Reviewer’s report

Title: Screening for thyroid dysfunction and treatment of screen-detected thyroid dysfunction in asymptomatic, community-dwelling adults: a systematic review

Version: 0 Date: 03 Jan 2019

Reviewer: Howard Tracer

Reviewer's report:

This is a very nice systematic review on screening for and the treatment of asymptomatic, screen-detected thyroid dysfunction.

I appreciate the opportunity to review it.

I have the following few comments and suggestions.

I'd suggest that the Abstract touch on findings for all the key questions.

So, on page 2, line 33, you might add "no studies on the treatment of screen-detected subclinical hyperthyroidism were found.

"If you add this, then you'll need to specify "subclinical hypothyroidism" on line 34.

Similarly, on line 37, you might add a sentence or phrase on the harms that were found (or that few/ none were found).

On page 6, line 119,

"TD affects...5% of people..." may be incorrect data.
The reference cited stated "5% of women and 3% of men"

On page 10,

Lines 202-203, you wrote "suggests that TSH tests are potentially overused..."

I understand that you wrote "potentially overused," however, overuse would depend upon knowing that there were no clinical indications for the TSH test.

On page 12, line 243.

I think that should read "or" b) intermediate outcomes.

On page 13, lines 273-275.

I was unclear about your population inclusion criteria of "no history of thyroid disease (except Hashimoto's thyroiditis, subclinical hypothyroidism or subclinical hyperthyroidism)"

I would think that for KQ1 (screening), the population included would be no history of any thyroid disease, and persons with "no history of thyroid disease (except Hashimoto's thyroiditis, subclinical hypothyroidism or subclinical hyperthyroidism)" might be the included population for KQ3 (and KQ4), treatment of screen-detected or subclinical TD.

If so, this should be clarified.

On page 22, lines 464-465,
You noted that "All of the...participants in Anderson 2016 had concomitant heart disease..."

If so, I wonder whether any outcomes that include this study (on pages 23-29) should be downgraded for indirectness (applicability of findings in a population with heart disease to the general population).

On pages 37 and 39,

Where you discuss the results for cholesterol and LDL cholesterol levels that were found in several RCTs of treating subclinical hypothyroidism, you note that "results were mixed" or that most studies "did not find a statistically significant difference..."

I would note that most of the studies found lower levels of cholesterol and LDL levels in those treated, though most of these were not statistically significant.

As you note on page 53, lines 958-961, the issue here may be that "small sample sizes...may not have...sufficient power..." - rather than a lack of effectiveness.

I know that in the "Data Synthesis" section (p. 16) you stated that "due to clinical and methodological heterogeneity...a meta-analysis was not completed..."

Still, I wonder if a meta-analysis might be appropriate for these intermediate outcomes, possibly by restricting the studies included in the meta-analysis to those that were more similar (eg. duration 6 months or longer, or 1 year or longer, etc...).

If you don't think a meta-analysis is appropriate, then a forest plot might be a good way to visually present this data to readers.
Related to this, on page 52, lines 937-946, you mention two systematic reviews with meta-analyses that found a small benefit of treating subclinical hypothyroidism on cholesterol and LDL levels.

It's my impression that the findings of this review are consistent with those two studies.

If you think they are not, then some discussion of these 2 reviews weaknesses (eg., do you think a meta-analysis was not warranted in those reviews), and why this review reached a different conclusion, would be helpful.

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