PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (http://bmjopen.bmj.com/site/about/resources/checklist.pdf) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

TITLE (PROVISIONAL)	Lung CAncer SCreening in French women using low-dose
	computed tomography and Artificial intelligence for DEtection: the
	CASCADE study protocol
AUTHORS	Revel, Marie-Pierre; Abdoul, Hendy; chassagnon, guillaume;
	Canniff, Emma; Durand-Zaleski, Isabelle; Wislez, Marie

VERSION 1 – REVIEW

REVIEWER	Snowsill , Tristan
	University of Exeter
REVIEW RETURNED	06-Oct-2022

GENERAL COMMENTS	This is a very well written protocol for a worthy study. It will add substantially to the literature and aid the translation of knowledge from trials into clinical practice. Many high income countries around the world are implementing or considering implementing targeted lung cancer screening and will be interested to know the results of this research. It is very important that the protocol be published so that it is widely known the study is being conducted.
	My comments below are minor suggestions:
	RECRUITMENT. The study is recruiting via social media and established media, but does not include recruitment via primary care records. This is expected to be a route by which smokers and ex-smokers are targeted in national lung cancer screening programmes in other countries (though perhaps not in France). Should be noted as a limitation.
	STATISTICS. No concerns from a statistical perspective. Multiple imputation using chained equations is state of the art for handling data which is missing at random. In their statistical analysis plan the investigators should specify any procedures they will use to explore the possibility data is missing not at random (MNAR). These details do not need to be reported in this publication.
	HEALTH ECONOMICS. From a health economic perspective I am generally happy. The purpose of this study is not to enable a cost- effectiveness analysis of targeted lung cancer screening, and that is reasonable. The health economic aims are in keeping with the study design and the findings will be valuable. It is not clear whether resource use for for consultations and examinations is coming from research case report forms or from administrative data. This could be clarified.
	Good luck with the study

VERSION 1 – AUTHOR RESPONSE

Reviewer Report:

Reviewer: 1 Dr. Tristan Snowsill, University of Exeter

Comments to the Author:

This is a very well written protocol for a worthy study. It will add substantially to the literature and aid the translation of knowledge from trials into clinical practice. Many high income countries around the world are implementing or considering implementing targeted lung cancer screening and will be interested to know the results of this research. It is very important that the protocol be published so that it is widely known the study is being conducted.

Thank you for this comment

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We don't rely exclusively on social and established media. As mentioned in the text, we will benefit from the invitation process for breast cancer screening, which was probably not explicit enough. Therefore, we have modified as follows: The same note will be included in the invitation letter for to breast cancer screening in the four participating French regions, sent by the Regional Cancer Screening Coordination Centers (Centres Régionaux de Coordination du Dépistage des Cancers, CRCDCs)

STATISTICS. No concerns from a statistical perspective. Multiple imputation using chained equations is state of the art for handling data which is missing at random. In their statistical analysis plan the investigators should specify any procedures they will use to explore the possibility data is missing not at random (MNAR). These details do not need to be reported in this publication.

Thank you for this comment and suggestion

HEALTH ECONOMICS. From a health economic perspective I am generally happy. The purpose of this study is not to enable a cost-effectiveness analysis of targeted lung cancer screening, and that is reasonable. The health economic aims are in keeping with the study design and the findings will be valuable. It is not clear whether resource use for for consultations and examinations is coming from research case report forms or from administrative data. This could be clarified.

We thank the reviewer for the comments on the economic analysis, and have followed the suggestions in order to clarify the source of the economic data. The text now reads as follows: '

These will be collected prospectively at the participant level only via the study case report form, administrative data will not be queried, partly due to regulatory difficulties but mainly because it cannot differentiate work-up/cancer costs from other costs.'

Good luck with the study

Thank you

Reviewer: 1 Competing interests of Reviewer: I declare that I have no competing interests.