this may bias the excision towards a smaller margin, whereas when a surgeon plans to reconstruct a defect with a skin graft then comparably a more liberal margin may be taken. These factors would be best explored using Bayesian techniques. With SCC the margin used in different

studies was infrequently reported in the larger studies.[17, 42, 59, 78, 107, 115, 125, 129] When it was reported, several studies found no association between wider margins and reduced proportion of incomplete excision,[92, 130] often as the deep margin was primarily affected.[92]

Audits of outcomes following NMSC excisions will undoubtedly continue throughout plastic surgery and dermatology units worldwide, of which the majority will never be published. Future published studies must be of higher methodological quality and should be prospective and include consecutive excisions as a minimum. Multi-centre, national, annual audits such as those performed by UK dermatologists[16, 17] provide the most useful data and other specialties and countries should follow suit. Our study has demonstrated the proportion of incomplete excision is substantially higher than previously reported. In light of these findings, guidelines should be updated, and action taken to improve the outcomes of the world's commonest malignancy.

Acknowledgements

None.

References

1. National Cancer Intelligence Network (NCIN). Non-melanoma skin cancer in England, Scotland, Northern Ireland, and Ireland. 2013.

2. National Cancer Registration and Analysis Service (NCRAS). Malignant melanoma: Incidence, mortality and survival rates in England, Wales, Scotland, and Northern Ireland. 2013.

3. Vallejo-Torres L, Morris S, Kinge JM, Poirier V, Verne J. Measuring current and future cost of skin cancer in England. *J Public Health (Oxf)*. Mar 2014;36(1):140-8. doi:10.1093/pubmed/fdt032

4. Pascal RR, Hobby LW, Lattes R, Crikelair GF. Prognosis of "incompletely excised" versus "completely excised" basal cell carcinoma. *Plast Reconstr Surg*. Apr 1968;41(4):328-32. doi:10.1097/00006534-196804000-00006

5. Park AJ, Strick M, Watson JD. Basal cell carcinomas: do they need to be followed up? *J R Coll Surg Edinb*. Apr 1994;39(2):109-11.

6. Goldberg DP. Assessment and surgical treatment of basal cell skin cancer. *Clin Plast Surg*. Oct 1997;24(4):673-86.

7. Griffiths RW. Audit of histologically incompletely excised basal cell carcinomas: recommendations for management by re-excision. *Br J Plast Surg*. Jan 1999;52(1):24-8. doi:10.1054/bjps.1998.3018

8. Tan PY, Ek E, Su S, Giorlando F, Dieu T. Incomplete excision of squamous cell carcinoma of the skin: a prospective observational study. *Plast Reconstr Surg*. Sep 2007;120(4):910-6. doi:10.1097/01.prs.0000277655.89728.9f

9. England N. 2013/14 NHS STANDARD CONTRACT FOR CANCER: SKIN (ADULT). 2013.

10. Motley R, Kersey P, Lawrence C, Dermatologists BAo, Surgeons BAoP, Royal College of Radiologists FcoCO. Multiprofessional guidelines for the management of the patient with primary cutaneous squamous cell carcinoma. *Br J Dermatol*. Jan 2002;146(1):18-25. doi:10.1046/j.0007-0963.2001.04615.x

11. Telfer NR, Colver GB, Morton CA, Dermatologists BAo. Guidelines for the management of basal cell carcinoma. *Br J Dermatol*. Jul 2008;159(1):35-48. doi:10.1111/j.1365-2133.2008.08666.x

12. Breuninger H, Dietz K. Prediction of subclinical tumor infiltration in basal cell carcinoma. *J Dermatol Surg Oncol*. Jul 1991;17(7):574-8. doi:10.1111/j.1524-4725.1991.tb03655.x

13. Wolf DJ, Zitelli JA. Surgical margins for basal cell carcinoma. *Arch Dermatol*. Mar 1987;123(3):340-4.

14. Kimyai-Asadi A, Goldberg LH, Jih MH. Accuracy of serial transverse cross-sections in detecting residual basal cell carcinoma at the surgical margins of an elliptical excision specimen. *Journal of the American Academy of Dermatology*. September 2005;53(3):469-474.

15. Brodland DG, Zitelli JA. Surgical margins for excision of primary cutaneous squamous cell carcinoma. *J Am Acad Dermatol*. Aug 1992;27(2 Pt 1):241-8. doi:10.1016/0190-9622(92)70178-i

16. Keith DJ, de Berker DAR, Bray AP, Cheung ST, Brain A, Mohd Mustapa MF. British Association of Dermatologists' national audit on nonmelanoma skin cancer excision, 2014. *Clinical and Experimental Dermatology*. 2017;42(1):46-53. doi:10.1111/ced.12990

17. Keith DJ, Bray AP, Brain A, et al. British Association of Dermatologists (BAD) National Audit on Non-Melanoma Skin Cancer Excision 2016 in collaboration with the Royal College of Pathologists. *Clin Exp Dermatol*. Jan 2020;45(1):48-55. doi:10.1111/ced.14034

18. Nolan GS, Wormald JCR, Kiely AL, Totty JP, Jain A. Global incidence of incomplete surgical excision in adult patients with non-melanoma skin cancer: study protocol for a systematic review and meta-analysis of observational studies. *Syst Rev*. Apr 2020;9(1):83. doi:10.1186/s13643-020-01350-5

19. Moher D, Liberati A, Tetzlaff J, Altman DG, Group P. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *BMJ*. Jul 2009;339:b2535. doi:10.1136/bmj.b2535

20. Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A. Rayyan-a web and mobile app for systematic reviews. *Syst Rev*. 12 2016;5(1):210. doi:10.1186/s13643-016-0384-4

21. Slater D, Barrett P. Standards and datasets for reporting cancers. Dataset for histopathological reporting of primary cutaneous basal cell carcinoma. Appendix F2019.

22. Hoy D, Brooks P, Woolf A, et al. Assessing risk of bias in prevalence studies: modification of an existing tool and evidence of interrater agreement. *J Clin Epidemiol*. Sep 2012;65(9):934-9. doi:10.1016/j.jclinepi.2011.11.014

23. Higgins J, Green S. *Cochrane Handbook for Systematic Reviews of Interventions*. The Cochrane Collaboration; 2011.

24. Terracciano L, Brozek J, Compalati E, Schünemann H. GRADE system: new paradigm. *Curr Opin Allergy Clin Immunol*. Aug 2010;10(4):377-83. doi:10.1097/ACI.0b013e32833c148b

25. Nyaga VN, Arbyn M, Aerts M. Metaprop: a Stata command to perform meta-analysis of binomial data. *Arch Public Health*. 2014;72(1):39. doi:10.1186/2049-3258-72-39

26. Miller JJ. The Inverse of the Freeman – Tukey Double Arcsine Transformation. *The American Statistician*. 1978/11/01 1978;32(4):138-138. doi:10.1080/00031305.1978.10479283

27. Harbord R, Higgins J. Meta-regression in Stata. *The Stata Journal*. 2008;8(4):493-519.

28. Higgins JP, Thompson SG. Controlling the risk of spurious findings from meta-regression. *Stat Med*. Jun 2004;23(11):1663-82. doi:10.1002/sim.1752

29. Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *BMJ*. Sep 2003;327(7414):557-60. doi:10.1136/bmj.327.7414.557

30. Adamczyk L, Simpkin A, Oxley J. What is the point of tips? *Journal Of Clinical Pathology*. 2014;67(1):40-44. doi:10.1136/jclinpath-2013-201802

31. Afridi RA, Ahmed E, Khan SA, Ali A. Demographics of basal cell carcinoma and its surgical management. *Journal of Ayub Medical College, Abbottabad : JAMC*. 2012 2012;24(3-4):141-143.

32. Ali I, Sri Prakash K, Eve B, Hollowood K, Reed J, Turner R. A significantly improved outcome for surgical excision of basal cell carcinoma as a result of the Audit process. *British Journal of Dermatology*. July 2009;161(1):110.

33. Ali S, Herron CC, Owens PW, et al. Adequacy of skin malignancy resection margins in a model 3 hospital. *Irish Journal of Medical Science*. February 2017;186 (2 Supplement 1):S112.

34. Alsharqi A, Wilson N. Will the introduction of new NICE guidelines change the management of basal cell carcinomas in the community? *British Journal of Dermatology*. July 2011;165(1):108.

35. Asif M, Mamoon N, Ali Z, Akhtar F. Epidemiological and excision margin status of basal cell carcinoma - three years armed forces institute of pathology experience in pakistan. *Asian Pacific Journal of Cancer Prevention*. 2010;11(5):1421-1423.

36. Babaye-Nazhad S, Amirnia M, Alikhah H, Khodaeyani E, Atapour N. Safety margin in excision of basal cell carcinoma. *Pakistan Journal Of Biological Sciences: PJBS*. 2009;12(21):1408-1414.

37. Baheerathan NN, Paraneetharan S, Abouserwel A, Bostanci G, Ilankovan V. Outcome of incompletely excised non-melanoma head and neck skin cancer from one unit. *British Journal of Oral and Maxillofacial Surgery*. October 2014;52 (8):e50.

38. Bariani RL, Nahas FX, Jardini Barbosa MV, Farah AB, Ferreira LM. Basal cell carcinoma: An updated epidemiological and therapeutically profile of an urban population. *Acta Cirurgica Brasileira*. 2006;21(2):66-73.

39. Başer NT, Bulutoğlu R, Barutcu AY, Karayel H, Terzioğlu A, Aslan G. Evaluation of basal cell carcinomas with positive surgical margins: A five year retrospective analysis. *Turkish Journal of Cancer*. 2008;38(1):16-19.

40. Bassas P, Hilari H, Bodet D, Serra M, Kennedy FE, García-Patos V. Evaluation of surgical margins in Basal cell carcinoma by surgical specialty. *Actas Dermo-Sifiliograficas*. 2013;104(2):133-140. doi:10.1016/j.ad.2012.06.001

41. Betti R, Radaelli G, Crosti C, Ghiozzi S, Moneghini L, Menni S. Margin involvement and clinical pattern of basal cell carcinoma with mixed histology. *Journal Of The European*

Academy Of Dermatology And Venereology: JEADV. 2012;26(4):483-487. doi:10.1111/j.1468-3083.2011.04104.x

42. Bovill ES, Cullen KW, Barrett W, Banwell PE. Clinical and histological findings in re-excision of incompletely excised cutaneous squamous cell carcinoma. *Journal Of Plastic, Reconstructive & Aesthetic Surgery: JPRAS*. 2009;62(4):457-461. doi:10.1016/j.bjps.2007.11.041

43. Bozan A, Gode S, Kaya I, et al. Long-term follow-up of positive surgical margins in basal cell carcinoma of the face. *Dermatologic Surgery*. 2015;41(7):761-767. doi:10.1097/DSS.0000000000000394

44. Brinkman JN, Hajder E, Van Der Holt B, Den Bakker MA, Hovius SER, Mureau MAM. The effect of differentiation grade of cutaneous squamous cell carcinoma on excision margins, local recurrence, metastasis, and patient survival: A retrospective follow-up study. *Annals of Plastic Surgery*. 2015;75(3):323-326. doi:10.1097/SAP.0000000000000110

45. Caresana G, Giardini R. Dermoscopy-guided surgery in basal cell carcinoma. *Journal Of The European Academy Of Dermatology And Venereology: JEADV*. 2010;24(12):1395-1399. doi:10.1111/j.1468-3083.2010.03652.x

46. Chadha V, Wright M. Small margin excision of periocular basal cell carcinomas. *The British Journal Of Ophthalmology*. 2009;93(6):803-806. doi:10.1136/bjo.2008.151183

47. Chambers M, Esdaile B, De Vos S, et al. The oxfordshire community dermatology service. *British Journal of Dermatology*. July 2012;167(1):97.

48. Chan LS, Scholes NJW, Jones M. Skin excisions: Not so simple for the regionally based general surgical trainee. *Australian Journal of Rural Health*. 2011;19(4):205-210. doi:10.1111/j.1440-1584.2011.01198.x

49. Chen P, Patel DC. Evaluation of surgical excision of non-melanoma skin cancers - A retrospective study. *Australasian Journal of Dermatology*. November 2011;52 (4):A9.

50. Cho M, Lee J, James CL, Marshman G, Huilgol SC. Scalp Basal Cell Carcinoma: Review of 2,202 Cases. *Dermatol Surg*. Jul 2016;42(7):834-41. doi:10.1097/DSS.0000000000000783

51. Chow VLY, Chan JYW, Chan RCL, Chung JHP, Wei WI. Basal cell carcinoma of the head and neck region in ethnic chinese. *International Journal Of Surgical Oncology*. 2011;2011:890908-890908. doi:10.1155/2011/890908

52. Chowdhry M, Shah R, Dziewulski P, El-Muttardi N. Excision of basal cell carcinoma: Who does it best? *International Journal of Surgery*. November 2015;23(1):S94.

53. Codazzi D, Van Der Velden J, Carminati M, et al. Positive compared with negative margins in a single-centre retrospective study on 3957 consecutive excisions of basal cell carcinomas. Associated risk factors and preferred surgical management. *Journal Of Plastic Surgery And Hand Surgery*. 2014;48(1):38-43. doi:10.3109/2000656X.2013.800526

54. Cole SJ, Howes R, Meehan C, Cole R. High-risk basal cell carcinoma excision in primary care: a retrospective observational study of compliance with NICE guidance. *BMJ Open*. 2018;8(11)doi:10.1136/bmjopen-2018-023299

55. Conner E, Munro Z, Weatherhead R. Complete excision rate of periocular basal cell carci noma in ateaching hospital. *Clinical and Experimental Ophthalmology*. October 2015;43 (Supplement 1):68.

56. Custódio G, Locks LH, Coan MF, Gonçalves CO, Trevisol DJ, Schuelter Trevisol F. Epidemiology of basal cell carcinomas in Tubarão, Santa Catarina (SC), between 1999 and 2008. *Anais Brasileiros de Dermatologia*. 2010;85(6):819-826. doi:10.1590/S0365-05962010000600007

57. Dalal AJ, Ingham J, Collard B, Merrick G. Review of outcomes of 500 consecutive cases of non-melanoma skin cancer of the head and neck managed in an oral and maxillofacial surgical unit in a District General Hospital. *The British Journal Of Oral & Maxillofacial Surgery*. 2018;56(9):805-809. doi:10.1016/j.bjoms.2018.08.015

58. Dewan P, Panagou E, Ajen S, Bewley AP, Sahota A, Gibbon K. Are NICE skin cancer guidelines being followed in primary care? A re-audit to review changes in practice in an inner city setting. *British Journal of Dermatology*. July 2010;163(1):65.

59. Dhepnorrarat RC, Lee MA, Mountain JA. Incompletely excised skin cancer rates: a prospective study of 31,731 skin cancer excisions by the Western Australian Society of Plastic Surgeons. *J Plast Reconstr Aesthet Surg*. Oct 2009;62(10):1281-5. doi:10.1016/j.bjps.2008.04.028

60. Dieu T, Macleod AM. Incomplete excision of basal cell carcinomas: a retrospective audit. *ANZ J Surg*. Mar 2002;72(3):219-21.

61. Duarte B, Vieira L, Pessoa E Costa T, et al. Predicting incomplete basal cell carcinoma excisions - a large multidisciplinary retrospective analysis in a tertiary centre. *The Journal Of Dermatological Treatment*. 2019:1-17. doi:10.1080/09546634.2019.1687815

62. Duggan DA, Joyce KM, Dorairaj JJ, Kelly JL. Does the use of loupe magnification reduce incomplete excision rates of facial basal cell carcinomas? *Irish Journal of Medical Science*. July 2015;184(7)(1):S260.

63. Durmus Kocaaslan FN, Alakus AC, Sacak B, Celebiler O. Evaluation of residual tumors and recurrence rates of malignant melanoma and non-melanoma skin cancer of head and neck region. *Marmara Medical Journal*. 2019;32(3):107-111.

64. Elliott BM, Douglass BR, McConnell D, Johnson B, Harmston C. Incidence, demographics and surgical outcomes of cutaneous squamous cell carcinoma diagnosed in northland, New Zealand. *New Zealand Medical Journal*. 18 May 2018;131(1475):61-68.

65. Erba P, Farhadi J, Wettstein R, Arnold A, Harr T, Pierer G. Morphoeic basal cell carcinoma of the face. *Scandinavian Journal of Plastic and Reconstructive Surgery and Hand Surgery*. 2007;41(4):184-188. doi:10.1080/02844310701282138

66. Farhi D, Dupin N, Palangie A, Carlotti A, Avril MF. Incomplete excision of basal cell carcinoma: Rate and associated factors among 362 consecutive cases. *Dermatologic Surgery*. October 2007;33(10):1207-1214.

67. Fatigato G, Capitani S, Milani D, et al. Risk factors associated with relapse of eyelid basal cell carcinoma: Results from a retrospective study of 142 patients. *European Journal of Dermatology*. 2017;27(4):363-368. doi:10.1684/ejd.2017.3026

68. Fernandes JD, de Lorenzo Messina MC, de Almeida Pimentel ER, Castro LGM. Presence of residual basal cell carcinoma in re-excised specimens is more probable when deep and lateral margins were positive. *Journal Of The European Academy Of Dermatology And Venereology: JEADV*. 2008;22(6):704-706. doi:10.1111/j.1468-3083.2007.02571.x

69. Filho RB, de Carvalho Fantini B, dos Santos CA, et al. Attributes and risk factors of positive margins on 864 excisions of basal cell carcinomas: a single-center retrospective study. *Journal of Dermatological Treatment*. 2019;

70. Fortuin S, Kadouch DJM, Kadouch JA, Decates T, Marck KW, Karim RB. Use of an audit to improve surgical treatment of facial basal cell carcinoma. *European Journal of Plastic Surgery*. January 2013;36(1):1-6.

71. Goto M, Kai Y, Arakawa S, et al. Analysis of 256 cases of basal cell carcinoma after either one-step or two-step surgery in a Japanese institution. *Journal of Dermatology*. 2012;39(1):68-71. doi:10.1111/j.1346-8138.2011.01306.x

72. Grassi S, Merlino M, Rosso R, Borroni G. Incomplete excision of basal cell carcinoma of the head region: Analysis of 724 consecutive cases. *Giornale Italiano di Dermatologia e Venereologia*. 2018;153(3):435-437. doi:10.23736/S0392-0488.16.05447-V

73. Greaney L, Mehmet S. Head and neck non-melanoma skin cancer margin clearance. *British Journal of Oral and Maxillofacial Surgery*. October 2014;52 (8):e44.

74. Gualdi G, Monari P, Crotti S, et al. Matter of margins. *Journal Of The European Academy Of Dermatology And Venereology: JEADV*. 2015;29(2):255-261. doi:10.1111/jdv.12504

75. Gudi V, Ormerod AD, Dawn G, et al. Management of basal cell carcinoma by surveyed dermatologists in Scotland. *Clinical And Experimental Dermatology*. 2006;31(5):648-652.

76. Hakverdi S, Balci DD, Dogramaci CA, Toprak S, Yaldiz M. Retrospective analysis of basal cell carcinoma. *Indian Journal of Dermatology, Venereology & Leprology*. 2011;77(2):251-251.

77. Hamada S, Kersey T, Thaller VT. Eyelid basal cell carcinoma: non-Mohs excision, repair, and outcome. *The British Journal Of Ophthalmology*. 2005;89(8):992-994.

78. Hansen C, Wilkinson D, Hansen M, Soyer HP. Factors contributing to incomplete excision of nonmelanoma skin cancer by Australian general practitioners. *Archives of Dermatology*. 2009;145(11):1253-1260. doi:10.1001/archdermatol.2009.270

79. Healy R, Rahman D, Gibbon K, Sahota A, Bewley A. Are NICE skin cancer guidelines being followed in primary care? A review of current practice in an inner city setting. presented at: 88th Annual Meeting of the British-Association-of-Dermatologists; 2008;

80. Ho SF, Brown L, Bamford M, Sampath R, Burns J. 5 years review of periocular basal cell carcinoma and proposed follow-up protocol. *Eye (London, England)*. 2013;27(1):78-83. doi:10.1038/eye.2012.230

81. Hoefkens MF, Fabré J, Küsters-Vandevelde HV. Does loupe magnification reduce the gap between the macroscopic and microscopic border of a Basal cell carcinoma?: a prospective clinical study. Controlled Clinical Trial; Journal Article. *Annals of plastic surgery*. 2014;72(5):579-583. doi:10.1097/SAP.0b013e31826524df

82. Hurley RJ, McInerney NM, Palmer EJ, et al. Squamous cell carcinoma excision in a tertiary referral centre the importance of the deep excision margin. *Irish Journal of Medical Science*. September 2013;182(7)(1):S339.

83. Husein-ElAhmed H, Aneiros-Fernandez J, Gutierrez-Salmeron MT, Aneiros-Cachaza J, Naranjo-Sintes R. Basal cell carcinoma: Analysis of factors associated with incomplete excision at a referral hospital in southern Spain. *Cutis*. 2014;93(3):155-161.

84. Ismail N, D'Adhemar C, Kirby B, Collins P, Sheahan K, Lally A. An audit of basal cell carcinoma in St Vincent's University Hospital. *British Journal of Dermatology*. December 2012;167 (6):e34-e35.

85. Ito T, Inatomi Y, Nagae K, et al. Narrow-margin excision is a safe, reliable treatment for well-defined, primary pigmented basal cell carcinoma: An analysis of 288 lesions in Japan. *Journal of the European Academy of Dermatology and Venereology*. 2014;

86. Janjua OS, Qureshi SM. Basal cell carcinoma of the head and neck region: An analysis of 171 cases. *Journal of Skin Cancer*. 2012;(no pagination)943472.

87. Jankovic I, Kovacevic P, Visnjic M, Jankovic D, Binic I, Jankovic A. Does incomplete excision of basal cell carcinoma of the eyelid mean tumor recurrence? *Anais Brasileiros de Dermatologia*. November-December 2010;85(6):872-877.

88. Jenkins GW, Kanatas AN, Smith AB, Telfer MR. Anatomical restrictions in the surgical excision of scalp squamous cell carcinomas: Does this affect local recurrence and regional nodal metastases? *British Journal of Oral and Maxillofacial Surgery*. June 2012;50(1):S16.

89. Keith DJ, Bray AP, Brain A, et al. British Association of Dermatologists (BAD) National Audit on Non-Melanoma Skin Cancer Excision 2016 in collaboration with the Royal College of Pathologists. *Clin Exp Dermatol*. Jul 2019;doi:10.1111/ced.14034

90. Khalid S, Spicer A, Gee B, Carr R. The impact of Improved Outcome Guidance (IOG) for skin cancer: A comparative re-audit of excision rates of basal cell carcinomas by general practitioners in South Warwickshire. *British Journal of Dermatology*. July 2009;161(1):109.

91. Khalid-Raja M, Mistry N, Anari S. Peripheral histological clearance of cutaneous BCC and SCC excised using the wet blotting technique. *JPRAS Open*. September 2018;17:39-48.

92. Khan AA, Potter M, Cubitt JJ, et al. Guidelines for the excision of cutaneous squamous cell cancers in the United Kingdom: the best cut is the deepest. *Journal Of Plastic, Reconstructive & Aesthetic Surgery: JPRAS*. 2013;66(4):467-471. doi:10.1016/j.bjps.2012.12.016

93. Kiely JR, Patel AJK. A retrospective study of 694 Basal Cell Carcinoma excisions to quantify deep margin documentation and clearance compared to histological type and surgical margin. *J Plast Reconstr Aesthet Surg*. Jun 2019;doi:10.1016/j.bjps.2019.06.002

94. Kiely J, Kostusiak M, Bloom O, Roshan A. Poorly differentiated cutaneous squamous cell carcinomas have high incomplete excision rates with UK minimum recommended pre-

determined surgical margins. *Journal Of Plastic, Reconstructive & Aesthetic Surgery: JPRAS*. 2019;doi:10.1016/j.bjps.2019.06.034

95. Kratky V, Johnson D, Hollands H, Farmer J. Does frozen or permanent section control in surgical management of periocular nodular BCCs result in better histological and clinical outcomes? presented at: COS 2012 Annual Meeting; 2008; http://clinicaltrials.gov/show/NCT00663650 18 Years

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Both

290

96. Kreuser-Genis I, Esdaile B, Acland KM. Skin surgical proformas improve documentation as well as clinical standards. *British Journal of Dermatology*. July 2012;167(1):94.

97. Kyrgidis A, Vahtsevanos K, Tzellos TG, et al. Clinical, histological and demographic predictors for recurrence and second primary tumours of head and neck basal cell carcinoma. A 1062 patient-cohort study from a tertiary cancer referral hospital. *European Journal of Dermatology*. May-June 2010;20(3):276-282.

98. Lara F, Garbers LEFM, Santamaría JR. Recurrence rate of basal cell carcinoma with positive histopathological margins and related risk factors. *Anais Brasileiros de Dermatologia*. 2017;92(1):58-62. doi:10.1590/abd1806-4841.20174867

99. Lim D, Tan WS, Chio TWM. An audit on the management of cutaneous squamous cell carcinoma at the national skin centre, Singapore. *Annals of the Academy of Medicine Singapore*. September 2013;42(9)(1):S160.

100. MacIburko SJ, Townley WA, Hollowood K, Giele HP. Skin cancers of the hand: A series of 541 malignancies. *Plastic and Reconstructive Surgery*. 2012;129(6):1329-1336. doi:10.1097/PRS.0b013e31824ecc58

101. Malik V, Goh KS, Leong S, Tan A, Downey D, O'Donovan D. Risk and outcome analysis of 1832 consecutively excised basal cell carcinoma's in a tertiary referral plastic surgery unit. *Journal of Plastic, Reconstructive and Aesthetic Surgery*. December 2010;63(12):2057-2063.

102. Masud D, Moustaki M, Staruch R, Dheansa B. Basal cell carcinomata: Risk factors for incomplete excision and results of re-excision. *Journal Of Plastic, Reconstructive & Aesthetic Surgery: JPRAS*. 2016;69(5):652-656. doi:10.1016/j.bjps.2015.12.024

103. Melo JC, Marques MEA, Vasconcelos L, Miot HA, Abbade LPF. Invasive head and neck cutaneous squamous cell carcinoma: Clinical and histopathological characteristics, frequency of local recurrence and metastasis. *Anais Brasileiros de Dermatologia*. July-August 2014;89(4):562-568.

104. Mirhadi S, Diaz C, Thomson M. Audit of incomplete BCC surgical excisions: How to improve patients' outcomes and services. *Journal of the American Academy of Dermatology*. September 2018;79 (3 Supplement 1):AB54.

105. Mirshams M, Razzaghi M, Ehsani AH, et al. Incidence of incomplete excision in surgically treated basal cell carcinomas and identification of the related risk factors. *Iranian Journal of Dermatology*. 2011;14(55):1-5.

106. Mirshams M, Razzaghi M, Noormohammadpour P, Naraghi Z, Kamyab K, Rad SS. Incidence of incomplete excision in surgically treated cutaneous squamous cell carcinoma and Identification of the related risk factors. *Acta Medica Iranica*. 2011;49(12):806-809.

107. Ni Dhomhnallain O, Hackett C, Ramsay B, Lynch M, Ahmad K. Surgical management of cutaneous squamous cell carcinoma in mid-west ireland: A retrospective study. *Irish Journal of Medical Science*. April 2018;187 (Supplement 4):S158.

108. Ocanha JP, Miot HA, Marques MEA, Dias JT, Stolf HO, Abbade LPF. Relapses and recurrences of basal cell face carcinomas. *Anais Brasileiros de Dermatologia*. 2011;86(2):386-388. doi:10.1590/S0365-05962011000200032

109. Palanivel JA, Macbeth AE, Dootson G, Graham R, Mahmood K, Garioch J. An audit of incomplete excision rates of basal cell carcinoma from four U.K. teaching hospitals. *British Journal of Dermatology*. July 2011;165(1):106.

110. Patel SS, Cliff SH, Ward Booth P. Incomplete removal of basal cell carcinoma: What is the value of further surgery? *Oral and Maxillofacial Surgery*. June 2013;17(2):115-118.

111. Pignatelli I, Poirier V, De Berker DAR, Verne J. Completeness of basal cell carcinoma excisions in an English region. *British Journal of Dermatology*. July 2010;163(1):69-70.

112. Pinto A, El-Basyuni S, Boyle M. A study of the incidence of involved excision margins in cutaneous head and neck basal cell carcinomas and the outcomes of re-excisions. *International Journal of Oral and Maxillofacial Surgery*. October 2015;44(1):e124.

113. Pua VSC, Huilgol S, Hill D. Evaluation of the treatment of non-melanoma skin cancers by surgical excision. *Australasian Journal of Dermatology*. August 2009;50(3):171-175.

114. Ramdas K, van Lee C, Beck S, et al. Differences in Rate of Complete Excision of Basal Cell Carcinoma by Dermatologists, Plastic Surgeons and General Practitioners: A Large Cross-Sectional Study. *Dermatology*. 2018;234(3-4):86-91. doi:10.1159/000490344

115. Robertson BF, Wokes JET, Siddiqui H. Management of Incompletely Excised Skin Tumors: Our Experience. *Dermatologic surgery : official publication for American Society for Dermatologic Surgery [et al]*. 2018;44(3):365-369. doi:10.1097/DSS.0000000000001323

116. Robinson AJ, Walsh M, Hill C. Histopathological variation of incompletely excised basal cell carcinoma's and the variation with the grade of surgeon - implications for revalidation. *Eur J Surg Oncol*. Jan 2015;41(1):165-8. doi:10.1016/j.ejso.2014.10.059

117. Santiago F, Serra D, Vieira R, Figueiredo A. Incidence and factors associated with recurrence after incomplete excision of basal cell carcinomas: a study of 90 cases. *Journal Of The European Academy Of Dermatology And Venereology: JEADV*. 2010;24(12):1421-1424. doi:10.1111/j.1468-3083.2010.03662.x

118. Sartore L, Lancerotto L, Salmaso M, et al. Facial basal cell carcinoma: Analysis of recurrence and follow-up strategies. *Oncology Reports*. 2011;26(6):1423-1429. doi:10.3892/or.2011.1453

119. Shah SA, Obaidullah, Fahimullah. An assessment of incomplete facial basal cell carcinoma excision. *Journal of the College of Physicians and Surgeons Pakistan*. 2005;15(3):149-151.

120. Shah K, Reid JAW, Parekh R, Telfer M. Peripheral margins for wide local excision of morpheic basal cell carcinoma (BCC). *British Journal of Oral and Maxillofacial Surgery*. September 2013;51 (6):e99-e100.

121. Shalom A, Westreich M, Schein O, Hadad E. Stretch test: Effectiveness in identifying basal cell carcinoma borders. *Annals of Plastic Surgery*. 2012;68(1):72-73. doi:10.1097/SAP.0b013e3182119126

122. Sherry KR, Reid LA, Wilmshurst AD. A five year review of basal cell carcinoma excisions. *Journal Of Plastic, Reconstructive & Aesthetic Surgery: JPRAS*. 2010;63(9):1485-1489. doi:10.1016/j.bjps.2009.09.007

123. van Loo E, Mosterd K, Krekels GA, et al. Surgical excision versus Mohs' micrographic surgery for basal cell carcinoma of the face: A randomised clinical trial with 10 year follow-up. *Eur J Cancer*. Nov 2014;50(17):3011-20. doi:10.1016/j.ejca.2014.08.018

124. Staub G, Revol M, May P, Bayol JC, Verola O, Servant JM. Excision skin margin and recurrence rate of skin carcinomas. A 844-cases prospective study. *Annales de Chirurgie Plastique Esthetique*. 2008;53(5):389-398. doi:10.1016/j.anplas.2007.07.015

125. Stewart TJ, Saunders A. Risk factors for positive margins after wide local excision of cutaneous squamous cell carcinoma. *Journal of Dermatological Treatment*. 03 Oct 2018;29(7):706-708.

126. Su SY, Giorlando F, Ek EW, Dieu T. Incomplete excision of basal cell carcinoma: A prospective trial. *Plastic and Reconstructive Surgery*. 2007;120(5):1240-1248. doi:10.1097/01.prs.0000279148.67766.e1

127. Sugrue C, McInerney N, Tarmey T, et al. Risk factors for incomplete excision of basal cell carcinomas: A review of 1423 consecutively excised basal cell carcinomas in a tertiary referral centre. *Irish Journal of Medical Science*. September 2013;182(7)(1):S339.

128. Sugrue CM, McInerney N, Joyce CW, Kelly JL. Tumor Margin Assessment with Loupe Magnification Enables Greater Histological Clearance of Facial Basal Cell Carcinomas Compared with Clinical Examination Alone. *Dermatologic Surgery*. 2017;43(6):805-809. doi:10.1097/DSS.0000000000001121

129. Taib M, Adams BM. Skin shop: A new model for high-volume skin cancer care. *Journal Of Plastic, Reconstructive & Aesthetic Surgery: JPRAS*. 2019;72(2):290-293. doi:10.1016/j.bjps.2018.10.014

130. Tan PY, Ek E, Su S, Giorlando F, Dieu T. Incomplete excision of squamous cell carcinoma of the skin: A prospective observational study. *Plastic and Reconstructive Surgery*. September 2007;120(4):910-916.

131. Teoh YL, Halpern SM, Shall L. Factors associated with incomplete excision of basal cell carcinomas. *British Journal of Dermatology*. July 2010;163(1):55-56.

132. Thomas DJ, King AR, Peat BG. Excision margins for nonmelanotic skin cancer. *Plastic and Reconstructive Surgery*. July 2003;112(1):57-63.

133. Tullett M, Whittaker M, Walsh S. Marking sutures to orientate specimens of basal cell carcinoma: do they really make a difference? *The British Journal Of Oral & Maxillofacial Surgery*. 2016;54(6):682-685. doi:10.1016/j.bjoms.2016.04.007

134. Unlu RE, Altun S, Kerem M, Koc MN. Is it really necessary to make wide excisions for basal cell carcinoma treatment? *The Journal of craniofacial surgery*. Nov 2009;20(6):1989-1991.

135. Van Rijsingen MCJ, Vossen R, Van Huystee BEWL, Gorgels WJMJ, Gerritsen MJP. Skin tumour surgery in primary care: Do general practitioners need to improve their surgical skills? *Dermatology*. 2015;230(4):318-323. doi:10.1159/000371812

136. Wade S, Gonzalez ML, Basra M. An audit of the diagnostic accuracy and complete excision rate for skin cancers in primary and secondary care in the Cardiff area. *British Journal of Dermatology*. July 2011;165(1):105.

137. Wavreille O, Martin De Lassalle E, Wavreille G, Mortier L, Martinot Duquennoy V. Histologic risk factors of basal cell carcinoma of the face, about 184 cases. *Annales de Chirurgie Plastique Esthetique*. 2012;57(6):542-548. doi:10.1016/j.anplas.2012.03.002

138. Weshah S, Smadi R, Helalat M. Basal cell carcinoma: A retrospective analysis of 76 patients. *Pakistan Journal of Medical Sciences*. 2007;23(4):556-560.

139. van Delft LCJ, Nelemans PJ, van Loo E, Abdul Hamid M, Kelleners-Smeets NWJ. The illusion of conventional histological resection margin control. *Br J Dermatol*. 05 2019;180(5):1240-1241. doi:10.1111/bjd.17510

140. Morris DS, Elzaridi E, Clarke L, Dickinson AJ, Lawrence CM. Periocular basal cell carcinoma: 5-year outcome following Slow Mohs surgery with formalin-fixed paraffin-embedded sections and delayed closure. *Br J Ophthalmol*. Apr 2009;93(4):474-6. doi:10.1136/bjo.2008.141325

141. Abide JM, Nahai F, Bennett RG. The meaning of surgical margins. *Plast Reconstr Surg*. Mar 1984;73(3):492-7. doi:10.1097/00006534-198403000-00030

142. Genders RE, Marsidi N, Michi M, Henny EP, Goeman JJ, van Kester MS. Incomplete Excision of Cutaneous Squamous Cell Carcinoma; Systematic Review of the Literature. *Acta Derm Venereol*. Mar 2020;100(6):adv00084. doi:10.2340/00015555-3441

143. Griffiths RW, Suvarna SK, Stone J. Basal cell carcinoma histological clearance margins: an analysis of 1539 conventionally excised tumours. Wider still and deeper? *J Plast Reconstr Aesthet Surg*. 2007;60(1):41-7. doi:10.1016/j.bjps.2006.06.009

144. Barry J, Oon SF, Watson R, Barnes L. The management of basal cell carcinomas. *Ir Med J*. Jun 2006;99(6):179-81.

Supporting information

Conflicts of interests:

None declared.

Funding statement:

None.

Patient consent:

Not applicable.

Contributor statement:

GSN wrote the protocol, JCRW, ALK and AJ revised this. GSN, ALK and JPT screened results, extracted the data and performed the risk of bias assessment. RGW and MA performed the meta-analyses and meta-regression. RGW and GSN interpreted the results. GSN wrote the first draft of the manuscript, JCRW and RGW revised this. All authors approved the final version. AJ and GSN conceived the project.

Data statement:

The extracted data are freely available via the Open Science Framework (https://osf.io/6znhb/) and the statistical syntax can be obtained from RGW/MA.

Figure legends

Figure 1: PRISMA flow diagram. (Adapted from Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097)

Figure 2: Risk of bias summary graph for included studies. Risk of bias was assessed using a tool specifically designed for observational prevalence/incidence studies.[22]

Figure 3: A forest plot of the summary estimates of the risk of incomplete excision for basal cell carcinomas (BCCs) split by specialty. General practitioners were more likely to incompletely excise BCCs than dermatologists (RR 3·9 [2·0-7·3] p<0·001, permuted p=0·002) and plastic surgeons (RR 2·4 [1·4-4·2] p=0·003, permuted p=<0·001). Dermatologists had a lower risk of incomplete excision than plastic surgeons (RR 0·4 [0·2-0·7] p=0·003, permuted p<0·001).

Figure 4: A forest plot of the summary estimates of the risk of incomplete excision for squamous cell carcinomas (SCCs) split by specialty. General practitioners were more likely to incompletely excise SCCs than dermatologists (RR 4·8 [1·0-22·8] p=0·05, permuted p<0·001) and plastic surgeons (RR 2·2 [1·2-8·5] p=0·021, permuted p=0·002). Dermatologists had a lower risk of incomplete excision than plastic surgeons (RR 0·3 [0·1-0·8] p=0·021, permuted p=0·002).

CHARACTERISTIC			NUMBER OF STUDIES	PERCENTAGE OF ALL STUDIES
STUDY DESIGN	Randomised controlled trial		3	3%
	Cohort	Prospective	10	9%
		Retrospective	47	43%
		Other	7	6%
	Case-series	Prospective	6	6%
		Retrospective	33	30%
		Other	4	4%
YEAR OF PUBLICATION	2000 – 2005		5	5%
	2006 – 2010		31	28%
	2011 – 2015		49	45%
	2016 – 2019		25	23%
COUNTRY OF ORIGIN	Europe		69	63%
	Asia		19	17%
	Oceania		14	13%
	South America		7	6%
	North America		1	1%
SPECIALTY	Plastic surgery		37	34%
	Dermatology		22	20%
	Maxillofacial surgery		10	9%
	General practice		8	7%

	Ophthalmology	4	4%
	Ear, nose & throat surgery	1	1%
	Other	28	26%
TYPE OF PUBLICATION	Full paper	79	72%
	Conference abstractions	28	26%
	Other	3	3%
TOTAL		**110**	**100%**

Table 1: Characteristics of included studies. Cohort and case-series 'other' includes studies with mixture of prospective and retrospective data collection and those where the text is unclear as to whether the data collection was retrospective or prospective. 'Other' specialty includes studies that reported multiple specialties in the same study. 'Other' publication type includes conference podium and poster presentations.

SPECIALITY	PROPORTION OF HEAD AND NECK EXCISIONS % (95% CI)	PROPORTION OF LESIONS RECONSTRUCTED WITH % (95% CI)		
		Direct closure	Skin graft	Flap
DERMATOLOGY	84·7 (74·7-92·6)	89·3 (85·5-92·6)	2·9 (1·8-4·4)	6·1 (4·7-7·7)
PLASTIC SURGERY	92·7 (86·2-97·3)	55·5 (42·8-66·8)	16·4 (9·9-24·2)	22·6 (11·6-36·0)
GENERAL PRACTICE	31·0 (20·0-43·1)	Not reported		
MAXILLOFACIAL SURGERY	97·7 (85·2-100)	48·6 (44·2-53·0)	24·6 (21·0-28·6)	26·8 (23·1-30·8)
EAR, NOSE AND THROAT SURGERY	100 (96·6, 100)	Not reported		
OPHTHALMOLOGY	100 (98·8-100)	72·2 (64·9-78·5)	13·0 (8·6-19·0)	11·1 (7·1-16·9)

Table 2: The proportion of lesions excised from the head and neck, and the way all lesions were reconstructed from the included studies. How lesions which were excised by general practitioners and ear, nose and throat surgeons were reconstructed was not reported in any studies.