

Response to Reviewers: Manuscript WJG 86335

Enduring association between IBS and war trauma in civilians from the Nicaragua Civil War period: A population-based study

Reviewer #1:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Major revision

Specific Comments to Authors: Overall, the manuscript presents an interesting study investigating the relationship between war trauma and Irritable Bowel Syndrome (IBS) development in civilians from the Nicaragua Civil War period. The topic is relevant and has potential implications for understanding the impact of war events on gastrointestinal health. However, some parts could benefit from further clarification and improvement:

1. **Introduction:** The introduction provides a general overview of IBS prevalence in different regions but lacks a clear statement of the research objective and the rationale for the study. It should clearly state the main research question and hypothesis, which will help readers understand the purpose of the study from the outset.
 - We appreciate this critique. We have added a focused statement to the Introduction.
2. You should cite relevant reviews on the association between IBS and psychological conditions (<https://pubmed.ncbi.nlm.nih.gov/31157418/>; <https://pubmed.ncbi.nlm.nih.gov/34927759/>).
 - We have reviewed the articles, and have added an appropriate citation (#7).
3. **Background and Literature Review:** The literature review on the association between IBS and war trauma is primarily focused on studies conducted on U.S. veterans. To strengthen the relevance of the study, it would be beneficial to include more literature on the association between war trauma and IBS in civilian populations, especially from other regions with similar conflict histories.
 - We fully agree with this observation, however, the literature focused on war trauma and IBS in civilian populations is extremely limited, particularly with a population-based study design. This study adds to the literature in this respect. We note that there is literature focused on PTSD and war experience.
4. **Methods:** The methods section needs more information about the specific inclusion and exclusion criteria for participants in the study. Clarifying the criteria for selecting individuals and households for the survey will help readers understand the representativeness of the sample. The number of participants selected for the study (1,600) and the number of eligible adults (1,000) need further justification or explanation. How were these specific numbers determined, and why were they considered adequate for the study?
 - We agree. The section has been modified in the manuscript: The current study is nested within a comprehensive study of the population prevalence of the FGIDs, based upon Rome 2 criteria, with final enrollment of 1,617 persons randomly selected from urban and rural areas. The sample size was based upon an estimated IBS prevalence of 11%, alpha 5%, and 5% losses to follow-up within the Leon-HDSS. Thereafter, individuals born before 1975 were selected to meet the criteria of having been at least 5 years of age during the peak war period of 1975-1979 in the Leon region (n=1,012).
5. **Variables and Instruments:** The description of the poverty index (UBN) used for socioeconomic status measurement needs more clarity. Provide a brief explanation of the four indicators and how they are combined to determine the poverty index score.
 - Thank you for this comment. The poverty index based on UBN is fully described in the added citations 16 and 17.
6. The methodology for the Rome II Modular Questionnaire (R2MQ) validation in Nicaragua needs to be elaborated further. Explain how the 400 individuals were selected, and provide more details about the physician interviews and blinding process.
 - We agree. This part has been modified in the manuscript. The 400 subjects were randomly selected per Leon-HDSS protocol. This was an independent sample, and subjects were not included in the core study. Each individual underwent two R2MQ interviews by different trained field coordinators. Case status was confirmed thereafter via interviews by trained physicians, who were blinded to the survey results.

7. Statistical Methods: The statistical methods section should include more details about the analysis plan and how the associations between war trauma and IBS were assessed. Specifically, provide information on the type of regression model used, covariates included, and statistical significance levels.

• We thank you for this input. Modifications have been made in the Statistical Methods section. The variable distribution by groups (gender and strata age) was analysed with Mantel-Haenszel chi square test for categorical variables. Multiple logistic regression model was adjusted for age, gender, education, and poverty level.

8. The ethics section mentions approval from the Institutional Review Boards of the University of North Carolina and UNAN-Leon, but it does not elaborate on the ethical considerations taken into account during the study. Include information on informed consent, participant confidentiality, and any potential conflicts of interest.

• We agree. Modifications have been made in this section.

Reviewer #2:

Scientific Quality: Grade B (Very good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: This is original research article about the relationship between war exposure and IBS prevalence. Overall, the manuscript is very well written. English language is great, the length of the text and its subdivision are appropriate, explanations are clear and tables are of a high standard. Referencing is very good and an appropriate set is included for readers to understand the relative background. I feel that results of the study have been overstated in some places, which seems to be common for this type of work. However, I believe that the study is worthy of publication. The authors could consider the following questions and comments:

1. Military personnel may experience different types of treatment during their participation in war, and this variability in treatment between populations may have contributed to the introduction of bias. This topic is worth exploring in the future.

• We agree, and this theme would be of interest in a future study.

2. Data collection in the form of questionnaires requires good compliance of subjects. This way of including patients may itself exclude residents with emotional problems caused by war (or other factors). This may introduce unnecessary bias.

• We agree. Our study employed experienced field coordinators who were part of the Leon-HDSS and were trained to try to minimize the potential loss of respondents.

3. The inclusion of patients needs to be explained graphically (why 1600 people were chosen for the total population), how patients were finally excluded, and how many patients were excluded at each step.

• We agree. The section has been modified in the manuscript: The current study is nested within a comprehensive study of the population prevalence of the FGIDs, based upon Rome 2 criteria, with final enrollment of 1,617 persons randomly selected from urban and rural areas. The sample size was based upon an estimated IBS prevalence of 11%, alpha 5%, and 5% losses to follow-up within the Leon-HDSS. Thereafter, individuals born before 1975 were selected to meet the criteria of having been at least 5 years of age during the peak war period of 1975-1979 in the Leon region (n=1,012).

4. Disclose the approval and approval number of the ethics committee in the text.

• The University of North Carolina, Chapel Hill IRB approval number has been added.