Reviewer’s report

Title: Do we know enough about the effect of low dose computed tomography screening for lung cancer on survival to act? A systematic review, meta-analysis and network meta-analysis of randomised controlled trials.

Version: 0 Date: 07 Feb 2019

Reviewer: Ali Usman

Reviewer's report:

The authors tried to answer the question "Do we know enough about the effect of low dose computed tomography screening for lung cancer on survival to act?", however, fell well short.

1. This review provides no additional information as compared to a recent systematic review by Ali.et al 2016 on "Screening for lung cancer: A systematic review and meta-analysis".

2. There are some serious methodological flaws in authors' approach to combining studies in conventional and network meta-analysis. First, NLST is essentially a head-to head lung cancer screening trial and should not be combined with other LDCT screening trials with usual care or no screening as comparison. Secondly, MILD study is essentially two trials in one i.e. Annual screening arm and Biennial screening arm and study reports very different results in terms of magnitude of effect on mortality for each when compared with usual care, so combining them in to a single comparison is methodologically not correct.

3. To properly answer the question on effect of LDCT screening on lung cancer mortality, one has to account for subsequent harms associated with screening as well such as over diagnosis, false positives and consequences of false positives, so an informed decision on effectiveness of screening can be made i.e. balancing benefits vs. potential harms.

4. Apart from doing risk of bias assessment for individual studies, authors have refrained from doing an actual quality assessment of body of evidence i.e. GRADE. The pooled estimates have little to no certainty if they are being informed through poor quality of evidence.

5. Authors also did not provide additional information on important subgroups of interest where a differential effect of screening may be present such as stage of lung cancer.

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