
Charles Darwin University

**Conceptual, statistical and clinical interpretation of results from
Cryosurgery combined with topical interventions for actinic keratosis: a systematic
review and metaanalysis**

Jayaraj, Rama; Kumarasamy, Chellan

Published in:
British Journal of Dermatology

DOI:
[10.1111/bjd.17772](https://doi.org/10.1111/bjd.17772)

Published: 01/08/2019

Document Version
Peer reviewed version

[Link to publication](#)

Citation for published version (APA):

Jayaraj, R., & Kumarasamy, C. (2019). Conceptual, statistical and clinical interpretation of results from: Cryosurgery combined with topical interventions for actinic keratosis: a systematic review and metaanalysis. *British Journal of Dermatology*, 181(2), 423-424. <https://doi.org/10.1111/bjd.17772>

General rights

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the public portal

Take down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

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

R. Jayaraj^{1*}, C. Kumarasamy²

1. Dr. Rama Jayaraj, PhD, GCTLHE, MPH(RJ)
Senior Lecturer - Clinical Sciences,
College of Health and Human Sciences, Charles Darwin University, Ellengowan Drive,
Casuarina, Northern Territory 0909, Australia
Email: Rama.Jayaraj@cdu.edu.au
2. Chellan Kumarasamy, B.Tech (CK)
The University of Adelaide,
North Terrace Campus, Adelaide, South Australia 5005, Australia.
Email: chellank54@gmail.com

*** Corresponding author**

Dr Rama Jayaraj PhD, GCTLHE, MPH (RJ)
Senior Lecturer - Clinical Sciences,
College of Health and Human Sciences, Charles Darwin University, Ellengowan Drive,
Casuarina, Northern Territory 0909, Australia.
E-mail: Rama.Jayaraj@cdu.edu.au

Keywords

Cryosurgery, Topical interventions, Actinic Keratosis, Methyl aminolaevulinate–
photodynamic therapy, Publication Bias, Publication bias, Effect size of clinical efficacy,
Meta-Analysis, and Systematic review

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/bjd.17772

This article is protected by copyright. All rights reserved.

**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 ¹. 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 ². 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 ³. 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.

Funding

No funding support received to conduct and prepare this study.

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

References

- 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

