Peer-Review comments and author responses

Reviewer 1

Comment: Dear authors, Congratulations for submitting this manuscript! I consider the topic as original, under-explored and of utmost importance for the scientific community. The text is overall very well structured. I outline below my comments and suggestions. In all the manuscript, please check for extra spaces between words.

Response: *Thank you for bringing this to our attention. The text was fully proofread and revised.*

1. Abstract

Comment: In the background: I would change the last sentence as follows: "However, the link between hepatitis immunization status and social support needs to be explored". The rest of the abstract is very well structured.

Response: *It now reads " However, the link between hepatitis immunization status and social support needs to be explored.", as you suggested.*

2. Introduction

Comment: Nothing to change, very well structured.

3. Methods

Comment: I would change the last sentence of the first paragraph as follows: "The composition and categorization of the rest of the variables are detailed in the appendix".

Response: *This phrase was removed since we moved the variables description to the methods section.*

Comment: I would rephrase the last 2 sentences of the second paragraph: "Clinically relevant confounders were included in the multivariate analysis (Andrea et al., 2015; Reeder et al., 2022; Y. Wang et al., 2024). Age, gender, race/ethnicity, family poverty index ratio (PIR), educational level, smoking status, alcohol consumption, food insecurity, sleep habits, physical activity, caffeine intake, comorbidities, and mental health status (PHQ-9 score) controlled for demographic, socio-economic, lifestyle and past medical history". I assume the last sentence is the enumeration of the clinical relevant confounders included in the model, but it isn't clear.

Response: *The text is now written in a more clear way: "The following clinically relevant confounders were included in the multivariate analysis: (Andrea et al., 2015; Reeder et al., 2022; Y. Wang et al., 2024). Age, gender, race/ethnicity, family poverty index ratio (PIR), educational level, smoking status, alcohol consumption, food insecurity, sleep habits, physical activity, caffeine intake, comorbidities, and mental health status (PHQ-9 score) controlled for demographic, socio-economic, lifestyle and past medical history. "*

4. Results:

Comment: Table 1:

The first and second rows (A and B at least 1 dose, and A and B full doses) are very hard to understand and confusing.

From my understanding, in the first row, the population who received 1 dose of hepatitis A and B vaccine was divided according to high vs low social support value in: patients who received only 1 dose of either hepatitis A or B vaccine (missing in any) and patients who received only 1 dose of both hepatitis A and B vaccine (1 dose of both).

In the second row, I assume the numbers refer to the population who have a full vaccine regime for both hepatitis A and B (2 and 3 doses, respectively, as specified in the methods section), therefore, under the category of complete, and the rest are considered as incomplete. Something that strikes me is that the sum of the absolute numbers of each subcategory (A and B at least 1 dose, and A and B full doses) don't add up to the total population of each subgroup (high vs low social support). Is there missing data? If so, this has to be acknowledged.
I therefore suggest re-constructing the first 2 rows of this table for more clarity.
I would move the second row A and B full doses to the top, and adding a legend at the bottom of table 1 clarifying what is considered by the subcategories complete and incomplete.
I would then place the row A and B at least 1 doses and rename it as follows: "A and B at least 1 dose". I would also rename the subcategories as follows: "missing in any" to "NO", and "1 dose of both" to "YES".

I would also change the legend next to Age at screening as follows: "(mean, SD, in years)". Similarly, I would change the legend next to PHQ9 as follows: "mean, SD)". Additionally, what does PIR ordinal mean? I would directly name the indicator PIR to avoid confusion, because the reader can already infer that the variable is ordinal, and specify what each subcategory refers to.

Finally, there is no need of including the p-value of each baseline characteristic, so I would directly delete that column.

Response: *We have updated table 1, according to your suggestions.*
Regarding missing data, we added a paragraph in the results section, describing it:

"Model 1 included 247 complete observations and Model 2, 217 complete observations. Data was missing for 11.2% of the complete vaccination, and 19.7% of the partial vaccination main independent variables. "

Updated Table 1:

	Low Social Support (N=1,352)	High Social Support (N=1,645)
Partial Vaccination		
no shots	1,023 (89.5%)	1,230 (90.4%)
partially HAV HBV	120 (10.5%)	131 (9.6%)
Complete Vaccination		
incomplete	1,107 (91.8%)	1,391 (93.0%)
complete HAV HBV	99 (8.2%)	104 (7.0%)
Age	60.6 ± 13.7	60.3 ± 13.6
Gender		
female	659 (48.7%)	827 (50.3%)
male	693 (51.3%)	818 (49.7%)
Education Level		
< High School	263 (19.5%)	185 (11.3%)
Some High School	235 (17.4%)	204 (12.4%)
Complete High School	338 (25.1%)	380 (23.1%)
Some College	327 (24.2%)	456 (27.7%)
Complete college or >	186 (13.8%)	419 (25.5%)
PIR		
0	274 (20.3%)	142 (8.6%)
PIR 1-2	389 (28.8%)	338 (20.5%)
PIR 2-3	194 (14.3%)	259 (15.7%)
PIR 3-4	155 (11.5%)	247 (15.0%)
PIR 4-5	82 (6.1%)	149 (9.1%)
PIR >5	258 (19.1%)	510 (31.0%)
smoking		
no	398 (51.2%)	563 (70.7%)
smoke	380 (48.8%)	233 (29.3%)
sleep hours		
sleep <6 hrs/day	420 (31.1%)	524 (31.9%)
sleep 6-9 hrs/day	735 (54.4%)	869 (52.8%)
sleep >9 hrs/day	197 (14.6%)	252 (15.3%)

TABLE 1:
Complete vaccination: 2 doses of HAV and 3 doses of HBV, Incomplete vaccination: at least one dose of both HAV and HBV vaccination. Frequency (%). Age: Mean ± Standard Deviation (in years), PIR: Poverty Index Ratio.

Comment: Univariate analysis: I would change this sentence "Immunization status was not associated with social support level in the univariate analysis" to "Full immunization status was not positively associated with high social support level".

Response: *Updated as you suggested.*

Comment: Table 2:

Well structured, but what does *, ** and *** next to the numerical results of the model mean?

Response: *The legend now reads: "HAV = Hepatitis A vaccine. HBV = Hepatitis B vaccine. PIR = Poverty Index Ratio. PHQ9 = 9-item depression scale. * = p<0.05, ** = p<0.01, *** = p<0.001"*

Comment: The discussion and conclusion sections are excellent!

Comment: APPENDIX:
Response: *First we would like to acknowledge that this paragraphs were moved to METHODS section*

Comment: Outcome - Social support assessment:
I would rephrase the first sentence as follows: "Five dichotomous social support variables were used to create a social support scoring index".

Response:*Updated.*

Comment: Covariates: Please expand on the Poverty Index Ratio (PIR), besides describing it as an ordinal variable. What does it take into account? Many readers might not be familiar with this indicator.

Response: *"The PIR income ratio is calculated by dividing family (or individual) income by the poverty threshold specific to each survey year and is an effective measure of income disparity closely related to human life and health (Jia et al., 2024)"*

Reviewer 2:

Recommendation: Revisions Required

Comment:
In this work, authors conducted an exploratory analysis to examine the potential predictors of social support. Please find below my comments:

- "Hepatitis A and B immunization as a predictor of social support" From this title, I am assuming that your exposure of interest is Hepatitis A and B immunization, and the outcome of interest is

social support. Is this hypothesis correct? Do we have literature supporting this hypothesis? Isn't it more natural to think that the level of social support may be a predictor of Hepatitis A and B immunization?

In addition, this title is not very informative. I would suggest providing more information to the reader of the context of this work. For example, I am missing the target population here.

Response: *We agree with your comment on the direction of the association. Since this is a cross-sectional study we can not infer causality from our results. However, since the vaccination most likely happened in infancy, while the questionnaires were filled by adults older than 40 years old, it is still logical to assume that immunization status would actually be the predictor of Social Support levels. Addressing your comments, the title now reads " Hepatitis A and B immunization association with social support among adults in the US population from the NHANES 2005-2006 cohort data.*

1. Abstract

Comment: - Background of the abstract: "Lack of social support is associated with chronic physical and mental diseases. On the other hand, high social support is an indicator of a healthier lifestyle, including vaccination adherence. Similarly, immunization is a widely available public-health statistic associated with healthier behaviors. However, the link between hepatitis immunization status and social support has yet to be explored." Here, you are treating social support as an exposure, which does not correspond to the title. Also, you are starting with a general statement followed by a contrast sentence ("on the other hand"), then followed by a positive statement ("similarly), and finishing with another contrast sentence ("however"). This is difficult to follow. In general, please try to organize better the ideas, so they follow a more natural order (for example, start with positive sentences, and then explain the counterpart to give an overview to the reader).

Response: *As noted in the previous comment, since ours and the mentioned studies were cross-sectional analyses, no causality is to be inferred, but the association, which could be directional. Regarding the writing, this section was rewritten to allow a better information flow and understanding:*

"High social support is easily assessed and has been associated with a healthier lifestyle, including vaccination adherence. Similarly, immunization is a widely available public-health statistic associated with healthier behaviors. However, the link between hepatitis immunization status and social support needs to be explored."

2. Methods

Comment: "The National Health and Nutrition Examination Survey (NHANES)…" I would start this sentence with "we conducted a multivariate logistic regression to explore…" or something along these lines. In general, we start the methods section by stating what we did, followed by how we did it and so on.

Response: *Thank you for bringing this to our attention. ""We evaluated the association between immunization against hepatitis A and B and levels of social support in the general US adult*

population through logistic regression. A secondary analysis of the 2005-2006 National Health and Nutrition Examination Survey (NHANES), a publicly available cross-sectional database, was performed (CDC, 2005-2006).

Comment: - "We hypothesize that hepatitis immunization may serve as a lifestyle surrogate, associated with mental, physical and social health indicators." Do we have literature available to support this hypothesis?

Response: *The hepatitis and social support association gap was presented in the previous paragraph of the introduction. There the relevant literature showing the association between vaccination and social factors is mentioned, in the influenza context. (Z. Wang et al., 2022; Wong et al., 2021),*

Comment: - "Age, gender, race/ethnicity, family poverty index ratio (PIR), educational level, smoking status, alcohol consumption, food insecurity, sleep habits, physical activity, caffeine intake, comorbidities, and mental health status (PHQ-9 score) controlled for demographic, socio-economic, lifestyle and past medical history." How were these variables treated? Please specify if they were continuous, categorical or ordinal variables.

Response: *Following your comments, we've added the codebook to methods section*

3.Results

Comment: - Table 1 includes covariates that were not included in the methods. I would suggest adding a brief description of these variables.

Response: *Table 1 was updated according to another reviewer's suggestion*
The following item was added to the methods section:
"Physical activity was a binary variable. "Yes" if the participant reported having performed any activity in the last 30 days."

Comment: Results: "Univariate analysis failed to show a significant association…" The univariate analysis didn't really fail, it showed what the evidence based in the data provided. Instead, I would express this in terms of the strength of evidence. In addition, I don't think it's relevant to report the results of the univariate analysis in the results section of the abstract.

Response: *Following your comments, we have removed the sentence from the abstract:*

"Multivariate analysis revealed significantly greater odds of high social support for participants fully or partially immunized against both hepatitis A and B: 3.15 (95% CI 1.03-9.66, p = 0.04) and 3.35 (95% CI 1.15-9.75, p = 0.03), respectively."

Comment - "...also were associated with better social support. Smoking status (aOR = 0.39, 95% CI 0.19-0.78, p=0.01)" How was the low social support coded? Please double-check this, but I think the interpretation is the opposite.

Response: *The main outcome was a binary variable, as stated in the methods section – The main outcome was social support, measured by a social support score, previously proven valid in other studies (Nicklett et al., 2012; Smith et al., 2017; Teoh et al., 2018; Y. Wang et al., 2024). It is composed of five variables: emotional support, financial support, religious service attendance, number of close friends, and marital status. Each positive answer contributed one point to the score, ranging from 0 to 5 (Wang et al., 2022). Participants with a score of 0–3 were classified as having low social support, whilst those scoring 4–5 were categorized as having high social support. – thus, having a aOR of less than 1 indicates higher odds of being in the low social support group.*

Comment: - "The global burden of Hepatitis A (HAV) and B (HAB)" These abbreviations are not standard in medical literature and may be confusing for the reader. If HAV stands for hepatitis A virus, what HAB stands for?

Response: *Thank you for bringing this typo to our attention. The abbreviation was corrected to HBV*

Comment: - "Beyond direct health benefits, vaccines may impact social determinants of health, such as income and education" Have you considered the possibility of reverse causation? Maybe people with higher income and higher education are more likely to be vaccinated, and not the other way around.

Response: *This sentence was reformulated to: "Beyond direct health benefits, vaccines may be associated with social determinants of health, such as income and education (Alsharif et al., 2022)."*

Comment:- "with millions of individuals affected worldwide" How many millions? Please try to be objective and provide figures.

Response: *Updated: "Worldwide, 387 million individuals were reported infected with HBV only. (Bhandari et al., 2024; Obeagu, 2023)."*

Comment: "It prevents serious infections that can lead to chronic liver failure and hepatocellular carcinoma (Hepatitis B), or diarrhea with life threatening dehydration (Hepatitis A)" You already defined Hepatitis A an B as HAV and HAB. Why not using these abbreviations, then?

Response: *Corrected to HAV and HBV*

Comment: "…This study analyzes NHANES 2005-2006.." You introduced the NHANES 2005-2006 without giving any context to the reader. Although this information is given in the first paragraph of the methods section, please avoid mentioning the dataset before giving prior information to the reader.

Response: *"This study performs a secondary cross-sectional data analysis on the association between hepatitis A and B vaccination status and social support among U.S. adults aged 40 and older."*

Comment: - "Hepatitis immunization status was measured by two different models". Please consider changing to "by two different approaches" to avoid confusion with statistical modelling.

Response: *Updated: "Hepatitis immunization status was measured by two different approaches"*

Comment: - "Clinically relevant confounders were included in the multivariate analysis" I understood we were constructing a predictive, rather than a causal model. That is, you are attempting to construct a model to predict lack of social support. If this is the case, the definition of confounders is hardly justified, because we haven't defined an exposure, unless we are doing an exploratory analysis? Please clarify this.

Response: *Our study is an exploratory analysis with a cross-sectional design, aiming to answer whether hepatitis immunization status is associated with social support levels.*

Comment: - "Statistical analysis was performed with Stata software version 18.5 (StataCorp, 2023), with a statistical significance of $p < 0.05$." This is not correct. What you are setting up here is the alpha critical value at the level of 0.05. This is different to the p value.

Response: *Updated: "Alpha was set at 0.05 and power at 80%".*

Comment: - "Continuous variables were described by means and standard error" The descriptive statistics uses mean and standard deviation for normally distributed variables. If you are reporting standard errors, then this is inferential statistics. Standard deviation is not the same as standard error.

Response: *Updated: "Continuous variables were described by medians and standard deviation."*
- "while adjusted OR (aOR)…" We don't normally abbreviate adjusted OR as aOR. This is not standard in literature.

We thank you for bringing this to our attention. After reviewing the literature we've found extensive literature support using aOR as an abbreviation of adjusted OR. The following link refers to a publication in the agency of healthcare research and quality jiournal, using this abbreviation.
https://www.ncbi.nlm.nih.gov/books/NBK410020/
Comparative Effectiveness Reviews, No. 182.
Chou R, Totten AM, Pappas M, et al.
Rockville (MD): Agency for Healthcare Research and Quality (US); 2017 Jan.

Comment: - Results: I am missing some information regarding the missing data here.

Response: *"Model 1 included 247 complete observations and Model 2, 217 complete observations. Data was missing for 11.2% of the complete vaccination, and 19.7% of the partial vaccination main independent variables. "*

Comment: - "The odds ratio of being in the high social support group when receiving full immunization against hepatitis A and B was 3.15 (95% CI 1.03-9.66, p=0.04) after adjustment." I

know this is reported in the tables, but please clarify which variables this model was adjusted for. In addition, please provide an interpretation of the OR.

Response: *It now reads " Receiving full immunization against hepatitis A and B was associated with high to social support. (OR 3.15, 95% CI 1.03-9.66, p=0.04)*

Comment: "The OR of high social support increased with PIR levels." What does it mean in plain words? Please provide and interpretation of the OR, and report confidence intervals + p value.

Response: *"Receiving at least one dose of vaccine for both hepatitis A and B was associated to a higher social support (OR 3.35, (95% CI 1.15-9.75, p=0.03)"*

The reader can find the OR and PIR univariate analysis in table 2, with p-values and OR.

Comment: - "Model 2: (At least one dose for both hepatitis vaccines)" You already explained your Model 2, no need to state this again in the subheading.

Response: *We appreciate your suggestion, but we believe this information may ease the information flow and understanding of the results, since the reader would not need to search for the model description in the methods section.*

Comment: - "The results of this exploratory analysis showed that being vaccinated against Hepatitis A and B is significantly associated with social support, after adjusting for potential confounders." This is the first time you are mentioning that this is an exploratory analysis, and this is stated in the discussion section. I recommend you should make it clear in the abstract, methods, results, and even in the title of this manuscript. The exploratory nature of this study is crucial to interpret the results.

Response: *As stated in the previous comments, we've modified the title and background to make the exploratory nature of the study more explicit.*

Comment: - "The results of this exploratory analysis showed that being vaccinated against Hepatitis A and B is significantly associated with social support, after adjusting for potential confounders." No need to clarify here that the results are adjusted for potential confounders. This was already mentioned in the results. More importantly, after reading your results, what would be the message for policy makers? Does it mean that we need to vaccinate more people for them to have a higher level of social support? What are the implications of lack of social support, and why policy makers should care about this?

Response: *We removed the sentence referring to the adjustment, following your comments. Regarding the impact for policy makers, it is described at the end of the discussion section: "Promoting HAV and HBV vaccination could provide the additional benefit of strengthening social support, leading to synergic health benefits. In addition, policymakers should direct resources into strategies that increase social support, benefiting also from increasing vaccination coverage and reducing chronic diseases in the general population. Future research should explore*

the temporal dynamics and causality between vaccination and social support to better understand this complex relationship. "

Comment: - "Since vaccination occurred before the social support establishment, our findings suggest that vaccination may positively influence building social support networks." This information is key for the interpretation of the paper, and I would suggest including it in the introduction. If vaccination occurred before social support, then we have directionality in this relationship.

Response: *We agree with your comment. However, we are taking this information with caution, due to the exploratory nature of this study. We have included the word "most likely" to this sentence.*

Comment: - "This engagement probably explains why individuals vaccinated against HAV and HBV had higher odds of high social support in our study. Here you changed the abbreviations. Previously you stated HAV and HAB.

Response: *This typo was corrected following your previous comments.*

Comment: "Wang et al., 2022, reported that vaccination fosters engagement with healthcare systems and community networks, strengthening social connections. This engagement probably explains why individuals vaccinated against HAV and HBV had higher odds of high social support in our study." What Wang et al concluded in their paper was that health status predicts vaccination behavior. That is, vaccination behavior was the outcome. In the present work, social support is the outcome of interest.

Response: *We appreciate you bringing this matter to our attention. This paragraph now reads:*

"Wang et al., 2022, reported that engagement with healthcare systems and community networks, strengthening social connections, is associated with vaccination acceptance. Due to the likely bidirectional association between these variables, this engagement probably explains why individuals vaccinated against HAV and HBV had higher odds of high social support in our study.

Comment: - "Among lifestyle factors, sleeping more hours a day was associated with higher social support. Possible reasons for this association are the known effects of sleep health inducing lower stress levels and better health status" From this statement, I understand that lower stress levels can be a mediator for the association between hours of sleep and social support. But we are not exploring causation here, as we are trying to construct a model to predict social support. Am I correct? Please clarify.

Response: *We are conducting an exploratory data analysis, assessing association only. Stress levels could be a confounder of this association, but we don't have the data to reject or confirm this hypothesis in our available dataset.*

Comment: - In general, the discussion section in this paper has been devoted to exploring possible associations between a number of covariates and the level of social support, possibly without having a specific hypothesis to explore. However, the main goal of the study was to predict the social support, not to explore causality. If causality is the main goal, then you need to define an exposure, and draw a direct acyclic graph (DAG).

The main goal of our study was to perform an exploratory data analysis of the association between hepatitis vaccination status and social support levels, not intending to establish causation.

More importantly, I am missing here the main advantages and limitations of this study. In particular, we should be focused on the possibility of selection bias, owing to observational nature of the study. If this is an exploratory analysis, it may be important to mention the possibility of residual confounding. i.e., the probability that the results are biased due to the impossibility to include confounding variables that were not collected in this study. This is of a particular importance in causal models.

Response: *We have included the following paragraphs, according to your comments:*
"This study has some limitations. The cross-sectional exploratory nature of our analysis can not establish causality. The secondary data analysis of cohort recruited not targeting our outcomes may introduce selection bias. In addition, final multivariate analysis had only 7.2%- 8.2% complete observation of the 2,997 total.only had 8.2%

Strengths of our study were the robustness of the result for both fully vaccinated and partially vaccinated participants. In addition, vaccination and social supportal temporal relationships may suggest a directional relationship in this association."
Regarding the Appendix:

Comment: -The information regarding covariates is crucial for the interpretation of results, and should be included in the main text.

Response: *It was moved to the main text, as you suggested.*

Comment: "Primary outcomes:
1- Full immunization: if the participant declared having 2 Hepatitis A doses and 3 Hepatitis B doses of vaccination. Having incomplete schemes or no doses were grouped together as "not fully immunized".
2- Some immunization: if the participant declared having at least 1 dose of both Hepatitis A and B vaccination. Lacking at least 1 dose of either Hepatitis A or B immunization was grouped together as "not vaccinated".
I understood throughout the paper that the immunization status was a predictive factor, but here you are treating these variables as the primary outcome. In addition, only one primary outcome needs to be selected. The others would be secondary outcomes. The only exception is in the context of composite outcomes, which is not the case for this study.

Response: *We apologize for the mistake. Social support is our main outcome and these are our main independent variables. The text was corrected accordingly:*
Independent variable - Hepatitis Immunization

Comment: Full immunization: if the participant declared having 2 Hepatitis A doses and 3 Hepatitis B doses of vaccination. Having incomplete schemes or no doses were grouped together as "not fully immunized".
2- Some immunization: if the participant declared having at least 1 dose of both Hepatitis A and B vaccination. Lacking at least 1 dose of either Hepatitis A or B immunization was grouped together as "not vaccinated".
- "Five dichotomous social support variables were used to form a social support scoring index. The structure and predictive effectiveness of this index for NHANES have been shown in previous studies. This score is composed of emotional support, financial support, frequency of attending religious services, number of close friends, and marital status (Nicklett et al., 2012; Smith et al., 2017; Teoh et al., 2018; Y. Wang et al., 2024)." In my opinion, this information should be included in the main text, and not in the appendix. The description of the outcome is crucial for the reader to interpret the results. The same applies for the description of covariates.

Response: *This information was moved to the Methods section, as you suggested.*

Comment: For Table 5, please clarify in the legend what is meant by VIF, tolerance and R squared.

Response: *The following legend was added for table 4 and 5 in the appendix:*
VIF= Variance Inflation Factor.

Comment: As a final suggestion, please adhere to the STROBE guidelines to report the results of the present study.

Response: *We've confirmed the article adheres to the STROBE guidelines and added the following sentence to the methods section.*

"Our article adheres to the STROBE guidelines for observational studies."

Reviewer 3:

Comment: Congratulations for this project! Below you find my comments section by section!

1. Introduction:

Comment: Good job, I think a clear explanation on how social support can be evaluated would guide the reader towards a better overall understanding of this part.

Response: *Thank you so much for your insightful suggestions, we describe social support in details in the methods section- Social support score was composed of 5 items:*

- emotional (YES or NO answer, if anyone it's a YES)
- support related to religion (attendances per month to church as a YES, 4 or less attendances as a NO)
- marital status (marriage or living together as YES and living alone or widow as a NO)
-financial support (YES or NO answer)
- social network (assessed as number of close friends, more than 4 was considered as a YES)

2. Methods:

Comment: it is a little confusing, the first sentence is more suitable for discussion section. Please follow the recommended outline:
Study design
Setting
Participants

Response: *"We evaluated the association between immunization against hepatitis A and B and levels of social support in the general US adult population through logistic regression. A secondary analysis of the 2005-2006 National Health and Nutrition Examination Survey (NHANES), a publicly available cross-sectional database, was performed (CDC, 2005-2006). The main outcome was social support, measured by a social support score, previously proven valid in other studies (Nicklett et al., 2012; Smith et al., 2017; Teoh et al., 2018; Y. Wang et al., 2024). It is composed of five variables: emotional support, financial support, religious service attendance, number of close friends, and marital status. Each positive answer contributed one point to the score, ranging from 0 to 5 (Wang et al., 2022). Participants with a score of 0–3 were classified as having low social support, whilst those scoring 4–5 were categorized as having high social support. Original data was collected in-home by trained interviewers, after the appropriate informed consent was obtained. This analysis included 2,997 individuals, aged 40 or older, who completed the NHANES social support and immunization questionnaires."*

Comment: .Variables: Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers; give diagnostic criteria, if applicable and data sources/measurement.
For each variable of interest, give sources of data and details of methods of assessment (measurement); describe comparability of assessment methods if there is more than one group.

Response: *Following your suggestion, we have moved the variables description to the METHODS section with the appropriate corrections. These variables were accounted in the multivariate models to isolate the true effect of immunization on social support. Some variables, such as PIR and mental health, overlapped each other as both predictors and confounders because they influence social support directly (as predictors) and also relate to immunization status (as confounders). This overlap is justified as their inclusion ensures both the adjustment for confounding effects and the evaluation of their independent association with social support, providing a comprehensive understanding of the relationships in the model. Potential effect modifiers, including PIR, smoking status, and PHQ-9 score, were considered for their ability to alter the strength or direction of the immunization-social support association, and interaction*

terms could be explored in future analyses.
All variables were coded as follows:

Independent variable - Hepatitis Immunization

1- Full immunization: if the participant declared having 2 Hepatitis A doses and 3 Hepatitis B doses of vaccination. Having incomplete schemes or no doses were grouped together as "not fully immunized".

2- Some immunization: if the participant declared having at least 1 dose of both Hepatitis A and B vaccination. Lacking at least 1 dose of either Hepatitis A or B immunization was grouped together as "not vaccinated".

Outcome - Social support assessment

Five dichotomous social support variables were used to create a social support scoring index. The structure and predictive effectiveness of this index for NHANES have been shown in previous studies. This score is composed of emotional support, financial support, frequency of attending religious services, number of close friends, and marital status (Nicklett et al., 2012; Smith et al., 2017; Teoh et al., 2018; Y. Wang et al., 2024).

More specifically, 1 point was assigned to the answer "yes" for the question on emotional support (Can you count on anyone to provide emotional support such as talking over problems or helping make a difficult decision?) and on the financial support (Could you count on anyone to help, for example, by paying any bills, housing costs, hospital visits, or providing with food or clothes?). The answers "no", "don't need," or "don't accept" were assigned as "0" (Nicklett et al., 2012; Smith et al., 2017; Teoh et al., 2018; Y. Wang et al., 2024).

In addition, 1 point was assigned for being married or living as married, attending at least four religious services per year (How often do you attend church or religious services?), and having four or more close friends (In general, how many close friends do you have?). In any of these questions, participants who refused to answer the question or answered "don't know" were considered as missing data. Answers that were not assigned 1 or missing data, were coded as "0" (Nicklett et al., 2012; Smith et al., 2017; Teoh et al., 2018; Y. Wang et al., 2024).

The sum of the social support score index ranged from 0 to 5. The social support score was then classified into two groups: Low social support: social support score = [0–3];and High social support: social support score = [4–5].

Covariates

Confounders associated with social-support were described in previous studies as age, sex, race, family poverty-to-income ratio (PIR), body mass index (BMI), marital status, educational attainment, and smoking status (Andrea et al., 2015; Reeder et al., 2022)). In addition, social support was also previously linked to cardiovascular diseases in a study that identified significant basal line differences in social support groups by age, BMI, education level, race, and smoking status (Y. Wang et al., 2024).

Demographic:
- *Age was a continuous variable.*
- *Gender was a binary variable: 0 for females and 1 for males.*
- *Race was described as a four level factor: non-Hispanic White; Mexican American and other Hispanic; non-Hispanic Black; Other.*

Socio-Economic:
- *Education Level was coded as five levels factor: including less than high school graduates, high school graduates or associate of arts degree, and college graduates*
- *The Family Poverty Index Ratio (PIR) was coded as a 6 level ordinal variable: [0-1];]1-2];]2-3];]3-4];]4-5]; [5+; The PIR is calculated by dividing family (or individual) income by the poverty threshold specific to each survey year (Jia et. al, 2024)*
- *Food Insecurity was coded as a binary variable: 1 if answering "yes", 0 if answering "no" to the question "have the Household eaten less for not having enough money?".*

Healthy Habits:
- *Smoking status: two questions from the NHANES were combined to determine whether participants smoke or not. Individuals who answered "yes" to questions "Have you smoked at least 100 cigarettes in life?" and "Do you now smoke cigarettes?"" were placed into the smoking group (Reeder et al., 2022; Y. Wang et al., 2024).*
- *Drinking status: two questions were combined to determine whether participants drink or not. Answering "yes" to questions "Have you drunk at least 12 drinks in the last year" and "Have you ever drunk 5 or more drinks a day?" were placed in the drinking group.*
- *Sleeping hours was coded as 3 factors ordinal category: Low: less than 6 hours a day; Average: 6-9 hours a day; High: 9 or more hours a day.*
- *Caffeine use in mg a day was transformed to a log10 base variable and later coded as a binary variable: low caffeine use if < log10(2.082) and High caffeine use if >= log10(2.082).*
- *Physical activity was a binary variable. "Yes" if the participant reported having performed any activity in the last 30 days.*

General and Mental Health:
- *Mental Health was coded as 5 levels ordinal variable, using PHQ9 questionnaire score: minimal or no symptoms of depression: 0-4, mild depression: 5-9, moderate depression 10-14, moderately severe depression: 15-19, 20 or more: severe depression).*
- *Other comorbidities: 1 if answering "yes", 0 if answering "no" to the question "Do you have any comorbidity?"*

Comment: Bias Describe any efforts to address potential sources of bias

Response: *"The following clinically relevant confounders were included in the multivariate analysis: (Andrea et al., 2015; Reeder et al., 2022; Y. Wang et al., 2024). Age, gender, race/ethnicity, family poverty index ratio (PIR), educational level, smoking status, alcohol consumption, food insecurity, sleep habits, physical activity, caffeine intake, comorbidities, and mental health status (PHQ-9 score) controlled for demographic, socio-economic, lifestyle and past medical history. "*

Comment: Study size Explain how the study size was arrived at

Response: *Thank you for your suggestion, it is stated in the METHODS section that the sample size of 2997 corresponds to 40 years old or more adults that have completed the Social Support questionnaire.*

"This analysis included 2,997 individuals, aged 40 or older, who completed the NHANES social support and immunization questionnaires"

Comment: Statistical methods when you describe the model you have to define the outcome variable and the predictors. For example it is unclear if the outcome is binary.

Response: *The description was updated. Now there are subheadings for each of these variables:*
"Independent variable - Hepatitis Immunization (binary)
"Outcome - Social support assessment (binary)"

Comment: Follow the strobe guidelines for reporting results too. Keep the same order as methods, so first description, then primary outcomes and then secondary outcomes.

Response: *We have included subtitles for each section, according to the STROBE guidelines*

Comment:. For all models I would suggest to describe which variables resulted as significant predictors of the outcome.

Response: *Thank you for your suggestion. We report it in Table 2 and Table 3.*

Comment: Here the question you want to answer is: is immunization able to provide higher odds of having higher level of social support ? Before running the models you should check the distribution of subjects in high and low social support and their immunization status. Do you see that almost all non immunized subjects has lower social support ? No you find similar proportion of subjects with with high level of social support in both immunized and non immunized category.

Response: *This comparison, including statistical tests were presented in Table 1.*

Comment: The model unadjusted is confirming that the odds of having higher social support are not influenced by immunization (please report the 95% CI). How to interpret this?

Response: *It is now reported in the results section: "Univariate analysis: Complete Iimmunization status was not positively associated with high social support level in both Model 1 (OR 0.84, 95% CI 0.63- 1.11, p = 0.22.) and Model 2 (OR 0.9, 95% CI 0.70-1.18, p = 0.47)**(Table 2)"***
We have included the following sentence in the DISCUSSION section:

"Of note, univariable analysis did not show a significant association with social support, probably due to the multiple confounders."

3. Results

Comment: Then when you adjust for other variables the OR change and it could gain significance. So what is the role of confounders? The results are reported in a confused way.

Response: The results section has been reformulated:
"Receiving complete immunization against hepatitis A and B was associated with highsocial support. (OR 3.15, 95% CI 1.03-9.66, p=0.04) after adjustment for income, food insecurity, education, race, age, gender, smoking status, caffeine consumption, sleeping hours, depression, and having comorbidities. Having a PIR between 2 to 3 (aOR = 4.42, 95% CI 1.41-13.93, p=0.01), sleeping more than 9 hours a day (aOR = 2.83, 95% CI 1.04-7.74), also were associated with better social support. Smoking status (aOR = 0.39, 95% CI 0.19-0.78, p=0.01) and eating less due to food insecurity were associated with lower social support (aOR = 0.26, 95% CI 0.11-0.57, p=0.001.
"Receiving at least one dose of vaccine for both hepatitis A and B was associated to a higher social support (OR 3.35, (95% CI 1.15-9.75, p=0.03) after adjustment for income, food insecurity, education, race, age, gender, smoking status, caffeine consumption, sleeping hours, depression, and having comorbidities.. Having a PIR between 2 to 3 (aOR = 4.27, 95% CI 1.21-15.11, p=0.02), also was associated with better social support. Smoking status (aOR = 0.39, 95% CI 0.18-0.84, p=0.02) and eating less due to food insecurity were associated with lower social support (aOR = 0.31, 95% CI 0.13-0.74, p=0.01) .

Comment: Please check that the text corresponds to tables. Please remember that CI95% can be helpful in correctly interpret results. Imagine you found: OR=1.60 == immunized patients are 60% more likely to have a high Social support than non immunized, and OR 1.01 means 1% more likely and if the CI is wide like 1.01 to 1.88 it means that in a future study investigating the same outcome in a similar population you can find that the immunized patients will be 1% to 88% more likely to have high social support: please think if it is useful for clinical decision making ? OR 0.89 means that ? immunized subjects are 11% less likely to have high social support.

Response: *The texts and tables were checked for typos.*

4. Discussion

Comment: Discussion should be reviewed in the light of correct interpretation of results and results should be compared with the literature, a final clinical recommendation should be give in the conclusion.

Response: *After reviewing the discussion section, the main results are interpreted in the first paragraph. The following paragraphs interpret and compare additional findings to the literature. We finish the conclusion with the following recommendation:*

"policymakers should direct resources into strategies that increase social support, benefiting also from increasing vaccination coverage and reducing chronic diseases in the general population."