

OPEN PEER REVIEW

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Peer Review Report for "Use of Complementary and Alternative Medicine Among Iranian Cancer Patients: A Prospective Cross-sectional Analysis of Prevalence, Patterns, and Drug Interactions"

Author(s): Mohsen Ebrahimifard, Mehran Sharifi, Ayda Moghadas, Azadeh Moghaddas

Review Timeline:

Submit Date:	25 Jan 2025
Revised Date:	11 Oct 2025
Accepted Date:	11 Oct 2025

Revision (0)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

Hossein Malekzadeh : Reviewer

18 Feb 2025

This manuscript presents a cross-sectional, descriptive-analytical study examining the prevalence and patterns of Complementary and Alternative Medicine (CAM) use, specifically medicinal herbs, among Iranian cancer patients. The study also assesses the potential for drug-herb interactions. Given the increasing use of CAM by cancer patients globally, and the potential risks associated with herb-drug interactions, this research addresses an important public health concern. The focus on the Iranian population, where cultural practices and access to healthcare may differ from Western countries, adds to the novelty and relevance of the findings.

REFEREE : Reviewer

20 Feb 2025

Dear Authors

I have reviewed this article carefully. My comments are as follows:

The first paragraph in the discussion section needs to add a reference.

In line 202, please delete the full form of CAM; the abbreviation is sufficient.

Please include some sentences about the limitations of this study in the discussion.

It is also suggested to add a figure to summarize the main findings of this study and cite it in the discussion.

REFEREE : Reviewer

24 Feb 2025

1. The title does not clearly state the study design. Adding "A Cross-Sectional Study" to the title would improve clarity. Also "Pattern and Frequency of Use as well as Drug-Herb Interactions" is wordy and it is better to be rewritten.
2. The keywords include relevant terms but should follow MeSH terms (e.g., "Herb Drug" is not a recognized MESH term; "Herbal Medicine" may be more appropriate).
3. The introduction could be more concise. It contains too many explanations for general concepts about CAM that are already well-known. Instead, the research gap should be more explicitly defined.
4. The study's novelty is slightly limited since similar studies exist, a stronger justification for novelty is needed.
5. The objectives are generally clear but could be stated at the end of the introduction.
6. Inclusion criteria are partially mentioned, but exclusion criteria are vague. Clarifying the specific selection process is necessary. The authors should explain how participants were recruited (randomized, voluntary, etc.).
7. Data collection methods (interviews, checklists) are described, but the potential for self-reporting bias should be discussed.
8. The study presents CAM usage statistics but does not critically assess whether CAM provided perceptible benefits (e.g., symptom relief, quality-of-life improvements).
9. The discussion should be refined by focusing more on clinical recommendations and patient safety.

OPEN PEER REVIEW

Revision (1)

Reply to Reviewers

Ideally, the reviewing process can significantly improve the submitted manuscripts by allowing the authors to take into account the advice of reviewers. Author(s) must reply to all reviewers' comments in a separate Word file, point by point. A "**Reply to Reviewers**" document is submitted along with revised manuscript during submission of revised files, summarizing the changes that the authors made in response to the reviewers' comments. The responses to reviewers' comments specifies how the authors addressed each comment the reviewers made.

You can read the authors' responses to the reviewers' comments in the next page.

Dear reviewers,

I really appreciate your valuable comments in the manuscript. We corrected the manuscript based on your comments.

We presented the revised manuscript in separated uploaded file. Also, we have highlighted the edited parts according to your comments. All changes are visible in track change format.

Thank you in advance

Reviewer 1:**Questions:****1:**

The first paragraph in the discussion section needs to add a reference. In line 202, please delete the full form of CAM; the abbreviation is sufficient. Please include some sentences about the limitations of this study in the discussion. It is also suggested to add a figure to summarize the main findings of this study and cite it in the discussion.

Response to reviewer;

Thank you for your consideration. We have revised the first paragraph of the discussion section and added both limitations and additional context to strengthen the discussion overall. These updates are visible in the highlighted sections. Furthermore, all abbreviations throughout the manuscript have been standardized.

The first paragraph changed to:

This study provides a novel contribution by combining a culturally specific analysis of CAM usage with a focused evaluation of potential drug-herb interactions among Iranian cancer patients—an area that has been underrepresented in the existing literature.

Herb consumption is on the rise in Iran, especially among patients with chronic diseases. Cancer management has become a primary focus of public health policies, claiming considerable healthcare resources. Despite advancements in conventional medical treatments, they often fail to fully address patients' needs. As a result, there has been a growing trend among cancer patients toward using medicinal plants (23). These are available either as unprocessed herbs (sold in traditional perfumeries) or as formulated herbal medicines (distributed in pharmacies). The use of CAM, including herbal remedies, varies significantly across cultures and regions due to differing perspectives and practices. Physicians' approaches to CAM also range widely, from active encouragement to skepticism or outright criticism (24).

Limitation section:

While this study has provided valuable insights, it is essential to reflect on the challenges faced and their potential impact on the results. CAM research is confronted with a lot of challenges. One limitation of the study is the absence of multivariate analysis to identify independent predictors of CAM use or drug-herb interaction risk. Another limitation is science gives science crucial tools for assessing CAM, but the scientific culture and scientists themselves can subvert meaningful assessment. Most of the initial clinical trials on CAM have serious methodological flaws such as low statistical power including poor controls and no comparisons. In this study, we face more constraints than other studies due to variations in treatments and non-standardized herbal medicines. Future research should include regression models to explore these associations more rigorously.

Reviewer 2:

Questions:

2:

1. *The title does not clearly state the study design. Adding "A Cross-Sectional Study" to the title would improve clarity. Also "Pattern and Frequency of Use as well as Drug-Herb Interactions" is wordy and it is better to be rewritten.*

Answer: It has changed to "Use of Complementary and Alternative Medicine Among Iranian Cancer Patients: A Cross-Sectional Analysis of Prevalence, Patterns, and Drug Interactions"

it

2. *The keywords include relevant terms but should follow MeSH terms (e.g., "Herb Drug" is not a recognized MESH term; "Herbal Medicine" may be more appropriate).*

Answer: It has changed to **"Keywords:** Cancer, Complementary Therapies, Alternative Medicine, Phytotherapy, Health Surveys, Prevalence"

3. *The introduction could be more concise. It contains too many explanations for general concepts about CAM that are already well-known. Instead, the research gap should be more explicitly defined.*

Answer: We completely re-write the introduction section, added some new information from recently published articles. All changes have been highlighted. (Page 3-4).

4. *The study's novelty is slightly limited since similar studies exist, a stronger justification for novelty is needed.*

5. *The objectives are generally clear but could be stated at the end of the introduction.*

Answer: we added this part to the introduction section:

Despite extensive global research, CAM use among Iranian cancer patients remains underexplored. In Iran, traditional herbal remedies are deeply embedded in cultural and religious practice, readily accessible through Attari shops and informal vendors. However, little data exists regarding clinical safety, particularly the potential for drug-herb interactions, which may compromise oncology care (14). Cultural beliefs, lack of patient-provider communication, and unregulated access pose unique challenges within this context. This study aims to address this critical gap by assessing the prevalence, patterns, motivations, and safety considerations—including interaction risks—of CAM use among Iranian cancer patients.

6. *Inclusion criteria are partially mentioned, but exclusion criteria are vague. Clarifying the specific selection process is necessary. The authors should explain how participants were recruited (randomized, voluntary, etc.).*

Answer: we added this part to the method's section: (Page 3, highlighted parts)

Eligibility criteria required that participants be Persian-speaking adults of any gender with a confirmed cancer diagnosis. They had to be aware of their diagnosis and either undergoing anticancer treatment—such as antineoplastic chemotherapy, endocrine therapy, radiotherapy, or surgery—at the time of the survey, or have completed such treatment within the preceding three years. Additional requirements included the ability to comprehend the survey questions, absence of any condition that would render questionnaire completion inappropriate or excessively burdensome, and a willingness to participate in the study.

7. Data collection methods (interviews, checklists) are described, but the potential for self-reporting bias should be discussed.

Answer: We added some explanation in data collection section, page 4

To enhance accuracy, responses were cross-checked with participants. However, we acknowledge the potential for self-reporting bias, which may affect the reliability of reported data due to recall errors or personal biases. Efforts to minimize this included training student researcher to probe for consistent responses and providing clear instructions to participants.

8. The study presents CAM usage statistics but does not critically assess whether CAM provided perceptible benefits (e.g., symptom relief, quality-of-life improvements).

Answer: The aim of this study was to identify and categorize the most probable CAM usage among cancer patients as a special group of patients. However, the outcome of using CAM should be checked in future studies. We added some explanation in discussion part, page 10.

9. The discussion should be refined by focusing more on clinical recommendations and patient safety.

Answer: the discussion part has been edited according to all comments and new data based on logistic regression's association.

Changes have been highlighted.

Associate Editor's Comments:

Associate Editor 1:

Comments to the Authors

1. In abstract section, be more specific about the implications of the findings. For example, instead of just saying "the likelihood of drug-herb interactions appears to be substantial," suggest a specific action (e.g., "underscores the need for improved communication between patients and oncologists regarding CAM use").

Answer: All parts were rephrased again as you can check the manuscript.

2. In introduction section, provide more specific rationale for focusing on the Iranian population. Discuss any unique cultural beliefs, healthcare access issues, or traditional medicine practices that make this population particularly relevant to study.

Answer: We added some information in page 2-3, introduction section.

3. In introduction section, While the introduction cites studies on CAM use in cancer patients, consider including more recent or impactful studies, particularly meta-analyses or systematic reviews, to emphasize the importance of the topics.

Answer: We added reference 12-14 with explanation in introduction part.

4. In methods section, provide a clear and concise definition of CAM used in the study to ensure consistent understanding among participants and readers.

Answer: We added some explanation in page 2 and definition in page 4, data collection part.

5. Elaborate on the specific questions included in the questionnaire related to drug-herb interactions. How were patients asked about their use of prescription medications and potential interactions?

Answer: We added Drug-herb interaction section in page 4-5.

6. Consider conducting multivariate analysis to identify factors independently associated with CAM use and the risk of drug-herb interactions.

Answer: We performed the Logistic regression to assess the likelihood of CAM use based on various demographic and clinical predictors. Information was added to page 6, 8, 12 and table 5.

7. Proofread the manuscript carefully to correct any typos or grammatical errors
8. Ensure that all references are accurate and complete, and that they follow the journal's style guidelines.
9. Define all acronyms at first use (e.g., CAM).

Answer: We edited the mention comments.

Kind regards,

Azadeh Moghaddas

Corresponding author

Associate Professor of Clinical Pharmacy

OPEN PEER REVIEW

Revision (1)

REFEREE : Reviewer

25 Sep 2025

Thank you for your careful revisions. In the abstract and title, you describe the work as “cross-sectional”, but in the methods (line 95), you call it a “prospective cross-sectional” study. I recommend clarifying the study design description for consistency. The limitation section contains unclear sentences, such as: “science gives science crucial tools for assessing CAM, but the scientific culture and scientists themselves can subvert meaningful assessment”. This should be revised for clarity.

REFEREE : Associate Editor

1 Oct 2025

The authors' response to the reviewers' comments and the subsequent revision of the manuscript demonstrate a high level of scholarly diligence and responsiveness. They systematically addressed all major concerns raised by Reviewer 1, Reviewer 2, and the Associate Editor. Key improvements include the addition of a clear study design (“A Cross-Sectional Study”) to the title, a more focused and concise introduction that better articulates the research gap particularly the lack of data on CAM use and drug-herb interactions among Iranian cancer patients and the inclusion of a formal definition of CAM based on NCCIH criteria. The methods section was substantially strengthened with explicit eligibility and exclusion criteria, details on recruitment (simple random sampling from inpatient and outpatient oncology settings), and clarification of data collection procedures using the culturally adapted I-CAM-IR questionnaire.

Importantly, the authors conducted both univariate and multivariate logistic regression analyses as requested, identifying significant independent predictors of CAM use: younger age, male gender, lower education level, metastatic disease, and longer treatment duration. These findings are now clearly presented in Table 5 and discussed in the results and discussion sections. The discussion was also refocused to emphasize clinical implications and patient safety, with specific examples of high-risk drug-herb interactions (e.g., garlic with warfarin or aspirin increasing bleeding risk). The authors acknowledged limitations such as self-reporting bias and the inability to assess clinical outcomes like symptom relief or quality of life, while appropriately calling for future interventional or longitudinal studies. However, a critical inconsistency remains in the limitations section (lines 432–433), where the authors state, “One limitation of the study is the absence of multivariate analysis...” despite having performed and reported multivariate logistic regression throughout the revised manuscript. This appears to be an oversight, likely resulting from incomplete editing of the original draft. Additionally, some adjusted odds ratios reported in the results (e.g., aOR = 0.003 for treatment duration predicting herb use)

are unusually low and may reflect typographical errors or misinterpretation; such values warrant careful verification, as they could confuse readers or undermine the statistical credibility of the findings.

So, the revised manuscript is significantly improved, with enhanced methodological rigor, clearer clinical relevance, and stronger contextualization within Iran's unique sociocultural landscape where traditional herbal remedies are widely accessible through Attari shops and often used without medical supervision. The high rate of non-disclosure (91.5%) and the identification of clinically significant herb-drug interactions underscore the urgent need for routine CAM screening in oncology settings. With minor corrections particularly to the erroneous statement about the lack of multivariate analysis and verification of statistical outputs the manuscript would be well-positioned for acceptance as a valuable contribution to the field of integrative oncology.

REFEREE : EIC

1 Oct 2025

Our impression is that the above-mentioned manuscript could become suitable for publication in JJNPP. However, the criticism from the referees requires that we defer a final decision until you have considered their remarks and revised your manuscript accordingly.

OPEN PEER REVIEW

Revision (2)

Reply to Reviewers

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You can read the authors' responses to the reviewers' comments in the next page.

Thank you for your thoughtful and constructive feedback. I have carefully reviewed all the comments and made the necessary revisions throughout the manuscript in green color. Each point raised has been addressed to ensure clarity, accuracy, and alignment with the reviewers' suggestions. I appreciate your time and effort in helping improve the quality of this work.

Dear reviewers,

I really appreciate your valuable comments in the manuscript. We corrected the manuscript based on your comments.

We presented the revised manuscript in separated uploaded file. Also, we have highlighted the edited parts according to your comments. All changes are visible in track change format.

Thank you in advance

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7. Proofread the manuscript carefully to correct any typos or grammatical errors
8. Ensure that all references are accurate and complete, and that they follow the journal's style guidelines.
9. Define all acronyms at first use (e.g., CAM).

Answer: We edited the mention comments.

Kind regards,

Azadeh Moghaddas

Corresponding author

Associate Professor of Clinical Pharmacy

OPEN PEER REVIEW

Revision (2)

REFeree : Reviewer

6 Oct 2025

Dear AE,

Thank you very much for giving me the opportunity to review this manuscript.

Here are my comments:

1. A minor language edit can further strengthen the manuscript.
2. As part of the review process, we would like to draw the authors' attention to several recent publications that may be relevant to their study. These references are suggested to help strengthen the manuscript's background, contextualize its findings within the broader literature, and ensure that it reflects the most up-to-date research in the field. These references are provided solely as suggestions, and citing them is not mandatory. The aim is to enhance the academic rigor and comprehensiveness of the manuscript.

These article(s) are as below:

A. Treatment of Complementary and Alternative Medicine in Patients with Chronic Viral Hepatitis from Somalia

* Reason: This study is highly relevant as it provides cross-cultural and cross-disease evidence of the widespread use of specific, culturally-informed CAM therapies, strongly reinforcing your finding that CAM use is a pervasive patient-driven phenomenon. Citing it would powerfully generalize your conclusions beyond an Iranian cancer context and highlight the universal need for clinician awareness and open communication about CAM across different medical conditions and cultures.

** Link: <https://brieflands.com/articles/hepatmon-150636>

B. Complementary and Alternative Medicine Use in Diabetic Foot Ulcer Patients at a Shiraz Diabetes Clinic: A Cross-Sectional Study

* Reason: This study is highly relevant as it provides robust, population-specific evidence that CAM use is extremely prevalent among Iranian patients with a different chronic condition (diabetic foot ulcers), powerfully reinforcing your finding that this is a widespread national health behavior. Citing it would strengthen your argument for routine clinical screening by demonstrating that the issue extends beyond oncology to other specialties, making it a systemic priority.

** Link: <https://brieflands.com/articles/semj-145592>

C. A Investigation of Medical Ethics in Clinical Trials Involving Herbal and Complementary Medicines

* Reason: This study is highly relevant as it provides direct, empirical evidence of ethical compliance and, crucially, a significant gap (24% of trials not mentioning consent) in clinical trials specifically involving herbal products and supplements. Citing it would powerfully substantiate your paper's conclusion by demonstrating that the lack of communication and oversight you identified is a systemic issue that even extends to formal research settings, thereby strengthening your call for

integrating ethical screening and documentation into routine oncology care.

** Link: <https://brieflands.com/articles/erms-161588>

Final Decision: Minor Revision

Kind Regards | Publishing Assistant

REFeree : Reviewer

8 Oct 2025

Thank you for the opportunity to review the revised manuscript. The authors have addressed previous comments effectively and improved the clarity of the paper, and the manuscript is suitable for publication with minor language polishing.

REFeree : Associate Editor

8 Oct 2025

The Ms needs some minor revisions before suitable for publication in JJNPP.

REFeree : EIC

8 Oct 2025

Our impression is that the above-mentioned manuscript could become suitable for publication in JJNPP. However, the criticism from the referees requires that we defer a final decision until you have considered their remarks and revised your manuscript accordingly.

OPEN PEER REVIEW

Revision (3)

Reply to Reviewers

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You can read the authors' responses to the reviewers' comments in the next page.

We sincerely thank both reviewers for their thoughtful and constructive feedback on our manuscript. We are grateful for the opportunity to revise and improve our work based on your insights.

Reviewer 0:

We appreciate your positive evaluation and are pleased that the revisions have addressed your previous concerns. In response to your suggestion, we have carefully reviewed the manuscript and performed additional language polishing to enhance clarity and readability. (Blue highlighted sentences)

Reviewer 1:

Thank you for your detailed and insightful comments. We acknowledge the importance of minor language edits and have revised the manuscript accordingly to improve fluency and precision.

We also appreciate the suggested references and recognize their relevance in strengthening the contextual framework of our study. Accordingly, we have incorporated the following citations into the revised manuscript to enhance its academic rigor and situate our findings within the broader literature: (Find the discussion part in blue highlighted sentences)

- The study on CAM use among patients with chronic viral hepatitis in Somalia (Hepat Mon, 2023) has been cited to support the cross-cultural and cross-disease relevance of CAM practices, reinforcing our conclusion that CAM use is a widespread, patient-driven phenomenon across diverse medical contexts.
- The cross-sectional study on CAM use in diabetic foot ulcer patients in Shiraz (SEMJ, 2023) has been referenced to highlight the systemic nature of CAM utilization in Iran, extending our findings beyond oncology and supporting the call for routine clinical screening across specialties.
- The investigation into ethical practices in clinical trials involving herbal and complementary medicines (ERMS, 2024) has been cited to substantiate our discussion on the lack of communication and oversight in CAM use, emphasizing the need for ethical screening and documentation in oncology care.

We believe these additions have strengthened the manuscript's background and discussion sections, and we thank you again for your valuable recommendations.

OPEN PEER REVIEW

Revision (3)

REFEREE : EIC

11 Oct 2025

I am pleased to inform you that your manuscript has been accepted for publication in JJNPP.

Your work underwent a rigorous peer-review process, and the reviewers and editorial board were impressed by the originality, scientific rigor, and relevance of your findings. We believe your contribution will be of significant interest to our readership and will advance the field of natural pharmaceutical products.

Before publication, our production team will contact you regarding final formatting, proofs, and any necessary administrative steps. Please ensure that all authors have approved the final version of the manuscript and that any required ethical or copyright documentation is in order.

On behalf of the editorial board, I congratulate you and your co-authors on this excellent work and thank you for choosing to publish in JJNPP.