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Charles Darwin University

## Conceptual, statistical and clinical interpretation of results from

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Article type : Letter to the Editor

**Conceptual, Statistical and Clinical interpretation of results from A Systematic Review and Meta-Analysis of Cryosurgery combined with Topical interventions for Actinic Keratosis**

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**Conceptual, Statistical and Clinical interpretation of results from A Systematic Review and Meta-Analysis of Cryosurgery combined with Topical interventions for Actinic Keratosis**

Dear Editor,

A study, recently conducted by Heppt and colleagues, was published in the British Journal of Dermatology <sup>1</sup>. We have a few points regarding this study, which we believe, will be of great interest to the readers of the British Journal of Dermatology.

**Conceptual interpretation of pooled effect size of the clinical efficacy of two treatments**

Furthermore, when conducting meta-analysis by pooling studies, the studies should be analysing the outcome of the same input effect (for ex. in a meta-analysis regarding efficacy of two treatments A & B, you cannot pool the results of a cohort that received treatment A with one that received treatment B, even though the outcome of both cohorts is measured in terms of Risk Ratio). Heppt et al.'s meta-analysis fails to comply with said point. In Fig.3 of Heppt et al.'s manuscript, we observe that studies assessing different treatments (5-FU, Imiquinod, Ingenol Mebutate, Diclofenac and ALA-PDT) have been pooled, to determine the overall Risk Ratio, which is incorrect. Similar points have been echoed by previous publications regarding the pitfalls faced while conducting a meta-analysis <sup>2</sup>. As it stands, the forest plots presented by Heppt et al, are not adequately representative of the actual pooled outcome effect (pooled RR).

**Publication bias of literature based meta-analysis on Cryosurgery combined with Topical interventions for Actinic Keratosis**

The authors have also not assessed for publication bias (Figure 1). Publication bias is a side-effect of the publication process, wherein small studies and negative results are often not published, as part of peer reviewed literature. If ignored, publication bias can severely affect the credibility of results <sup>3</sup>. We strongly recommend, Heppt et al. and future researchers to include publication bias assessment as a major part of meta-analyses.

This letter is intended to inform the authors, as well as open up discussion regarding issues that may arise while conducting a meta-analysis, so that these issues are avoided in future similar studies.

## Declarations

### Ethics approval and consent to participate

Not applicable.

### Consent for publication

Not applicable.

### Availability of data and materials

Not applicable.

### Competing interests

None has been declared by the authors.

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### Authors' contributions

RJ is principally conceived of this review and led the growth of the letter to the editor. Both RJ and CK wrote the first draft of the letter, and critically revised and edited sequential drafts of the manuscript. RJ and CK read and approved the final version of the manuscript

### Acknowledgements

Not applicable

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- 1 Heppt MV, Steeb T, Ruzicka T *et al.* Cryosurgery combined with topical interventions for actinic keratosis: a systematic review and meta-analysis. *The British journal of dermatology* 2018.
- 2 Greco T, Zangrillo A, Biondi-Zoccai G *et al.* Meta-analysis: pitfalls and hints. *Heart, lung and vessels* 2013; **5**: 219-25.
- 3 Jayaraj R, Kumarasamy C, Ramalingam S *et al.* Systematic review and meta-analysis of risk-reductive dental strategies for medication related osteonecrosis of the jaw among cancer patients: Approaches and strategies. *Oral Oncol* 2018; **86**: 312-3.

**Fig. 1** Funnel plot assessing publication bias for Heppt et al.'s study, for the meta-analysis of studies involving 100% clearance of AK in patients.

This figure shows the funnel plot which was slightly asymmetric (existence of publication bias) across clinical efficacy of two treatment studies. It indicates the possible bias among the included intervention studies and each point indicates an individual intervention study that was included for the generation of the forest plot (Figure 3 in the study of Heppt and colleagues).

Figure. 1

