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Manuscript Title	Risk of Pancreatic Cancer in Individuals with Celiac Disease in the United States: A Population-Based Matched Cohort Study
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The reviewers' comments were helpful, and we have incorporated these comments into the revised text. We are thankful for all the critical input, as these suggestions have greatly enhanced the quality of our manuscript. I hope we have adequately addressed the comments raised by the reviewers. Below are our responses to each point raised by the reviewers.

Reviewer #1:

Specific Comments to Authors: Although personally I do not like the topic of this article. I must congratulate the authors for successfully doing this research and confirming the finding that patients with CD were at increased risk of PC. The research is well done. Just some language problems and references problems.

Comment: We thank the reviewer for taking the time to review our manuscript and sharing your comments. We appreciate your time. We have revised the manuscript and improved the manuscript as recommended. We have done meticulous proofreading and revisions to ensure the correction of all grammatical, syntactical, formatting, and other errors.

Question R1#1: Language problem: 1. In the introduction section: "Nevertheless, despite the magnitude of the risk remaining debatable, the unequivocal association between CD and PC." This sentence is incomplete and may lack a verb.

Answer: Thank you for pointing it out. We have corrected the sentence, and the error happened during the submission. We have done careful proofreading to double-check it.

Question R1#2: Methods Section: The sentence, "Details of the data source, quality checks, and diagnosis codes used for patient selection are described in the supplementary materials", appeared twice.

Answer: Thank you for pointing it out. We have corrected the repetition, done careful proofreading, and revised the manuscript.

Question R1#3: Study participants section: "All patients with the diagnosis of CD from January 1, 2005, to December 31, 2021, were identified." The word "identified" might replace as well. Because "TriNetX has received a waiver from Western IRB as it only provides de-identified information".

Answer: Thank you for the recommendation.

Question R1#4: Baseline Characteristics section: "After PSM, both cohorts (134680 patients each) were well-matched and balanced (Supplementary Figure 1). However, compared with the CD cohort, the control cohort had a higher prevalence of rheumatoid arthritis (1.8% vs. 5.9%)." The word "However" should be rephrased.

Answer: Thank you for pointing it out. We modified the conjunctive adverbs "however" for better readability and rephrasing.

Question R1#5: Discussion section: "Patients with CD were found to have a modest excess risk of PC. Results indicate that CD is associated with an increased risk of PC." These two sentences look same to me.

Answer: We have revised the conclusion.

Question R1#6: Conclusions section. The last sentence, "Further, our study confirms that CD is associated with a significantly increased risk for pancreatic cancer." looks redundant to me.

Answer: Thank you for pointing it out. We have revised the conclusion section.

Question R1#7: There are several other minor language problems, such as what are BS and EMR. Language should be polished.

Answer: We have done meticulous proofreading and revisions to ensure the correction of all grammatical, syntactical, formatting, and other errors. Hence, we believe that the revised manuscript would meet the requirement as Grade A for the final publication.

Question R1#8: References problems. 1. Introduction section: "In the two most recent matched studies that included data on PC risk in CD, a higher risk of PC diagnosis was observed in CD patients; however, discordant results were obtained regarding whether PC risk persists long-term after CD diagnosis [5]." There is only one reference, which has the similar findings with the present study. Reference should be added.

Answer: Thank you for pointing it out. We have included both references and have included a statement to explain the difference between these two studies.

Question R1#9: Discussion section: "Two hypothetical explanations have been proposed in the literature to explain this finding". Please provide references.

Answer: We have included the references for both the point that we included in the discussion as a hypothetical explanation.

Reviewer #2:

Specific Comments to Authors: In this manuscript the authors report a population-based cohort study about the risk of pancreatic cancer in individuals with celiac disease in the United States. The title reflects the main subject of the manuscript. The Introduction is well resourced and the subject is presented very well. The abstract

summarizes and reflects the work described in the manuscript. The abstract is compatible with the main text. The keywords reflect the focus of the manuscript. The figures are ok. The references are up-to-date. Overall, this manuscript represents a useful contribution to the medical literature. The style, language and grammar are ok

Comment: We thank the reviewer for taking the time to review our manuscript and sharing your comments. We appreciate your time.

Reviewer #3:

Specific Comments to Authors: Manuscript NO: 81484 Title: Risk of Pancreatic cancer in Individuals With Celiac Disease in the United States: A Population-Based Matched Cohort Study Summary: The objective of this paper was to investigate the magnitude of the risk of pancreatic cancer (PC) associated with celiac disease (CD) from large populations in the United States. A population-based, multicenter, propensity score-matched cohort study was conducted using well designed methods and statistical analyses. A total of 389980 patients were identified for this study. Among them, 155877 patients were identified to have CD, and the remaining 234103 individuals without CD were considered a control cohort. The results revealed that patients with CD were at increased risk of PC. Risk elevation persisted beyond the first year after diagnosis to reference individuals without CD from the general population. This is a well written article.

Comment: We thank the reviewer for taking the time to review our manuscript and sharing your comments. We appreciate your time. We have revised the manuscript and improved the manuscript as recommended. We have done meticulous proofreading and revisions to ensure the correction of all grammatical, syntactical, formatting, and other errors.

Question R3#1: Some Specific concerns: 1.In the "Introduction" section: Of "In the two most recent matched studies that included data on PC risk in CD, a higher risk of PC diagnosis was observed in CD patients; however, discordant results were obtained

regarding whether PC risk persists long-term after CD diagnosis [5].-----Only one reference available. Please add another one, and more details had better be added for the "discordant results".

Answer: Thank you for pointing it out. We have included both references and have included a statement to explain the difference between these two studies.

Question R3#2: In the "Discussion" section: Of "In the reports by Lebwohl et al. and Ladgren et al., an adjusted Hazard ratio of 1.98 (1.29-3.06) and 2.27 (1.22-4.23) were described; and we noted HRs of 1.29 and 1.56 for PC in our cohort of CD patients [4,9]."- -----Please check "Lebwohl et al. and Ladgren et al", "1.98 (1.29-3.06) and 2.27 (1.22-4.23)" and [4,9] .

Answer: Thank you for pointing it out. We have rewritten the stamen and included the accurate hazard ratio details for both the reference compared to our study outcome-related hazard ratio.

Question R3#3: In the "Discussion" section: "Our results are largely consistent with prior observations of elevated PC risk in CD." -----references should be given.

Answer: Thank you again for pointing it out. We have included the references for this statement.

Question R3#4: In the "Discussion" section: some more address should be added to the "Strengths and Limitations", such as----not exclude or associated with "patients with other severe diseases (chronic diarrhea, chronic gastritis, peptic ulcer, abnormal bowel flora, SLE, liver cirrhosis, renal failure, chronic obstructive pulmonary diseases, IgG4-related disease, immune deficiency syndrome, some endocrine syndrome, and so on)", for there many other factors may associate with the PC.

Answer: Thank you for sharing a valuable point regarding th potential confounder. We have addressed this issue in the limitation section and have included the statement as

"Some residual confounding can exist, and we cannot exclude any possible confounding factors not controlled for in our study that may have an effect on the risk of PC."

Question R3#5: In the "Abstract" section: Of "CONCLUSION: In this large propensity-matched analysis, we observed that patients with CD were at increased risk of PC. Risk elevation persisted beyond the first year after diagnosis to reference individuals without CD from the general population.", which had better be "CONCLUSION: Patients with CD are at increased risk of PC. Risk elevation persists beyond the first year after diagnosis to reference individuals without CD from the general population.", or other appropriate expressions.

Answer: Thank you for sharing your recommendation. We have revised the abstract's conclusion as recommended.

Question R3#6: In the "Abstract" section: Of "Key Words: Celiac disease, Cancer; Epidemiology; Pancreas; Pancreatic cancer; Malignancy; Carcinoma", which may be "Key Words: Celiac disease; Epidemiology; Malignancy; Carcinoma; Pancreas; Pancreatic cancer",

Answer: Thank you for sharing your suggestion. We have rearranged the keywords as recommended.

Question R3#7: As the revision process results in changes to the content of the manuscript, language problems may exist in the revised manuscript. Thus, it is necessary to perform further language polishing that will ensure all grammatical, syntactical, formatting and other related errors be resolved, so that the revised manuscript will meet the publication requirement (Grade A).

Answer: We have done meticulous proofreading and revisions to ensure the correction of all grammatical, syntactical, formatting, and other errors. Hence, we believe that the revised manuscript would meet the requirement as Grade A for the final publication.