Author’s response to reviews

Title: Medical complexity and time to lung cancer treatment - a three-year retrospective chart review

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Author’s response to reviews:

We appreciate the thorough work by the reviewers and have adjusted our manuscript and figures according to their comments.

Reviewer #1:

The article by Stokstad et al. from St Olavs Hospital- Trondheim University Hospital, Trondheim, Norway describes a three-year retrospective review of charts to assess the impact of medical complexity on time to treatment for lung cancer. Norwegian recommendations are that >70 percent of patients should start surgery or radiotherapy within 42 calendar days and systemic therapy within 35 days. The authors sought to determine the extent to which their hospital achieved the recommended timeframes by treatment modality and, in particular, the proportion of non-complex patients who did not achieve the target. The information was then to be used to improve organizational efficiency.

A retrospective chart review was conducted on all patients diagnosed with lung cancer at the University Hospital from the beginning of 2011 to the end of 2013. The authors defined non-complex patients as patients who had one or fewer tissue diagnostic procedures, no comorbidities, no intercurrent diseases that would delay treatment or complications from diagnostic procedures of more than three days.
The chart review found that 19% of patients received no treatment for lung cancer and 58% of patients were noncomplex. On the other hand, 32% of the 449 cases analyzed had more than one tissue diagnostic procedure; 15% had medical delays greater than three days.

The key finding was that even amongst the noncomplex patients the median number of days until surgery/ radiotherapy was 41 and only 56% of noncomplex patients started their radiotherapy or underwent surgery within 42 days. On the other hand, 80% of the noncomplex patients received systemic therapy within the recommended time frame of 35 days.

Given the fact that there is no evidence that shorter wait times lead to better outcomes for patients with lung cancer, the authors should comment on how and why the current Norwegian recommendations were decided upon.

*It has not been possible to identify any public documentation on the rationale for the chosen maximum timeframes in Norway. This information has been added to the manuscript on lines 96-98 page 13.

They should also comment on whether it is reasonable to use the same metric for both the start of surgery and radiotherapy. The resources needed to undertake a surgical intervention include access to diagnostic facilities including interventional radiology and PET-CT, the schedule of multidisciplinary case conferences, the timeliness of pathology review, the hospital’s OR capacity, number of thoracic surgeons available, availability of OR time, and patient volumes, whereas timely access to radiotherapy is dependent on access to diagnostic resources, consultation with a radiation oncologist, availability and timeliness of treatment planning resources, the complexity of the treatment and the availability of appropriate radiotherapy treatment machines. Timely access to systemic therapy treatment is dependent on many of the same diagnostic resources but also access to molecular diagnostics and the availability of chemotherapy chair time. So understanding what is behind the apparent delays in access to treatment services requires a much greater understanding of the resources available at the St. Olav hospital and these are not described in the paper.

The article would also be strengthened by a better description of the processes of diagnostic workup. The manuscript states (line 69 -70 p3) that the first hospital appointment should be offered within seven calendar days of receiving a referral letter. How is the initial consultation organized? To whom would a referral be directed? Is there a centralized intake process for suspected lung cancer cases? Is there a diagnostic assessment unit for lung cancer?
As mentioned, we have not been able to find any documentation for the Norwegian timeframes. Thus, it is not easy to discuss whether it is reasonable to use the same metric for both surgery and radiotherapy - or whether the metric for systemic therapy is reasonable.

We agree that in order to understand delays, the organization at our hospital and the processes of diagnostic workup need to be analyzed. This was beyond the scope of the present study, but will be the subject for the next article in this PhD-project.

All facilities for appropriate diagnostic workup, with the exception of PET CT, were available at St. Olavs Hospital during the study period. This information has been added to the manuscript on lines 100-101 page 5.

On page 5, reference is made to a weekly regional multidisciplinary tumor board and the various participants are listed including a lung oncologist. Is this individual a radiation oncologist or medical oncologist? Does the pulmonary physician who is the leader of the multidisciplinary team specialize in lung cancer treatment or is lung cancer only one of many interests?

Oncologists in Norway are trained in both radiotherapy and medical oncology. The pulmonologist who leads the multidisciplinary team specialize in diagnosis and staging and medical treatment of lung cancer. This information has been added to the manuscript on lines 108-109 and 113-115 page 5.

The start time of the diagnostic workup was defined as the date the referral letter for suspected lung cancer was received or alternatively the date when the diagnostic workup started for patients with a single pulmonary nodule. It would seem to this reviewer that these are very different start points with the potential to confound the analysis. It could be expected that using the date of the referral letter might introduce additional time dependent on access to necessary diagnostic procedures. Similarly, the date a treatment decision was arrived at was determined either from documentation in the EMR or the date of the last diagnostic procedure. Again this may confound the analysis as there may be delays until a multidisciplinary case conference occurs or the clinic visit can be arranged to discuss treatment with the patient etc.

We agree that defining the date the referral letter was received as the start date for the diagnostic work-up is incorrect. This date is, however, the start of the timeframes defined by Norwegian health authorities. We have now made this clear the manuscript on lines 152-154 page 7.
We also agree with the reviewer regarding the definition of time for treatment decision and have revised the definition (lines 154-155 on page 7) and re-run our analyses using this revised definition.

On line 146, page 6, reference is made to an adjustment in the multivariate analysis for PET CT which apparently was performed outside of the Central Norway health region during most of the study period. Please provide a description of how this adjustment was made.

*Whether PET CT was undertaken or not was included in the model for multivariate logistic regression analysis of associations of complexity with timely treatment (lines 257-259 page 12). The reference on page 6 has been removed, and the rationale for including whether PET CT was performed or not is now explained in the Statistics-section (lines 163-165 on page 7).

In the results section, it is interesting to note that the percentage of patients who are older than 70 years was considerably higher in 2013 than in the preceding two years. The authors should discuss if there was practice change that resulted in more elderly patients being referred for diagnosis and treatment.

*The proportions of patients aged <70 decreased (48%-42%-33%); age between 70 and 74 increased (12%-19%-26%); while there was no change in the proportions of age ≥75 years (40%-38%-41%). We have no reasons to believe that the observed variation was due to a practice change. We have included this information in the result section of the manuscript on lines 183-185 page 8.

It is also noteworthy that 18% of patients diagnosed over the three years received no cancer treatment. In this reviewer's view that percentage is low but perhaps this is due to the fact that St. Olav is a referral hospital and patients with advanced disease, poor performance status and older age may not actually be referred for consideration of treatment.

*As mentioned in our discussion, the proportion of lung cancer patients who receive cancer treatment varies substantially between countries. It was beyond the scope of the present study to investigate why the proportion receiving lung cancer treatment in our cohort was relatively high. A possible explanation is that most patients live within 30 minutes of travel from the hospital.
97% of the study population lives in the primary catchment area of St Olav's Hospital. Thus, the explanation suggested by the reviewer is not the reason. We have commented on this in the discussion on lines 306-310 page 14.

On pages 9 and 10 where data on time intervals are presented, there is so much data presented that the reader may have difficulty reading and digesting it. The authors might consider reorganizing this section and describe the time intervals for surgery/radiotherapy altogether and then have a separate section to describe systemic therapy time data.

*We agree and have reorganized the “Interval” chapter.

The summary data in this section (lines 243 to 247) is helpful but the explanation for the differences observed, particularly the reasons for palliative treatment being accessed in a more timely fashion than curative treatment deserves explanation.

*We agree, but in order to understand this, the organization at our hospital and the processes of diagnostic workup need to be analyzed. This was beyond the scope of the present study, but will be the subject for the next article in this PhD-project.

The discussion would benefit from a more robust interpretation of the results rather than just a summary of the findings and a presentation on guidelines in other jurisdictions.

The authors acknowledge that a limitation the study is its retrospective design but it should also be noted that the data are institution-based rather than population-based, which this reviewer considers to be a significant weakness also.

*We agree and have added this to the discussion on lines 333 and 344-349 on page 15.

Although the authors indicate that they have data on the timelines for each step of the diagnostic workup and that these data will be presented in another manuscript, it would be helpful if the reader was provided with some insights as to where the greatest delays occur and how investigators hope to improve their metrics. Otherwise, the reader can only conclude that in this
one institution, timelines for access to treatment of lung cancer cases are less commonly met than expected by Norwegian guidelines. Without some insights into the reasons for the observed data, the data by themselves are likely of limited interest.

Presumably, the authors have plans for next steps such as value stream mapping to determine where the delays are occurring. The discussion in the paper would be enriched by the authors laying out their future plans having obtained this data.

*We agree, but as mentioned, this will be covered in our next article. We have added information about our follow-up studies on lines 342-344 page 15.

There is one large table and four complex figures. I would suggest omitting Figure 1. Figure 2 suggests that something occurred between 2012 and 2013 that resulted in a much greater proportion of patients achieving the targeted timeframe for systemic therapy. The authors should comment on what may have occurred. Was additional staff hired for example? Similarly, wait time metrics for the surgery/radiotherapy patients, particularly those who are noncomplex was much better in 2011 than in the following two years. Can the authors offer an explanation?

*We agree and have revised our figures. The difference between 2012 and 2013 in proportions of timely systemic therapy was not statistically significant (2011: 25 (60%); 2012: 26 (57%); 2013: 35 (74%); p=0.16). The explanation for why surgery and radiotherapy was offered more timely in 2011 than 2012 and 2013 was the increasing use of PET CT. The average time from referral for PET CT until the result was available was 20 calendar days, and the multivariate analysis revealed that the use of PET CT was significantly negatively associated with timeliness. This information has been added on lines 275-279 page 12-13.

In my view, the results of this work would be more valuable to readers if the authors made a greater attempt to understand and explain their data. Although wait times measured in days are unlikely to have much impact on clinical outcomes, they are a source of anxiety to patients and their families and are frequently a sensitive political issue. As a result, many jurisdictions are trying to facilitate access to care and reduce wait times. Providing readers with a greater understanding of where delays are likely to occur and how they might best be addressed could be helpful to those who struggle with this issue. Otherwise, the data set is really only of use to those involved in the care of lung cancer patients at St. Olav where it will serve as the starting point for quality improvement initiatives.
*We agree, and as mentioned, this will be described in our next article. We do, however, still believe that our work should be of interest, since this is the first article describing complexity of patients. Since we have not found any rationale for the timeframes in Norway or other countries, our study provides the first data on the proportion that could easily start cancer treatment within the recommended timeframes.

Reviewer #2:

The authors are to be congratulated on a really very interesting paper that is both an extremely important question but also very well designed and executed. I do however have a few questions.

1) In your methodology you use greater the one tissue procedure as a cut off. If a patient had a TTNB for their lung mass and an EBUS to investigate a PET positive mediastinal node. This would meet most countries guidelines as appropriate care but in your structure would make it "complex.” Do you think this is appropriate as it is a pretty common occurrence in the treatable patient. Do you think this could influence your results or at least lump together different patient groups with differing quality gaps?

*We agree that the cut-off at one tissue procedure can be debated, since there is no established definition of “complex” patients. The main reason for this cut-off value was that it is hard to argue that patients who only need one tissue procedure are “complex”. This is important since some people argue that the timeframes for starting cancer treatment cannot be met because so many patients are complex. Our study clearly demonstrates that it is not all about complexity, but also organization.

That said, the results do not change significantly if the cut-off is set at two tissue procedures. The proportions of timely treatment in non-complex if the cut-off =1 tissue procedure was 66%, and 58% if the cut-off is changed to 2. We have added this information to lines 321-325 on page 14.

2) Do you have protocols that can limit your timeliness? For instance the temporal relationship between pet and biopsy. Some regions have a set time between the two. Is that present in your area and would geographic and institutional factors influence your results.

*There were no protocols that limited our timeliness, but in the study period, patients had to be referred to other cities for PET CT (we now have PET CT at our hospital), and the use of PET CT increased significantly during the study period due to increasing capacity. Thus, we have
adjusted for use of PET CT in our multivariate analyses. There is no set time between PET CT and biopsy, and we do not believe that there are geographic or institutional factors influencing the results of our single-center study. We have added this information to lines 96-97 on page 4 and line 113 on page 5.

3) Can you explain why a statistically significant more patients got treatment who were complex? Does this suggest a bias?

*Patients who did not receive any treatment underwent less diagnostic procedures, mainly because their general condition was so poor that no beneficial treatment was considered available. Thus, it is likely that some of these patients did not undergo a proper diagnostic workup, and would have been classified as complex if they would have been eligible for treatment. This has been added to the discussion on lines 326-330 page 14-15.

4) I thought the discussion was appropriate and well balanced. More work into the why of the problems is needed but likely is out of scope for the publication.

*We agree, and are, as mentioned, already working on analyzing the why. The results will be presented in a separate article.

Editors comments:

1. While there is reference to materials from several countries on suggested wait time targets, what is the basis (patient convenience, workflow management, or some biological progression hypothesis) for current recommended Norwegian intervals for waits and is there merit in suggesting any refinement to these intervals in the conclusion?
*As mentioned in our response to Reviewer #1, we have not been able to find any documentation on the rationale for the timeframes in Norway. This information has been added to lines 96-98 on page 13.

The target is that at least 70% should start timely treatment. Our results show that 56% of those patients who started treatment were non-complex. Thus, it seems appropriate that at least these patients start treatment within the given timeframes. This has been added to lines 347-349 on page 15.

2. Given the finding that the time to treatment was longer than recommended in the cohort, please discuss briefly what kind of forward planning is considered to create patient flow improvements, through some form of workflow mapping and interventions to reduce serial waits which slow the process of diagnosis and treatment.

*To have any opinions on the actual timeframes, the times for each step of the diagnostic workup need to be analyzed. As mentioned in our response to the reviewers, we are currently analyzing these timelines as well as the organization. These results will be published in our next paper. We have added information about our plans in the manuscript on lines 342-344 page 15.