Author’s response to reviews

Title: Impact of radiographer immediate reporting of chest X-rays from general practice on the lung cancer pathway (radioX): study protocol for a randomised control trial

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Author’s response to reviews:

Many thanks to the reviewers for providing positive feedback and constructive criticism of our study protocol. We have addressed each comment sequentially with changes in the manuscript highlighted in RED.

Reviewer #1: OVERALL

Thank you for asking me to review this manuscript protocol for consideration for publication in Trials. It describes a single-centre randomized trial of a revised reporting pathway for chest x-rays requested from general practice when lung cancer is suspected. I note the study has been funded by CRUK’s EDAG programme. Generally, it is a clear and well-written protocol. I have some concerns around the primary outcome and purpose of the trial, the description of the intervention, and its external applicability which I outline in my comments below. As a general point it seems unlikely to me that the trial will have a meaningful impact on clinical outcomes
for lung cancer - I think the authors need to be much stronger in the introduction and discussion why they think it will. It would, however, seem likely to have a greater impact on patient satisfaction and I'm a little surprised that wasn't the primary outcome.

BACKGROUND

The background to the trial is reasonably well-described. However, it would be useful (line 72) to quantify the impact of time to clinical report on diagnostic delays and whether these delays are clinically meaningful?

Amended.

Line 65-68

A clinical report of imaging examinations is essential to guide diagnostic and treatment decisions. Time to a clinical report can be a serious factor in diagnostic delays1-3 with recognition that small delays for lung cancer diagnosis may contribute to higher stage at diagnosis4 and also a deterioration in performance status that may influence suitability for treatment.

Line 79 - the authors cite that radiographers have been trained to report CXRs. A bit more detail on how effective this has been would appear to be essential - i.e. how do they compare to radiologists?

Amended. Additional information on accuracy of radiographer CXR reporting added.

Line 76-80

There is some limited evidence to date that has evaluated CXR accuracy rates of trained reporting radiographers in comparison with radiologists. Reporting radiographers (n=40) were found to have high sensitivity (95.4%; 95% CI 94.4% - 96.3%) and specificity (95.9%; 95% CI
94.9% - 96.7%) at an objective structured examination of 100 CXRs at the completion of an accredited training programme.5

METHODS

Line 85 - Has any feasibility testing of the intervention been attempted up to this point? Are any of the outcomes assessing feasibility for a larger UK-trial, or is this trial simply for local service improvement?

Additional information provided.

Line 82-88

Recent work found poor compliance with suggested optimal diagnostic investigations for lung cancer, with 23% of patients in England receiving investigation and results within the recommended timeframes with significant variation between regions.6 This study aims to evaluate the impact of radiographer reporting on the timeliness, accuracy and quality of CXR reports, as well as the impact on the overall lung cancer pathway in comparison with radiologists. These parameters have not previously been studied in lung cancer patients. The current study could act as a pilot study for a larger, multisite evaluation if results are positive

Line 94 - It's not entirely clear why a comparison is being made with Newham University hospital? What will be gained from this? What is the basis for the choice of comparator site? Why not randomize there too, presumably that could quite efficiently give a more powerful trial.

Additional information provided.

Line 107

Newham does not currently have CXR reporting radiographers and does not offer straight to CT for CXRs suspicious for lung cancer.
Line 100 - I'm struck that the study will not directly recruit patients. How will patient's be informed that their data is being used in a clinical trial - more details on this would be important?

Additional information provided.

Line 115-119

Patient identifiable data will not be available outside of the direct clinical care team, only anonymised data will be used. Patients will be assigned a unique study identifier at time of CXR by the clinical care team. Block randomisation, institutional rather than patient enrolment and the use of de-identified data is in line with previous research that has examined the order of interpretation between readers.7

Line 106 - What has been the effect of radiographer reporting at other sites? Why do the protocol authors feel this study is necessary in the light of those experiences?

Additional information provided.

Line 121-126

Radiographer reporting, including CXRs, has been shown to create additional diagnostic capacity at centres that have embedded this into the imaging department.8-10 However, the published evidence on radiographer reporting of CXRs is limited. Furthermore robust methods of evaluating diagnostic reports (including actionability and usefulness) of radiographers and radiologists using independent experts has not previously been attempted.

Line 129/148 - The protocol seems to suggest that the new pathway will only reduce diagnostic delays by a few days - I think it would be useful for the authors to explicitly state somewhere what sort of reduction in delay they think they will achieve.

Anticipated improvements in time to first treatment are outlined in the sample size calculations.

Line 281-288
For the primary endpoint in this pilot study, time to treatment decision for lung cancers, if we expect an eleven day advance in time to first treatment decision, with a standard deviation of 14 (previous audit data suggest this degree of variation), 26 cancers in each group will confer 80% power (2-sided testing, 5% significance level), for the internal randomized comparison. We expect around 50 cancers per year in HUH, so we will have adequate power for this difference. A reduction in time to diagnosis of two weeks was found to improve mortality of lung cancer patients so this difference could be clinically significant in the current pilot study. If we anticipate a 12-day instead of 11-day advance in diagnosis, we would only need 22 in each arm, 44 cancers in all, for 80% power.

Line 150 - I would have thought patient satisfaction would have been the most appropriate primary outcome for the trial. It would be good to see a stronger justification for powering the study on what could be clinically insignificant gains in diagnostic delay.

Patient satisfaction is an important aspect of any imaging service and will be evaluated. The primary outcome in the current study is time to diagnosis (or discharge) of lung cancer. Even short reduction in time to diagnosis of lung cancer has shown improvements in outcomes.

See response above

Line 153 - do the authors envision a larger definitive trial? If so I would have thought stage at diagnosis was an important outcome to collect too?

Agreed. Stage at diagnosis will be collated for all lung cancers diagnosed in the study.

Line 179

iv. Stage at diagnosis of lung cancer

Line 168 - considerably more detail on the methods planned to assess patient satisfaction are required.
Included.

Line 306-307

Comparison will be made between patients who received an immediate and routine CXR report. The patient satisfaction survey to be used has been included as Appendix 1.

Line 169/170 - as above a clearer explanation of the rationale for the comparison with a second site not taking part in the study, and how this data will be used, would be important.

Please also see above

Line 107

Newham does not currently have CXR reporting radiographers and does not offer straight to CT for CXRs suspicious for lung cancer.

Line 182 - I'm a little confused by the section on "Off Protocol Radiographer Reporting." This suggests that when a serious pathology is suspected during immediate radiographer report, then that patient will be subsequently excluded from analysis. But surely that can only occur in those randomized to control, and would that not then be a source of bias? Perhaps I'm misinterpreting this, but it needs to be clarified.

Agreed. Modification made.

Line 212-213

All such occurrences will be identified, included in the intention to treat principle but we will also carry out sensitivity analysis excluding them. In view of randomisation, we expect the same rates of such cases in intervention and control sessions.

Line 258 - The study is powered on an eleven day reduction in diagnostic interval. Is there evidence that this is clinically meaningful?
Clarification provided.

Line 281-288

For the primary endpoint in this pilot study, time to treatment decision for lung cancers, if we expect an eleven day advance in time to first treatment decision, with a standard deviation of 14 (previous audit data suggest this degree of variation), 26 cancers in each group will confer 80% power (2-sided testing, 5% significance level), for the internal randomized comparison. We expect around 50 cancers per year in HUH, so we will have adequate power for this difference. A reduction in time to diagnosis of two weeks was found to improve mortality of lung cancer patients so this difference could be clinically significant in the current pilot study.11 If we anticipate a 12-day instead of 11-day advance in diagnosis, we would only need 22 in each arm, 44 cancers in all, for 80% power.

Line 261 - the study is powered on 26 cancers in each group. It appears that the expectation of 50 lung cancer each year gives very little margin on this power calculation. That's not a problem if this is a feasibility study, but it doesn't look that way?

Please see above

Line 275 - I think patient satisfaction is potentially the most important outcome from this study in my view. Much more information is required around how this will be collected. The instrument should be included as an appendix.

Patient satisfaction survey has been included as an appendix.

Line 306-307 and 495

Comparison will be made between patients who received an immediate and routine CXR report. The patient satisfaction survey to be used has been included as Appendix 1.

Line 285 - The health economic assessment is very briefly described. It is not clear to me that data will be collected on primary care costs if costs are being calculated from an NHS
perspective. Have the triallists assumed the intervention will be cost neutral in primary care? It may not be.

Additional information included. The model has recently been published and reference provided. Line 309-310

Adaptation of a health economic model that examined the impact of radiographer CXR reporting on the lung cancer pathway will be performed.12 [Reference added]

Reviewer #2: I appreciate the effort the authors have gone to in revising their manuscript again. This block randomised control trial will investigate the time to diagnosis of lung cancer when the radiology aspect of the national optimal lung cancer pathway is implemented.

1. The authors should briefly described the intervention different between the experimental and the control group.

Information included. Line 96-98

The intervention group will receive an immediate CXR report and be offered a CT for CXRs suspicious for cancer. The control group will have the CXR reported no later than next working day in line with current protocols

2. I would also like to thank the authors for clarifying a couple of points in this version of the manuscript.