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: 21 Jan 2019

Reviewer: Michael LeFevre

Reviewer's report:

Overall this is a well done comprehensive review that will serve a guideline panel well in deliberations about screening for thyroid dysfunction. Specific comments/questions follow.

Line 273-275.

Eligibility criteria are confusing as worded; I cannot tell whether those listed in parentheses are explicitly included or excluded. Similarly, the "no" preceding "history of thyroid disease" could be interpreted to extend to "uninvestigated nonspecific symptoms…"

Line 308-310.

This sentence, as well as the category of excluded studies in the appendix suggests that if RCTs were available, observational studies were not used.

That does not appear to be the case for multiple outcome, and seems to contradict line 298.

Line 457 (and line 709).

I find no forest plots in Additional file 2.

Line 496-505.
I am confused by the judgements made.

The phrase "moderate certainty that no statistically significant difference exists" in mortality for adults > age 65, appearing in the conclusions and in the evidence table seems to mask the large imprecision of the estimate with a HR that is clinically meaningful.

Perhaps your real conclusion is no statistically significant reduction in mortality? Much tighter precision exists in the cohort based gender sub analysis; ruling out a change in mortality of 1 per 1000 is a high bar with a large sample size.

Line 528.

Inconsistency as well?

Discussion section:

line 902-905.

This statement seems to express a certainty that contradicts the described methods which include explicit predetermined clinically important differences.

Ignored here is the primary question of whether the precision and consistency of null findings are sufficient to conclude that no clinically significant difference exists.

It is perhaps left to a guideline panel to draw conclusions in this domain.

Line 908.
Although "prospective" determination of clinically important differences is not possible retrospectively, I was somewhat surprised by the lack of estimates of clinically important benefits.

I agree it is hard.

The USPSTF made an attempt in the evidence review for the Behavioral Counseling to Promote a Healthy Lifestyle for Cardiovascular Disease Prevention in Persons With Cardiovascular Risk Factors ([https://www.ncbi.nlm.nih.gov/books/NBK241535/#ch4.s2 - see section on Clinical Interpretation of Benefit and Harms Given Paucity of Direct Health Outcome Data](https://www.ncbi.nlm.nih.gov/books/NBK241535/#ch4.s2)).

I admit this is loose and may have exaggerated health effects.

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