Title:

Systematic Reviews in Orthodontics: A fresh look to promote renewal and reduce redundancy.

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Systematic reviews are intended to collate and analyze the evidence regarding a specific aspect of clinical practice in a drive for evidence-based health care.[1] Unfortunately, many systematic reviews in medicine and dentistry [2,3] conclude by stating that further evidence is required through well-designed randomized clinical trials.[4,6] It has been mooted that within orthodontics, systematic reviews considerably outweigh the number of clinical trials[7] with evidence that a substantial proportion of the former are limited or inconclusive. This is due in many cases to low quality studies preventing or limiting meta-analyses.[8]

When several systematic reviews exist on a topic, it is possible to evaluate
and collate their findings in an overview or 'umbrella' review.[9] Within overviews, however, considerable duplication and unnecessary overlap have been identified which represents significant research waste.[10]

To address these shortcomings, is there a need to revisit what a researcher should do when a systematic review is completed? Although the Cochrane Collaboration has adopted the concept of living systematic reviews (LSR)[11] with creation of a Living Evidence Network (LEN), this involves continual update of the review as new evidence becomes available, rather than providing a direct stimulus for the improvement of the primary evidence in a subject area.

The limited yield from systematic reviews, meta-analyses and umbrella reviews has prompted us to make the following suggestions:

1] When a clinical systematic review is completed, aside from making recommendations as to how evidence should be improved, the authors should lead by example and ideally undertake a randomized controlled trial (RCT) but if not feasible or appropriate, another high quality study for example a prospective cohort study.This would hopefully lead authors to reflect on why they did the review in the first place, presumably to improve their clinical practice and that of others, rather than completion and publication of the review as the primary academic exercise.

2] All orthodontic systematic reviews should adopt the PRISMA guidelines for write-up and include a link to a peer-reviewed protocol for the "ideal" study in the area of interest. This would include a

sample size calculation for the most clinically important outcome, timepoint at which the data are to be collected, an explicit list of secondary outcomes based on the orthodontic core outcome set [12] and detail the prescribed methodology as well as the optimal statistical analyses required. The predetermined
study protocol should be published on PROSPERO or in an open access journal such as Clinical Trials. It should also be made available on the authors' own webpages.
We feel that this approach would have several advantages:

- It would facilitate the conduct of RCTs on a specific topic by having a peer-reviewed protocol to hand that may be used for local ethical applications.
- Several operators / centres could undertake the same trial contemporaneously or in succession in different settings to improve the generalizability of findings. Such multi-centre collaboration is to be encouraged.[13,14]
- Most importantly, methodological variation would be reduced and hopefully confounders identified as well as accounted for in the sampling strategy or analyses.
- With the adoption of the same trial design, similar participants and outcomes being assessed preferably from the orthodontic core outcome set[12] at the same timepoints, meta-analyses would be performed to potentially increase the certainty of findings.

This would maximize yield from our clinical trials.[15] For reviews incorporating comparisons of several
interventions, defining a protocol for a subsequent trial is challenging. In those instances, focus would have to be directed at trialling what are regarded as the most clinically important outcomes.
It is essential to emphasize that we continue to recognize the importance of well-conducted systematic reviews with meta-analyses, as these are the pinnacle of the hierarchy of evidence. We also acknowledge that we are guilty in almost all cases of not having followed our own systematic reviews with related clinical trials and indeed the views portrayed here are not intended to be critical of investigators.
As has often been said "If you always do what you always did, you will always get what you always got" and it is our duty as researchers to generate meaningful quantitative and qualitative data with the aim of improving clinical decision-making. Systematic reviews are a pivotal, complex and evolving
field, and making progress will be challenging but ultimately rewarding. We can but try.

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References

1. Sackett Dl, Rosenberg WMC, Gray JAM, Haynes RB, Richardson WS. Evidence based medicine: what it is and what it isn't? BMJ 1996;312-71.
2. Glenny A-M, Esposito M, Coulthard P, Worthington HV. The assessment of systematic reviews in dentistry. Eur J Oral Sci 2003;85–92.
3. Bassani R, Kahil G, Pereira R, Page MJ, Tricco AC, Moher D, Sarkis-Onofre R. Systematic reviews
in dentistry: Current status, epidemiological and reporting characteristics. J Dent 2019;71-84.
4. Fleming PS, Seehra J, Polychronopoulou A, Fedorowicz Z, Pandis N. A PRISMA assessment of the
reporting quality of systematic reviews in orthodontics. Angle Orthod 2013;158–163
5. Pandis, N., Fleming, PS, Worthington, H and Salanti, G. The quality of the evidence according to GRADE is predominantly low or very low in oral health systematic reviews. PloS one 2015;e0131644
6. Littlewood SJ, Millett DT, Doubleday B, Bearn DR, Worthington HV. Retention procedures for stabilising tooth position after treatment with orthodontic braces. Cochrane Database of Systematic Reviews 2016, DOI: 10.1002/14651858.CD002283.pub4.
7. Papageorgiou SN, Eliades T. Evidence–based orthodontics: Too many systematic reviews, too

few trials. J Orthod 2019;9-12.
8. Koletsi, D., Fleming, P. S., Eliades, T., Pandis, N. The evidence from systematic reviews and metaanalyses
published in orthodontic literature. Where do we stand?. EJO 2015;603-609.
9. Lewis R, Hendry M, Din N, Stanciu MA, Nafees S, Hendry A, Teoh ZH, Lloyd T, Parsonage R, Neal
RD, Collier G, Huws DW. Pragmatic methods for reviewing exceptionally large bodies of evidence: systematic mapping review and overview of systematic reviews using lung cancer survival as an exemplar. Syst Rev 2019;8-171.
10. Lunny, C, Zhang, JH, Chen, A, Neelakant, T, Shinger, G, Stevens, A, Tasnim, S, Sadeghipouya, S,Adams, S, Zheng, YW and Lin, L. Topic duplication and research waste at the 'Overviews of systematic reviews' level: Survey of overlapping overviews, 29 June 2021, PREPRINT (Version 1) available at Research Square https://doi.org/10.21203/rs.3.rs-665009/v1
11. Elliott, JH, Synnot, A, Turner, T, Simmonds, M, Akl, EA, McDonald, S, Salanti, G, Meerpohl, J, MacLehose, H, Hilton, J and Tovey, D Living systematic review: 1. Introduction—the why, what, when, and how. J Clin Epidemiol 2017;23-30.
12. Tsichlaki A, O'Brien K, Benson PE, Marshman Z, Johal A, Colonio-Salazar FB, Harman NL, Fleming
PS. Development of a core outcome set for use in routine orthodontic clinical trials. Am J Orthod Dentofacial Orthop 2020;650-660.
13. Bellomo R, Warrillow SJ, Reade MC. Why we should be wary of single-center trials. Crit Care Med
2009;3114-3119.
14. Bafeta A, Dechartres A, Trinquart L, Yavchitz A, Boutron I, Ravaud P. Impact of single centre status on estimates of intervention effects in trials with continuous outcomes: metaepidemiological study. BMJ 2012;344.
15. Chalmers I, Glasziou P. Avoidable waste in the production and reporting of research evidence. Lancet 2009;86-89.