

Subject: [15728] Manuscript Submitted to Dove Medical Press for Clinical Epidemiology

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Date: Tue, 23 Nov 2010 14:31:43 +1300

To: "harri.hemila@helsinki.fi" <harri.hemila@helsinki.fi>

Dear Dr Hemila

On behalf of the Editor in Chief, I regret to inform you that he has declined to accept your manuscript for Clinical Epidemiology.

If you agree to revise your manuscript in line with reviewer comments (below), you can submit it as a new paper to another Dove journal, where it will be treated as a new manuscript and subject to peer review.

We would like to suggest that your paper be considered for one of our sister journals, either Nutrition and Dietary Supplements or Clinical Pharmacology: Advances and Applications. Please note: the publication processing fee for both journals is €1249.

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I look forward to hearing from you whether you intend to submit to either of these alternative journals.

Kind regards

Jane

Jane Vardy

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Dear Dr Hemila

Journal Name: Clinical Epidemiology

Title: Zinc Lozenges May Shorten the Duration of Colds: a Systematic Review

ID: 15728

Author: Dr Hemila

Please find below the peer review report on your submission.

I regret to inform you that your manuscript is currently not suitable for publication in our journal.

REVIEWER 1 EVALUATION

There are a number of grammatical errors that need to be corrected before the paper can be accepted for publication.

P. 5 "web of science, October 21, 2009", should read "web of science, October 21, 2010", this analysis should have taken place after the other searches not before.

Background, nature, scope and importance of the problem that led to the review/meta-analysis is well described.

It was not clear if the review/meta-analysis was guided by a written protocol, the paper was silent on this point, it should be addressed.

The aims/research questions could be more clearly described.

The populations studied in which the results are to be generalised could be more specifically described, including a trial with children while all others involved adults diluted this aspect of the research and I note an analysis on adult only trials was not undertaken but would enable generalisability to this target population to be more clearer than the current mixing of population groups in the current presentation of results.

The literature search was very basic, and raises the question if any trials were missed in the review. The time period for the searches was not provided, this needs to be inserted into the manuscript.

One trial yielded 3 comparisons so there were 11 trials providing data for 13 trials which potentially increases publication bias in reporting, but this was not addressed in the review. Also there is confused reporting of the number of trials vs comparisons, for example, page 11 states "13 zinc lozenge trials" when it should have stated "13 zinc lozenge comparisons", this needs addressing.

The data extraction processes were well described. How missing data were handled was not described in the review.

No measures were taken to identify or reduce the selective reporting of results within study reports or the selective reporting of studies themselves (publication bias), such as a funnel plot analysis.

There seems to be a lack of reporting of the optional information size needed to detect the desired treatment effect.

Statistical heterogeneity was examined and reported to be high for the overall results and the high dose subgroup but not for the low dose subgroup. The author failed to interpret the high heterogeneity effect in terms of the results and generalisation, yet argued against previous research that demonstrated high heterogeneity. This needs to be addressed.

There was no discussion about the process of simply combining significance tests (P values) as the author did in this review. For example, studies with P values greater than 0.05 are published less often, making this method more prone to publication bias.

In terms of inclusion of papers, there was no mention if one or two reviewers undertook this process, no kappa value was reported in terms of inter-rater agreement.

The results were placed in context and implications for the results presented but the paper needs further re-working before it can be accepted for publication.

REVIEWER 2 EVALUATION

This systematic review with a meta-analysis examines whether dosage of zinc lozenges impacts the duration cold symptoms. The introduction is succinct and provides adequate background and justification for the review. The search strategy employed appears to be relevant and comprehensive.

It is unclear whether the primary author is the sole reviewer of the studies to be included in the analysis or whether a second reviewer was involved (as per 3rd paragraph in the methods section).

The "statistical methods" section is too long. Some of the narrative detail covering justification for methods may be better placed in the discussion or left out all together.

The discussion is quite lengthy. The section on "previous reviews", for example, could be reduced substantially. A statement or section dedicated to explicitly stating strengths and limitations of this review should be included in the discussion.

The second sentence in the "conclusion" section of the abstract does not appear to fit. The addition of a statement of what this study adds to the state of knowledge in this area would add substantially to the abstract.

REVIEWER 3 EVALUATION

General comments:

1. I would suggest the use of first person "I" be dropped
2. Throughout the presentation of methods, results and discussion there is a great deal of mixing. The author needs to revise this and avoid excessive interpretation when describing the methods and results.
3. The text accompanying the figures and tables is far too complex + lengthy and requires the reader to move back and forth between them and even the supplements. These require major revision.
4. The text is excessive in length and quite rambling.

Abstract: "results" missing

The conclusion does not follow from what was addressed in this review.

Introduction:

Omit the first paragraph. Considerable controversy remains regarding the zinc-ARI relation.

There is no mention of previous reviews in the introduction, nor is a clear case made for the need of this review. In the discussion two reviews are critiqued, however there are others, including the Cochrane systematic review of zinc treatment for common colds.

Methods:

The decision to apply % reduction as the primary outcome does have statistical merits, but is not of pragmatic utility. The author does need to address the absolute reduction in illness duration.

Was an intention to treat analysis an inclusion criteria? What proportion of subjects stopped taking zinc due to side effects and how did this differ between high and low dose zinc subgroups?

Results:

Table 1: incomplete presentation of effect column. This should include 95% CIs.

Table 2 not necessary

Figure S1 should not be a supplement.

Yours sincerely

Dr Henrik Toft Sorensen

Editor-in-Chief

Clinical Epidemiology

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