

Peer Review File

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Reviewer A

Comment 1: This paper reminds us of an important issue – the disparities faced by people with intellectual disabilities in identifying cancers of the colon and rectum. As such, it is highly relevant to the readers of this journal.

Reply 1: The authors thank reviewer A for his/her evaluation of the letter and the constructive comments.

Comment 2: The methodological approach is well-described, but I am confused by the reference to ‘Chi-square Mann Whitney’ tests; in my view these are two different tests - Mann-Whitney is for situations involving a categorical independent variable and an ordinal (rank) dependent variable. Chi-square is for situations where both the independent and dependent variables are categorical. Due to this lack of clarity, I am unsure of the robustness of the comparative (general population) statistical data.

Reply 2 - We corrected this error regarding the statistical tests.

Changes in the text: The Chi-square statistical test was used in the analyses (paragraph 2). The words "Mann Whitney" have been deleted.

Comment 3: The data about people with intellectual disabilities highlights a number of important points: young age at diagnosis; late diagnosis, often before the person was eligible for a screening programme; and diminished opportunity for successful treatment. It might have been helpful if these points were more clearly made e.g. the final paragraph states that participation in screening with fecal occult tests was lower in this population than in the general population, but it makes no mention about screening policies and related age limits.

Reply 3 - We added a sentence about the policy for colorectal cancer screening in France.

Changes in text: (paragraph 1): "In France, colorectal cancer screening is practiced with FOBT every two years, from age 50 to age 74 years."

Reviewer B

Comment 1: This is an important study that have potential improvement on CRC early detection through timely screening among those with intellectual disability. There are some minor or moderate suggestions for this letter.

Reply 1: The authors thank reviewer B for his/her evaluation of the letter and the comments, which have led us to improve the message. The authors agree with the suggested modifications

Comment 2. 1st paragraph: Please describe the CRC screening (fecal occult blood test) recommendation in France, including age and frequency for having CRC screening. Does fecal occult blood test is a gold standard screening in France? Given there are many CRC screening options, it is important to indicate clearly.

Reply 2: We have added a description of the colorectal cancer screening policy in France.

Changes in the text: (paragraph 1): "In France, colorectal cancer screening is practiced with FOBT every two years, from age 50 to age 74 years."

Comment 3. 1st paragraph: It might be great to include percentage to compare how lower screening use among adults with ID and general population.

Reply 3: We have added the value in paragraph 1, as suggested.

Changes in the text: "For example, in Canada (4) and France, FOBT screening is practiced 29% less frequently in people with ID than in the general population (34% vs. 24%) (5).

Comment 4. 1st paragraph: Study aim need to be rephased. Study purpose should be "We aimed to examine CRC outcomes among adults with ID. " The value of early detection and screening seems to be your study implication. However, whether including general population is not clear.

Reply 4: We modified the sentence in the 1st paragraph as suggested.

Changes in the text: "This retrospective study aimed to examine colorectal cancer outcomes among adults with ID and compare them to the outcomes observed in the general population."

Comment 5. 3rd paragraph: It might be great to include p-value for all comparisons.

Reply 5: We have added p-values in the 3rd paragraph for comparisons of stage I/II and stage III tumors

Changes in the text: Only one patient had a stage I/II carcinoma (7.1% vs. 48.7% in the general population; $p < 0.0001$), four patients had stage III tumors (28.6% vs. 21.2% in the general population; $p = 0.2953$)

Comment 6. 2nd-4th paragraphs: Authors used chi-square Mann-Whitney test to compare the relationship between stage at diagnosis and treatment. However, there were no clear information regarding this in results. Moreover, authors indicated p -value=0.0017 for comparison between those with stage IV with peritoneal carcinomatosis and general population. Which test was used? Is it Mann-Whitney test? Need clear information on 2nd paragraph.

Reply 6: We corrected this error regarding the statistical tests.

Changes in the text: The chi-square statistical test was used in all the analyses. The words "Mann Whitney" have been deleted.

Comment 7. 2nd -3rd paragraphs: It is a little confused whether this study included general population. In results, authors indicated comparison with general population. If this is the case, I think it should be described in 2nd paragraph and study aim.

Reply 7: We clarified this, as suggested.

Changes in the text: (Study aim) "This retrospective study aimed to examine colorectal cancer outcomes among adults with ID and compare them to the outcomes observed in the general population."

(2nd paragraph) "Those data were compared to corresponding data from the

general population with the Chi-square statistical test."

Comment 8. Last paragraph (conclusion): May consider including implications for screening guideline in France. It is important that recommendations should include those with ID as a high-risk factor. This is also critical for patient and physician communication.

Reply 8: We added the notion that ID is a risk factor.

Changes in text: (last paragraph) "Therefore, it is critical to strongly encourage and promote colorectal cancer screening for individuals with ID (Fig. 1), because they are at higher risk of developing this malignancy."

Reviewer C

The authors thank reviewer C for his/her comments.

Comment 1: This study reports a case series of 14 individuals with colon or rectal cancer, drawn from cross-referencing a registry of cancer cases with a registry of individuals with intellectual disability. Twelve cases presented at an advanced stage with poor outcomes. One case was diagnosed through surveillance in a high risk family. The circumstances of diagnosis for the 14th case are not presented.

Reply 1: The circumstances of diagnosis could not be found for one patient.

Changes in the text: We added: "The circumstances of diagnosis could not be found for one patient".

Comment 2: The authors also conducted a literature review of other series of patients with colorectal cancer and intellectual disability. In one country that reportedly is more meticulous about screening than others, cancers were found in earlier stages. In the other countries, diagnosis at an advanced stage were the rule. Of note, the average age of diagnosis was in the 60's. No denominator of the total number of people included in the intellectual disability registry was provided. The authors leverage these observations to call for a screening program that includes individuals with intellectual disability.

The strength of this small case series is that it derives from what appear to be fairly complete registries - although one has no way to know how many people with disability may not be included. The lack of patients diagnosed at an early stage, certainly suggests that there might be a benefit to screening. We don't have knowledge about the life expectancy of these individuals before the diagnosis of colorectal cancer. The fact that these patients presented with symptoms is not surprising; in the absence of screening, presentation with symptoms is to be expected.

This letter can be improved by providing more information about the number of people with disability in the registry.

Reply 2: We agree with the reviewer in those three points: 1) the idea that some people with ID are not included, mainly those living with their families; 2) the observation that life expectancy is not known for people with ID living in Hérault; and 3) That presentation with symptoms is due to cancers discovered at a late stage. As suggested, we indicated the number of all patients with colon and rectal cancers in the registry to elucidate the proportion with ID.

Changes in the text: "We cross-linked all colon and rectum cancers in the registry

(n=7023) with a list of 3433 adults with ID that lived in Hérault".

Comment 3. Given the increasing incidence of colorectal cancer in younger individuals, starting colorectal screening at age 60 may be too late to prevent some of the deaths - this should be made more clear.

Reply 3: We fully agree.

Changes in the text: "Screening for colorectal cancer began at age 60 years during the study period in the UK. However, this may have been too late, because 43% of individuals with ID died of lower digestive-tract cancer at ages 18-59 years."

Comment 4. Some discussion of the barriers to screening this population would be interesting.

Reply 4: We added a description of the barriers to cancer screening for persons with ID.

Changes in the text: "Studies have shown that the main barriers to cancer screening for individuals with ID included a lack of recommendations from physicians and professional caregivers, a lack of accessible information, reduced accessibility to screening procedures, and the need for support to complete the test (3, 4).

Comment 5: The details of the cases which were presented in the letter aren't really needed. The point is that the patients presented late and didn't survive long.

Reply 5: Two lines have been deleted concerning patient symptoms.

Comment 6. Some elements could easily be eliminated to make this letter shorter which would then allow some discussion of barriers to screening and issues of screening age initiation.

Reply 6: We deleted the details of patient symptoms and added the suggested points.
