

October 17<sup>th</sup>, 2023

Editorial Office,  
World Journal of Methodology

Dear Editors,

Thank you for finding our paper acceptable for publication. Please find our point by point response to the comments of the reviewers, as requested:

**Company editor-in-chief:**

I recommend the manuscript to be published in the World Journal of Methodology. Before final acceptance, when revising the manuscript, the author must supplement and improve the highlights of the latest cutting-edge research results, thereby further improving the content of the manuscript. To this end, authors are advised to apply a new tool, the Reference Citation Analysis (RCA). RCA is an artificial intelligence technology-based open multidisciplinary citation analysis database. In it, upon obtaining search results from the keywords entered by the author, "Impact Index Per Article" under "Ranked by" should be selected to find the latest highlight articles, which can then be used to further improve an article under preparation/peer-review/revision".

**-According to the request, we have applied the Reference Citation Analysis tool, and added the following reference to the revised manuscript [reference 35]:**

**Niewiadomski O, Studd C, Wilson J, Williams J, Hair C, Knight R, Prewett E, Dabkowski P, Alexander S, Allen B, Dowling D, Connell W, Desmond P, Bell S.** Influence of food and lifestyle on the risk of developing inflammatory bowel disease. *Intern Med J* 2017;**46**:669-76.

**Reviewer #1:**

I have a few comments on the manuscript – particularly the introduction section which needs to be improved and there is an error in the table that needs to be corrected.

**-We have made changes to the introduction section according to the specific comments as specified below. The error in the table (“prevalence- crude rate”) was corrected.**

**Reviewer #2:**

In the manuscript entitled “Inflammatory bowel diseases among First Generation Immigrants in Israel: a nation-wide epi-Israeli IBD Research Nucleus (epi-IIRN) study”, the authors show that among immigrants to Israel the IBD prevalence increased with longer time since immigration, and was related to the risk of IBD in the origin country. The manuscript is well written and the findings of this study are of interest. Their appeal to the readership of this journal is a little bit limited to warrant publication. To overcome this limitation and make the article more persuasive, the authors need to demonstrate the following issue. Like Fig.2, please separate the bar charts in Fig.1 into UC and CD, respectively.

**We adjusted Figure 1 as suggested and added *p-values* between the UC and CD bars as well.**

### **Reviewer #3:**

This study is novel and is very meaningful. And the manuscript is well organized. It is recommended that the authors address the following minor issues before this manuscript being accepted.

#### Abstract Section

1. L 47: Regarding “epi-IIRN cohort”, please provide original words of “epi-IIRN”. **The abbreviation is now defined, as suggested.**
2. L 52: Revise “ $p < 0.001$ ” to “ *$p < 0.001$* ”. Note italics and spaces please. **Revised as suggested and implemented throughout the manuscript.**
3. L 54: Revise “ $\geq 1990$ ” to “ $\geq 1990$ ”. Note space please. **Revised as suggested.**
4. L 54: Revise “ $p = 0.043$ ” to “ *$p = 0.043$* ”. Note italics and spaces please. **Revised as suggested.**
5. L 58: Revise “among non-immigrants prevalence was” to “non-immigrant prevalence was”. **Revised as suggested.**
6. L 64: Revise “Inflammatory bowel diseases, IBD” to “Inflammatory bowel diseases”. **Revised as suggested.**
7. L 64: Revise “environmental.” to “environment”. **Revised as suggested.**

#### Introduction Section

8. L 69: Regarding “vice versa (e.g. from the Faroe Islands to Denmark)”, “vice versa”? **Indeed, there is evidence that the excess UC risk among immigrants from Faroe Islands (which has record high IBD rates) to Denmark (which has considerably lower IBD rates) disappears over 1-2 generations. We clarified this within the text.**
9. L 72: Revise “hampering the ability to focus on the environmental effect” to “hampering attention to environmental effect”. **Revised as suggested.**
10. L 90: Revise “Israel affected” to “Israel affects”. **Revised as suggested.**

#### Methods Section

11. L 116: Revise “1990-2001 and 2002-2020” to “1990-2001, and 2002-2020”. **Revised as suggested.**
12. L 129: Revise “Date of death” to “The date of death”. **Revised as suggested.**

#### Results Section

13. L 148: Revise “n=28” to “n = 28”. Note spaces please. **Revised as suggested and implemented throughout.**
14. L 153: Revise “are detailed” to “were detailed”. **After consulting with a professional English language editor, it was decided to keep the present tense.**
15. L 156: Regarding “USSR countries”, please supplement original words of “USSR”. **The abbreviation was defined, as suggested.**
16. L 158: Revise “characteristics are displayed” to “characteristics were displayed”. **After consulting with a professional English language editor, it was decided to keep the present tense.**
17. L 161: Revise “are displayed as” to “were displayed as”. **After consulting with a professional English language editor, it was decided to keep the present tense.**
18. L 161: Regarding “Table 1”, please revising to a three-wire table with two thick and one thin. **The table was graphically rearranged as requested.**
19. “median (IQR)” on line 161 and “IQR interquartile range” on line 164? **The definition was moved to the earlier place.**
20. L 164: Delete “IBD Inflammatory bowel diseases”. **Removed, as suggested.**
21. L 186-187: Move “Figure 1. IBD prevalence among Jewish Israel-born and first-generation immigrants on June 2020” to line 188. **The Figure was moved as suggested, and is presented after the in-text citation.**
22. L 200: Revise “by duration of residence in Israel.” to “by duration of residence in Israel”. **The period was removed as suggested, also for Figure 3 and Supplemental Figure 1.**

#### Discussion Section

23. L 234-235: “As in our study, most of these studies”? **This sentence was rephrased for clarification.**
24. L 252: Revise “, urbanization and” to “, urbanization, and”. **Revised as suggested.**
25. L 252: Revise “Vangay et al” to “Vangay et al.”. **Revised as suggested.**
26. L 257: Revise “Our study has” to “Our study had”. **Revised as suggested.**
27. L 257-258: Revise “the immigrant versus” to “the immigrants versus”. **Revised as suggested.**
28. L 261: Revise “, IBD type and” to “, IBD type, and”. **Revised as suggested.**
29. L 176: Regarding “we did control for IBD risk at the country of origin”, How does the authors control IBD risk at the country of origin? **IBD risk was controlled by stratification, as shown in Figures 2 and 3. This was clarified in the text.**

#### Conclusion Section

30. L 279: Revise “high prevalence rates of IBD” to “high prevalence rate of IBD”. **Revised as suggested.**

#### Reviewer #4:

Israel has a high rate of Jewish immigration and a high prevalence of inflammatory bowel diseases (IBD). In this nationwide study the authors aimed to compare IBD prevalence in first-generation immigrants versus Israel-born Jews. It is not an interesting manuscript. Authors cannot succeed to present their idea in a clear way adding information to the existing literature. What are the original findings of this manuscript? What are the new hypotheses that this study proposed?

**In this nationwide study, we compared IBD rates between first-generation immigrants originating from countries of varying IBD risk, versus Israel-born residents. Our focus on the Jewish population was aimed at narrowing the genetic variation of IBD that is usually present in immigration cohorts. We found that the prevalence rate was lower among patients from intermediate-and low-risk regions compared to patients from high-risk regions but in both, the prevalence increased in association with duration in Israel after immigration. This finding, especially among immigrants from intermediate- and low-risk countries, lends support toward the role of environmental factors in IBD pathogenesis in Israel. This is the first time this is shown in Israel and the uniqueness is the broadly similar genetic background of Israeli-born and the immigrants, unlike other similar studies around the globe. This is now better clarified within the discussion.**

Sincerely yours,

Dan Turner MD, PhD and Mira Stulman

Shaare Zedek Medical Center

The Hebrew University of Jerusalem

Jerusalem, Israel