Reviewer A

The authors evaluate the impact of a patient's refusal of surgery for non-metastatic rectal adenocarcinoma on overall survival. They found that those who refused surgery were more likely to be older, Black, have non-private insurance, and have larger tumors. Refusal of surgery was associated with shorter overall survival by approximately 40 months. Among those who refused surgery, the following factors were associated with decreased survival: age > 70, CCI > 2, rural treatment center, larger tumors.

Comments revisions:
- The authors should clarify the clinical question this study is designed to answer. This clinical question should be included in the introduction.

Reply: This would be a helpful addition to the manuscript.

Changes in the text: A sentence was added to the last paragraph of the introduction. The clinical question this study was designed to answer is now explained as: "The purpose of this study was to investigate factors associated with patients who decline rectal cancer surgery and the subsequent impact of this decision on overall survival (OS). This clinical information could help practitioners counsel and better understand the possible reasons why a patient may decline a recommended surgical intervention."

- Further clarity would be helpful regarding the cohort of almost 12,000 patients who did not receive surgery and did not refuse surgery. Does this include the 'watch and wait' group?

Reply: Thank you for this thoughtful comment. There were 11,928 patients excluded from analysis that did not receive surgery, but it was not coded as patient refusal. 9,700 of 11,928 (81.3%) of patients did not receive surgery because "surgery of the primary site was not performed because it was not part of the planned first course of treatment." It is likely that many patients were in the 'watch and wait' group. It's also possible that many of this patients received chemotherapy and/or radiotherapy as their first course of treatment and that surgery was delayed for other reasons, but was performed later. 1,477 of 11,928 (12.4%) of patients did not receive surgery because it was not recommended/performed because of patient risk factors (comorbid conditions, advanced age, tumor progression). 392 of 11,928 (3.3%) died prior to surgery and 359 of 11,928 (3.0%) did not receive surgery and the reason was not documented. We agree that this would be helpful information to include.

Changes in the text: We added a sentence to the text in methods under cohort selection. This now reads: "Patients were also excluded if the reason they did not receive surgery was anything other than patient refusal (n = 11,928). Of the patients that did not receive surgery

for reasons other than refusal, 81.3% were coded as surgery not being part of the planned first course of treatment and 12.4% were due to patient risk factors (comorbidities, advanced age, tumor progression, etc).

- Additional description of the methods used for the propensity matching analysis would be useful. Please describe the demographics of those patients who refused surgery and were not matched (about 300 patients). In addition, the authors should report standardized differences after propensity score matching to ensure that there is sufficient similarity between the case-matched cohorts. This can either be included as a separate table or an additional column in your Table 1. And finally, the caliper of 0.0001 used for the propensity matching is quite small. The authors might consider a wider caliper with 3:1 or 4:1 matching to increase the power of this analysis.

Reply: We created a supplemental table showing the demographics of the propensity matched groups along with the standardized differences to show there were no differences between the two matched groups. Since the survival results of the propensity matched analysis were very consistent with the overall analysis, we hadn't thought to increase the caliper size or change to a 3:1 or 4:1 matching for more statistical power. When we tried this based on the reviewer suggestion, the significance of the findings remained but the similarity between the case-matched cohorts dropped significantly. For this reason, we prefer to keep the analysis as is.
Changes in the text: The supplemental table was referenced in the 4th paragraph of the results section and the table itself was added to the last page of the manuscript.

- The authors should report the survival analysis results in the >70 cohort as well and comment on these findings as compared to the younger cohort.

Reply: This analysis was also completed.

Changes in the text: We added a sentence at the end of the 4th paragraph in the results section: "In comparison, an analysis limited to patients who were 70 years old and above also showed a survival detriment associated with declining surgery (HR 2.43, 95% CI 2.15-2.75, p<0.01)." We also added the following to the discussion: Interestingly, while older patients were more likely to refuse surgery, those who did still experienced a survival detriment as shown in our subset analysis."

- The authors should explain why age was converted to a categorical variable and how the delineations of 18-49, 50-69 and >70 were chosen. The cohort that refused surgery has considerably more older patients and this might encourage further stratification of the >70 cohort.

Reply: Analysis of age as a continuous variable is associated with refusal of surgery. We defined age as a categorical variable to lend applicability of the results among different age groups. We could certainly further stratify the ≥70 year old cohort, but we don't wee a signal

that this analysis would add much information to our results.

Changes in the text: None

- The last sentence of the discussion section of the abstract is appropriate for the full manuscript, but not for the abstract. The discussion section of the abstract should include a summary of findings and is not necessarily a shorter version of the discussion section in the manuscript.

Reply: This sentence will be deleted from the abstract.

Changes in the text: The last sentence of the conclusions section in the abstract was deleted.

- The use of the word 'invalid' in line 49 is offensive and should be removed.

Reply: The word was removed from the text.

Changes in the text: The sentence now reads "There are many other potential reasons as to why a patient may elect to not undergo surgery including the need to care for another family member, loss of income that would devastate the family, and no resources for post-operative care."

Although I enjoyed reading the manuscript, some clarifications are needed.

Introduction: I am not sure whether the authors have fully recognized the background for the watch and wait for principle among rectal cancer patients? Please remember that approximately 10% of the patients receiving neoadjuvant radiochemotherapy have a complete response of the tumor after neoadjuvant (i.e. preoperative radiochemotherapy). Many of those patients are included in clinical trials. Please specify how you define the watchful waiting group.

Reply: We agree that the watch and wait approach is a major theme in the treatment of rectal cancer. We will make it clearer that analyzing this group of patients is not the intent of this manuscript where we analyze patients that decline a recommended definitive surgery, rather than pursue a provider-directed watch and wait approach. We did not specifically define a watchful waiting group, but we tried to exclude these patients from the cohort of patients we analyzed. We excluded 11,928 patients that did not receive surgery, but were not coded as having refused surgery. 83% of these patients were coded as "surgery of the primary site was not performed because it was not part of the planned first course of treatment." It is possible that a majority of these patients were in the watchful waiting group.

Changes in the text: We added a sentence to the text in methods under cohort selection. This now reads: "Patients were also excluded if the reason they did not receive surgery was anything other than patient refusal (n = 11,928). Of the patients that did not receive surgery for reasons other than refusal, 81.3% were coded as surgery not being part of the planned first course of treatment and 12.4% were due to patient risk factors (comorbidities, advanced age, tumor progression, etc). We also added a sentence to the introduction making our study purpose more clear as described above.

Methods: what is the rationale for excluding T1N0 ? This is a large group (n=26 000) and should receive either local excision or TME. You might miss important information by excluding T1 patients. Please elaborate.

Reply: We excluded patients with T1N0 disease because these patients could potentially be treated with local excision alone, which is not a surgical intervention that is coded as definitive surgery in the NCDB. Therefore, we felt we couldn't reliably include these patients in our analysis and trust the results.

Changes in the text: None

Regarding missing: I know from other NCDB studies that missing is a methodological challenge. 3.5% missing is remarkably low. Please confirm that 3.5% is correct.

Reply: We looked at our data again and calculated 3.5% missing data. A possible explanation for this low level of missing data in our patient population is that when we selected our patient population we excluded patients that had unknown stage, unknown histology, unknown if definitive surgery was performed, unknown if chemotherapy or radiotherapy was given, and unknown survival data. Therefore, we selected a patient population where a majority of that key clinical data was known.

Changes in the text: We changed the text to the following: "After excluding patients with unknown stage, unknown histology, and unknown treatments, only 3.5% of values were missing across all variables. Therefore, missing values for each variable were treated as missing values and no imputation was performed."

Discussion: You have identified several sociodemographic variables that are associated with the refusal of surgery. Are there any variables that are not included in the data set, but ideally should be there? Is this a limitation? Conclusion: Refusal of surgery was more common later in the study, why?

Reply: This is an excellent point. Many additional variables could be included that that might give more insight about why patients refuse surgery. We mention a few variable in the second to last paragraph in the discussion section including "surgical fitness [and] patient values." However, as we mention in the second paragraph of the discussion: "It is important to note that the decision-making process regarding treatment between the patient and their healthcare

providers is complex with nuance that is difficult to capture in an aggregate database." A rare situation such as the refusal of surgery requires a lot of patients to analyze lending itself to an aggregate database study, which doesn't capture all these nuances. In terms of why refusal of surgery was more common later in the study, our best guess is that patients became aware of a 'watch and wait approach' even when it was not recommended by their provider.

Changes in the text: We added three sentences to paragraph 6 of the discussion with a possible explanation as to why the refusal of surgery was more common later in the study: "A potential reason as to why patients seem to be refusing surgery more frequently may be related to knowledge of the 'watch and wait' approach. It is possible that some patients prefer organ preservation, but might not necessarily be the best candidates. These patients may elect for 'watch and wait' anyway even though their treatment team is recommending surgical intervention."

Figure 1: Please include n of T1N0

Reply: Figure 1 includes the n for clinical T1N0 disease (n = 26,484) that were excluded from the analysis. This is located in the first box on the right side.

Changes in the text: None

Figure 2: This is hardly new, it is well known for decades that surgery improves survival. Please consider moving this to the supplement section.

Reply: We favor keeping Figure 2 in the main manuscript because it illustrates novel information about the subset of patients who actually refuse surgery. However, we are happy to move the figure to the supplemental section if desired.

Changes in the text: None

Please consider a Figure/Kaplan Mayer curve illustrating the impact of sociodemographic status on survival among those who refused surgery

Reply: While it is true that our study found that patients with a lower socioeconomic status (insurance type and income) are more likely to refuse surgery, there is no difference in OS in the refusal cohort only when it comes to race, insurance type, income, or residents without a high school degree.

Changes in the text: None