Overall comments

The authors thank the reviewers for their comments.

Responses to comments of Reviewer 1

Comment 1: It is not clearly explained why the authors restricted the sample of patients to those with colonoscopy in the diagnostic procedure. It is not explained in the paper and it should be. Also, the reason for not being diagnosed by colonoscopy would be worth to know.

Response 1: Our aim was to investigate the period between diagnostic procedures and treatment. Colonoscopy was a common and measurable starting point for this period. Of the 569 cases with hospital and Medicare data available for analysis, 94% had a colonoscopy at any time in the study period and 89% had one up to and including in the month of diagnosis, so the cases who had a colonoscopy represent the vast majority of those for whom we have data. We have revised the following text in paragraph 11 of the Methods section to reflect this.

“The primary outcomes of interest were the time between colonoscopy diagnosis and surgery treatment, and whether or not the patient received surgery in a specialist cancer centre, as defined by an institution having radiotherapy facilities. Colonoscopy was used as the indicator for diagnosis and an appropriate surgical procedure as the treatment.”

Comment 2: The fact that the data available did not include radiotherapy and chemotherapy is a severe drawback of this study. It is well known that the accepted therapeutic strategy for rectal cancer involves radiotherapy and chemotherapy preoperatively. Lack of this information did not allow us to interpret the interval between colonoscopy and surgery in a proper way. It might happen that the treatment is not appropriate and it is not possible to know with the present database. The fact that there is no association with centres with radiotherapy available and the relevance of private practice in small clinics mentioned by the authors adds relevance to this point.

Response 2: We have acknowledged that not being able to include pre-operative radiotherapy or chemotherapy is a limitation of the study in the paper. This paper provides an overview of the timing between colonoscopy and surgery, and the possible mediating factors are discussed. This includes pre-operative radiotherapy and chemotherapy (paragraphs 2 and 4 of Discussion). As described in our response to the reviewer’s comment 5, we have revised paragraph 4 of the Results section as follows:

“For cases with colon cancer, who should not require pre-operative radiotherapy or chemotherapy, there were no major differences in the time to surgery across the subgroups compared. The period was marginally longer for those…”
Responses to comments of Reviewer 1 (continued)

Comment 3: The definition of a reference centre or specialized centre as the one with radiotherapy is quite unusual. It would have been better use volume of cases, which is more common as an independent variable. I would suggest a reanalysis taking volume into consideration.

Response 3: The definition of a specialist centre was debated at length by the authors. We agree that hospital volume, if accurate, would be informative. Unfortunately, we don't have patient volume data for these hospitals overall, only the number of cases in our sample. Therefore defining a high-volume centre is difficult. In our data nine centres had the highest patient volumes with 10 to a maximum of 26 surgical procedures for colorectal cancer across the three-year study period, which does not accord with the patient volumes reported in the literature. The definition of a specialist centre as one with a radiotherapy unit was a surrogate for having all cancer treatment modalities available at the one centre, thereby making it a more specialised facility, plus the importance of being able to offer radiotherapy for rectal cancer in particular.

Comment 4: Finally, I am not sure that the best definition of this study design would be retrospective cross-sectional. My proposal would have been retrospective cohort study.

Response 4: We have changed the study design to “retrospective cohort study” in the title and abstract as requested by the reviewer.

Comment 5: The research question is beyond the scope of these variables. The restriction to colonoscopy and the impossibility of having radiotherapy and chemotherapy available makes discussing of the data very difficult. A possible suggestion would be to restrict the analysis to colon cancer, although the sample will be lower.

Response 5: As described in our response to the reviewer’s second comment, we are not claiming that this study provides a comprehensive assessment of all the factors influencing the time interval between diagnosis and surgery. We have described these limitations in the Discussion.

The results for colon cases (265 cases, or 65% of the sample) are given in the paper, in the paragraph 4 of the Results section and in Table 3. We have revised the following text in paragraph 4 of the Results to emphasise that the results for colon cancer are less likely to be affected by other treatment types prior to surgery.

“For cases with colon cancer, who should not require pre-operative radiotherapy or chemotherapy, there were no major differences in the time to surgery across the subgroups compared. The period was marginally longer for those…”
Responses to comments of Reviewer 1 (continued)

Comment 6: Previous evidence is quite scarce and it is not well considered in the discussion.

Response 6: As described in the paper, most existing research on this topic has focused on delays prior to diagnosis and this is one of the first studies to examine the pathway between colorectal cancer diagnosis and surgical treatment. Hence there is limited previous evidence to discuss. We have added text in paragraph 3 of the Introduction and paragraph 2 of the Discussion, referring to a recent paper by Torring et al.

Introduction: “A recent prospective study reported that 3-year mortality for CRC patients increased with diagnostic delay beyond one month, particularly for those presenting with serious symptoms.”

Discussion: “However we should be mindful that these small delays may compound delays in diagnosis for groups such as migrants and people living in remote areas who have lower screening rates, and that diagnostic delay is associated with increased mortality for patients with CRC.”

Responses to comments of Reviewer 2

Comment 1: The introduction summarises the literature reasonably well, although it may strengthen the paper if they were to refer to an important paper by Torring et al demonstrating associations in time to diagnosis and colorectal cancer mortality (British Journal of Cancer (2011) 104, 934 – 940).

Response 1: We have added the following underlined text to paragraph 3 of the Introduction and paragraph 2 of the Discussion, referring to the paper by Torring et al.

Introduction: “A recent prospective study reported that 3-year mortality for CRC patients increased with diagnostic delay beyond one month, particularly for those presenting with serious symptoms.”

Discussion: “However we should be mindful that these small delays may compound delays in diagnosis for groups such as migrants and people living in remote areas who have lower screening rates, and that diagnostic delay is associated with increased mortality for patients with CRC.”

Comment 2: The study uses data from the 45-and-Up Cohort study of approximately 10% of the total eligible NSW population, linked to health data from the Cancer Registry, hospital admissions data (APDC) and Medicare Benefit Schedule (MBS) data. It would be useful to clarify which sources of data were used to identify the date of colonoscopy (the APDC or MBS or both).

Response 2: The following line has been added to paragraph 11 of the Results section.

“Over 90% of the relevant colonoscopies and surgical procedures were identified in the APDC, with just over half of these also identified in the MBS. The remaining colonoscopies were recorded in the MBS only.”

Comment 3: In the description of the datasets it should also be stated that this did not allow identification of dates of radiotherapy or chemotherapy. This is brought up in the discussion but I think it should be stated in the methods as it is an important limitation of the data available.

Response 3: We had stated the following in paragraph 9 of the Methods section.

“Chemotherapy and radiotherapy are generally performed on an outpatient basis, for which data were not available, so they were not included in the analysis.”
Responses to comments of Reviewer 2 (continued)

Comment 4: On page 12 [second paragraph of Results] the description of key dates is a little confusing. There is no specific definition of the date of diagnosis, only that it was available to the nearest month. Was the date of diagnosis based on the Cancer Registry date, which will often be based on the date of the pathological specimen obtained at colonoscopy? The date of colonoscopy is defined as the last pre-surgery colonoscopy no earlier than two months prior to the month of diagnosis. Without a clear definition of date of diagnosis, this is potentially problematic.

Response 4:
Date of diagnosis used in the analysis was the date recorded by the Central Cancer Registry, supplied to us as month and year only. This is based on the information available in notifications sent to the Registry including pathology reports and hospital forms. For colorectal cancer the date of diagnosis is likely to be based on the pathology form for the specimen obtained via colonoscopy. The following line in paragraph 10 of the Methods has been revised to indicate this.

“The CCR provided data regarding month and year of colorectal cancer diagnosis (the date of the most definitive cancer notification, likely to be based on the pathology form for the specimen obtained via colonoscopy), age at diagnosis, …”

Comment 5: Under the section Sociodemographic and clinical characteristics, it should be clarified if the place of residence was at the level of postcode or collecting district, the latter giving more precise information about socioeconomic disadvantage.

Response 5: The place of residence used in the analysis was the Local Government Area of residence at the time of diagnosis, as recorded by the Central Cancer Registry. We felt this was more relevant to the diagnosis and management of colorectal cancer than the place of residence at the time that the 45 and Up Study questionnaire was completed. We have removed the latter from the list of Sociodemographic and clinical characteristics and amended the text to “place Local Government Area of residence at diagnosis” in the description of the variables obtained from the Central Cancer Registry (paragraph 10 of the Methods).
Responses to comments of Reviewer 2 (continued)

Comment 6: While this is described as a population cohort it should be recognised that the final analysed sample actually represents less than 4% of all colorectal cancers diagnosed during the study period. Furthermore, the sample was more likely to be male, Australian-born, have localised disease, live in a rural area and be more disadvantaged socioeconomically. This probably needs to be acknowledged further as a limitation of the study.

Response 6: We have added the following sentence to the section on limitations (paragraph 4 of the Discussion) to reflect this.

“…study participants are not representative of the population due to people in rural areas being oversampled and a possible “healthy volunteer” effect. Our sample of cancer patients represent 4% of all colorectal cancers diagnosed in NSW and were also more likely to be male, Australian-born and have localised disease.”

Comment 7: The results are well presented, although there is no discussion about potential problems of multiple statistical testing.

Response 7: We have added the following sentence to the section on limitations (paragraph 4 of the Discussion) to reflect this.

“Some of the marginally statistically significant associations may have arisen by chance due to the large number of variables included in the analyses, but this is not likely to be an explanation for associations with small p-values.”

Comment 8: Rectal tumours had a longer pre-surgical treatment interval than colon tumours, although the crude median difference was only 4 days which is unlikely to be clinically important. However, the overall median time of 19 days could be important in the context of additional likely delays along the total diagnostic pathway.

Response 8: The following sentence has been added to paragraph 2 of the Discussion.

“The overall median time to surgery for all cases was 19 days and this could also be important in the context of additional delays along the total diagnostic pathway.”
Responses to comments of Reviewer 2 (continued)

Comment 9: The interpretation of differences between rectal and colon cancer is slightly limited in having no data on radiotherapy or MDT assessment. As discussed, the longer time may represent more detailed treatment planning for rectal cancer, which is potentially more important than the duration of the pre-treatment interval. This could perhaps be discussed further.

Response 9: We have revised the following sentence in paragraph 2 of the Discussion to reflect this.

“It may reflect referral to a CRC surgeon rather than a general surgeon, assessment by a multidisciplinary team, or the use of or a referral for assessment of pre-operative radiotherapy for rectal cancer, each of which could lead to better patient outcomes. Further, the crude difference in median time was only four days…”