Peer Review File

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Reviewer A

Comment 1: Abstract: The abstract in its current form lacks information on the key findings of the work. I would suggest that it is structured in a introduction, material and method as well as a result and conclusion section. The result section should summarize the key findings and in the conclusion section the relevance of the findings for daily practice should be indicated. Specifically, the 5-year mortality rate of LC should be correctly stated. The number given reflects mortality of locally advanced and metastasized cancers but the 5-year survival for the entire group of lung cancer is higher these days.

Reply 1: Thank you for this comment. In the guidelines for authors of TLCR, we found that for review articles, there should be no subheaders in the abstract. That's reason why we didn't structure the abstract in an introduction, material and method and conclusion section. However, we adapted the abstract now, so that the information requested by the reviewer is included. We agree with the reviewer that the five-year survival rate for lung cancer for the entire group of lung cancer is higher. We changed this in the abstract as follows:
'*The five-year survival rate for lung cancer depends on the stage at which it is diagnosed. It is over 50% for cases detected in a localized stage but when the disease has spread to other organs, the five-year survival rate is only 5%. Unfortunately, only 16% of lung cancer cases are diagnosed at an early stage*.' – Information from the Lung Cancer Fact Sheet – American Lung Association – www.lung.org.
Moreover, we included more specific conclusions with relevance for daily practice.

Comment 2: Introduction: Here some of the comments made for the abstract apply as well. Some expression should be more specific, e.g. not "LDCT can reduce…." but rather "screening with chest LDCT can reduce" (see line 48 for example. Statements to other screening programs such as breast cancer screening or colon cancer screening are oversimplified which should not be the case in a paper where screening is the focus, e.g. lines 54-57. Also the number participants in the US lung cancer screening program needs to be revisited. The cited source of information is not the most recent one. More recent work reports different findings (see my comment in line 60) .

Reply 2: We agree with the reviewer, that 'screening with chest LDCT' is more specific. We changed this in the manuscript.
We also deleted the reference to the existing cancer screening programs in the former lines 54-57. We also added data on the uptake in the US lung cancer screening program (Yong et al, 2020), which showed a much higher uptake of 16.3%. Probably, this publication was not yet publicly available when we closed our literature search.

Comment 3: Materials and Methods: Aside from using the term "lung cancer screening and participation" one should also apply the search term "uptake or uptake rate". This will add additional valuable literature to the search. I strongly suggest to run a search maybe by combining the terms "participation" and "uptake" in the advanced search function in e.g. pubmed. The sentence in line 74 to 78 is not quite clear to me and should be rephrased. Also a link to the following figure 1 should be given.

Reply 3: We fully agree with the reviewer that including the search term 'uptake' could yield additional valuable literature to the search. We followed the advise of the reviewer and combined the terms 'participation' and 'uptake' in the advanced search function of PubMed. This yielded 72 publications of which nine met the inclusion criteria of our review and were not yet included. Several of these publications were published after we had closed the search for our review article. To complete our search, we also did the same exercise in Web of Science, which yielded 14 publications of which one met the inclusion criteria and was not yet found in the PubMed data base. This means that an additional number of nine publications were included in our review:

Rai AV, Doria-Rose P, Silvestri GA, Yabroff KR. Evaluating Lung Cancer Screening Uptake, Outcomes, and Costs in the United States: Challenges With Existing Data and Recommendations for Improvement. J Natl Cancer Inst 2019;111(4):djy228. https://doi.org/10.1093/jnci/djy228

Jiang L , Chung S, Wei EK, Luft HS. New recommendation and coverage of low-dose computed tomography for lung cancer screening: uptake has increased but is still low. BMC Health Serv Res 2018;18:525. https://doi.org/10.1186/s12913-018-3338

Quaife SL, Vrinten C, Ruparel M, Janes SM, Beeken RJ, Waller J, McEwen A. Smokers' interest in a lung cancer screening programme: a national survey in England. BMC Cancer 2018;18:497. https://doi.org/10.1186/s12885-018-4430-6

Quaife SL, Ruparel M, Dickson JL, Beeken RJ, McEwen A, Baldwin DR, Bhowmik A, Navani N, Sennett K, Duffy SW, Wardle J, Waller J, Janes SM. Lung Screen Uptake Trial (LSUT): Randomized Controlled Clinical Trial Testing Targeted Invitation Materials. Am J Respir Crit Care Med 2020;201(8):965–75. https://doi.org/10.1164/rccm.201905-0946OC

Han PKJ, Lary C, Black A, Gutheil C, Mandeville H, Yahwak J, Fukunaga M. Effect of Personalized Risk Information on Patients Referred for Lung Cancer Screening With Low-Dose CT. Med Decis Making 2019;39(8):950-961. https://doi.org/10.1177/0272989X19875966

O'Brien MA, Sullivan F, Carson A, Siddiqui R, Syed S, Paszat L. Piloting electronic screening forms in
primary care: findings from a mixed methods study to identify patients eligible for low dose CT lung cancer screening. BMC Fam Pract 2017;18:95. https://doi.org/10.1186/s12875-017-0666-5

Hudson JN, Quinn GP, Wilson LE, Simmons VN. Evaluation of Promotional Materials To Promote Low-Dose Computed Tomography (LDCT) Screening to High-Risk Consumers and Health Care Providers. J Canc Educ 2018;33:1043–1051. https://doi.org/10.1007/s13187-017-1204-9

Eberth JM, Ersek JL, Terry LM, Bill SE, Nirupama Chintanippu Carlos R, Hughes DR, Studts JL. Leveraging the Mammography Setting to Raise Awareness and Facilitate Referral to Lung Cancer Screening: A Qualitative Analysis. J Am Coll Radiol 2020 available online 26 February 2020. https://doi.org/10.1016/j.jacr.2020.02.001

Norman R, Moorin R, Maxwell S, Robinson S, Brims F. Public Attitudes on Lung Cancer Screening and Radiation Risk: A Best-Worst Experiment. Value Health 2020;23(4):495-505.

The PRISMA flow chart was adapted accordingly.
The sentence in lines 74 to 78 was deleted, since it is confusing and redundant because it is already included in the PRISMA flow chart.
We also included a link to Figure 1 and specified the title.

Comment 4: Results: The result section is a summary of all findings. Though this is relevant, I sometimes felt a little bit lost in all the detailed summaries of the papers. I suggest that the authors should create summary tables per section with the key findings they discussed. This will increase the "take away" from reading significantly and help to achieve the overall objective of the paper which is to understand how to reach the hard to reach.

Reply 4: We thank the reviewer for this suggestion. A table was inserted with the most important findings for each section, which indeed gives a better overview.

Comment 5: In line 103, I don't agree with the presentation of the inclusion criteria of the Nelson study – see my detailed comment in the PDF.

Reply 5: We changed the inclusion criteria according to what is mentioned in the article of Zhao et al., 2011, as suggested by the reviewer (Zhao YR, Xie X, de Koning HJ, Mali WP, Vliegenthart R,Oudkerk M. NELSON lung cancer screening study. Cancer Imaging 2011;11:S79-S84. https://doi.org/10.1102/1470-7330.2011.9020).

We have also taken into account the more detailed comments of the reviewer mentioned in the PDF.

Comment 6: In line 142, I think it would be a good spot to elaborate on the role of the GPs. It is the current believe that they are key in the shared decision making with potential screening candidates but also motivate them to attend. However, GPs themselves need to be more educated about lung cancer screening, so in fact they should be reached as a target group for educational efforts as well.

Reply 6: We agree with the reviewer. In our manuscript, we already mentioned this when referring to Ersek et al., 2016 and Kanodra et al., 2016. We have now included an extra sentence in the Discussion part to stress this point:
However, since it was shown that there are substantial gaps in knowledge about LCS guidelines and reimbursement in family physicians and other PCPs and that they are not well-informed (Ersek at al., 2016; Kanodra et al., 2016), PCPs also have to be considered as a target group for education. Not only patient but also provider education should be developed to aid in shared decision-making opportunities (Hudson et al., 2018).

Comment 7: Discussion and conclusion: Here I have no specific comments but would like to see, that this section would be more "to the point" and highlights & discusses the key findings of the literature search.

Reply 7: We made several changes in the Discussion and Conclusion section. Moreover, by following the suggestion of the reviewer to include a table with the most important messages, we are convinced that it has become much easier for the readers to grasp the heart of the matter.

Reviewer B

Comment 1: The paper addresses an interesting topic. LDCT screening is recommended for Lung Cancer early detection, but some prospective candidates from the high-risk group ignore this recommendation. Why it happens and what to do? Interesting topic.
Nevertheless, the presentation of the material, the argumentation, and the structure of the paper should be largely improved.
First, the abstract. The abstract is one of the most important parts of the paper. It must reveal clearly what is the problem you are focused on, what is the goal of the paper, how did you solve the problem, what result you got. Currently, the abstract starts with an error. You say that the mortality of Lung Cancer is 90% and that 85% of Lung Cancer cases are associated with smoking. As a citation, you used the work of De Groot (reference #3). In the work, De Groot stated that 5-year survival ration is 15% (85% mortality) and 90% of Lung Cancer cases are associated with smoking. In other words, you mixed up the numbers.
Moreover, the goal of the paper is unclear. The statement "The aim of this review is to find out what is already known about reaching the hard-to-reach for LCS and how participation can be improved …" is confusing and unclear. What does it mean "to reach"? Who is or what is "hard-to-reach"?

Reply 1: Thank you for this comment. The abstract was thoroughly adapted with more focus on the problem, the goal of the paper and the results we got. The reference to the mortality rate has also been changed into a more differentiated picture according to the lung cancer stage.
Regarding the aim of the review which is confusing and unclear, we changed 'hard-to-reach' in the abstract by 'target group for lung cancer screening'. 'reached' was replaced by 'contacted'. In the further text, it becomes clear that the target group for lung cancer screening is not an easy one to convince to participate. 'hard-to-reach' is a terminology often used in this context (e.g. Field JK, Devaraj A, Duffy SW, et al. CT screening for lung cancer: Is the evidence strong enough? Lung Cancer 2016;91:29-35.). Moreover, the guest editors asked us to write a review with the title: 'Lung cancer screening: Targeting the hard to reach'.

Comment 2: Second, the introduction. In the introduction, you should show that there is a problem, who faces this problem and why it is important. Right now, it is unclear to whom you write this paper. Why there is a problem with the fact that people refuse to participate in screening? In your case, you may want to divide the problem into categories (shared decision-making, logistics, financial problems, etc.) and define what does each category means. Right now, you used the term shared decision-making multiple times in the paper, and after several pages of discussion how important it is you provide the definition of what it is.

Reply 2: In the introduction, we corrected the mistake you mentioned about the percentage of lung cancers whereby smoking is implicated (more than 90%) and the mortality due to lung cancer (85%). Thank you for mentioning this.
We agree with the reviewer that it was not very clear in the introduction what the problem is we wanted to solve. We therefore included the following paragraph:
A problem (cancer) screening programs can face, is that the target group does not attend, which endangers the existence of the program. Although it is clear that people can always refuse to participate after being well-informed about the benefits and harms of a (cancer) screening program, oftentimes other issues are playing a role. In these cases, more than unwillingness to participate, a lack of knowledge, not being familiar with the program or practical issues can be the reasons of non-attendance. In these cases, removing the barriers regarding these issues can help increase the

participation rate. Therefore, this review will present an overview of these reasons of non-attendance and what can be done about it.

The reviewer is right that the definition of shared decision-making has to be mentioned earlier in the manuscript. We have now put it under the heading *Recruitment: extra barriers specific for (ex-)smokers?* much earlier in the text, where it is addressed for the first time.

Comment 3: Third, the "body" of the paper. In Table 1 you just repeat the information from references. There is no reason for that. What is possible to do is to briefly describe each paper in two-three small sentences. But, even though, it is better to move the table into supplementary materials.

Reply 3: We agree with the reviewer and will move the table into supplementary materials.

Comment 4: Fourth, the conclusion. The conclusion states the result of the paper. This part is missing. Right now, the paper consists of the statements that were revealed by other authors. You need to perform the analysis of these results and highlight what is missing in these studies or what can be improved or something else. For example, you can create a table where columns are reasons why people do not participate in screening and rows are social groups and fill out the table to show which groups are studied and which are missing. Or which groups have dominating reasons. The analysis is needed otherwise there is no novelty besides collecting results from the other authors.

Reply 4: The conclusion part has been thoroughly rewritten. Moreover, a table has been included with an overview of the barriers on the one hand and the possible solutions to get into contact and motivate the target group for lung cancer screening on the other. We think this can also clarify the conclusions of the review.

Comment 5: Fifth, the writing. There are stylish mistakes in the paper. For example, a sentence from the abstract: "The definition and locating of the target group …". It should be or "the definition and location of the target group …" or "Defining and locating of the target group …". Another example, two sentences from the introduction: "Lung cancer (LC) is the leading cause of cancer death in the USA for both men and women (1). However, worldwide, lung cancer is also the commonest cause of cancer death (2)". The word "however" is not the right choice to connect these two sentences.

Reply 5: We thank the reviewer for these remarks and changed this accordingly.