Comprehensive Health and Biomedical Studies
Volume 3 · Issue 3 · e158042
OPEN PEER REVIEW

Patterns of Methadone and Opium Syrup Use in Drug Abuse Treatment in Rasht

Anita Mosavat, Amirali Soleymani Nejad, Negar Vahdani, Zohreh Kazempour Keleshteri, Alireza Badsar, Saeed Biroudian, Koroush Delpasand

SUBMITTED	REVISED	ACCEPTED	DOI
28 Jun 2024	30 Nov 2024	26 Jan 2025	10.5812/chbs-158042

About this report

This open peer review (OPR) report shows the public comments made on this article during peer review, by the reviewers, the associate editor and the editor-in-chief, for every revision round, together with the authors' replies. Comments appear only with the consent of the people who wrote them. Reviewers who chose to sign their report are named; the others are shown as "Referee". Comments are edited for language only, and confidential remarks to the editors are not included.

More about open peer review: brieflands.com/knowledgebase/opr

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1 Original submission

2 comments · 24 Nov 2024 – 25 Nov 2024

Referee 1 Reviewer

MINOR REVISION 24 Nov 2024

Dear Editor
Thanks to the research team. Some comments are provided to improve the manuscript titled “Patterns of Methadone and Opium Syrup Use in Drug Abuse treatment: A Study in Rasht City”:
1. The title needs editing. Usually, after “ : ” it is better to state the type of study rather than the location of the study.
2. In the Methods section of the abstract, state that you obtained the information from the patient or files, as mentioned in the Methods section of the article. The sampling method should also be mentioned.
3. Considering that men are mentioned in the conclusion, it is better to state the ratio of women to men in the results.

4. The inclusion and exclusion criteria for the study should be mentioned in the methods.

5. Please check your keywords with Mesh.

6. It is not recommended to use subject pronouns in the text of articles. It is better to rewrite these sentences.

7. The introduction is not structured and only presents relevant statistics. There is no explanation of what the gap in studies in this field is and why the authors want to conduct this study. The purpose of the introduction is to answer the question: What will the results of this study contribute to science in this field? The last paragraph also needs to be revised.

8. The references are written twice.

9. It is recommended that the entire text be re-edited by an English-language editor.

Please highlight all the amendments in your manuscript or indicate them by using tracked changes.

Referee 2 Reviewer

MAJOR REVISION 25 Nov 2024

Greetings and regards
The writing of the article is at an acceptable level, but the value of its findings is limited.
Inclusion and exclusion criteria should be mentioned in the article's methodology.

2

Revision 1

AUTHORS' RESPONSE TO REVIEWERS

Authors' reply to reviewers

The next pages contain the authors' point-by-point reply to the comments of this revision round, as submitted with the revised manuscript. It is published as the authors wrote it.

In response to the article review

the manuscript titled: “Patterns of Methadone and Opium Syrup Use in Drug Abuse treatment: A Study in Rasht City”:
1. The title needs editing. Usually, after “ : ” it is better to state the type of study rather than the location of the study. Thanks for your insightful comment, it has been corrected.”
Patterns of Methadone and Opium Syrup Use in Drug Abuse Treatment in Rasht ”
2. In the method of the abstract, write that you completed the information from the patient or files, as mentioned in the article method. The sampling method should also be mentioned. Thanks for your insightful comment, it has been corrected.” Data were collected using a checklist from patient records included demographic characteristics such as age, sex, marital status, occupation, place of residence, and education level**.** The sampling method was convenience”
3. Considering that men are mentioned in the conclusion, it is better to state the ratio of women to men in the results. it has been corrected” These findings underscore the need for gender-specific interventions and preventive strategies to address the unique challenges faced by men compared to women in substance abuse contexts.”
4. The inclusion and exclusion criteria for the study should be mentioned in the methods.

Inclusion criteria included patients diagnosed with Methadone or Opium Syrup abuse and indivisuals aged 18 years and older. Exclusion criteria included incomplete or partially completed patient records. Additionally, patients with concurrent psychiatric disorders and those who were simultaneously using multiple substances other than methadone or opium syrup were excluded from the study.

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Keywords: Methadone, Opium, Substance-Related Disorders
6. It is not recommended to use subject pronouns in the text of articles. It is better to rewrite these sentences. it has been corrected

7. The introduction is not structured and only presents relevant statistics. There is no explanation of what the gap in studies in this field is and why the authors want to do this. The purpose of the introduction is to answer the question: What will the results of this study contribute to science in this field? The last paragraph also needs to be revised.
Thanks for your insightful comment, it has been corrected

Iran's substance abuse research landscape has undergone substantial transformation, paralleling socioeconomic transitions and urbanization trends. While retrospective investigations have suggested correlations between opium consumption and diverse health complications, a notable absence of comprehensive prospective studies exists regarding mortality implications.(16).

This research aimed to provided a comprehensive assessment of substance abuse patterns in Rasht county. Generated empirical data on methadone and opium syrup usage.Also, developed evidence-based insights for targeted intervention strategies.

8. The references are written twice. it has been corrected

9. It is recommended that the entire text be re-edited by an English-language editor. it has been corrected

Please highlight all the amends in your manuscript or indicate them by using tracked changes. it has been corrected
Reviewer 2:
Greetings and regards
The writing of the article is at an acceptable level, but the content value of its findings is few
Inclusion and exclusion criteria should be mentioned in the article's methodology it has been corrected

Inclusion criteria included patients diagnosed with Methadone or Opium Syrup abuse and indivisuals aged 18 years and older. Exclusion criteria included incomplete or partially completed patient records. Additionally, patients with concurrent psychiatric disorders and those who were simultaneously using multiple substances other than methadone or opium syrup were excluded from the study.

2 Revision 1

0 comments

No public comments in this round.

3

Revision 2

AUTHORS' RESPONSE TO REVIEWERS

Authors' reply to reviewers

The next pages contain the authors' point-by-point reply to the comments of this revision round, as submitted with the revised manuscript. It is published as the authors wrote it.

Major Comments:

- The abstract lacks detailed information on the study size and how it was determined. Thanks a lot, We acknowledge the reviewer's comment. The abstract will be revised to include the total sample size (n=149) and to briefly mention that this represented a full census of eligible cases within the treatment centers during the study period.
- There is no mention of efforts to address potential sources of bias. Thanks a lot, We agree that addressing potential biases is crucial. The abstract will be updated to acknowledge the use of convenience sampling and to note that this may introduce selection bias. The full text will include a more detailed discussion of potential biasesand limitations.
- The abstract does not discuss the limitations of the study or the generalisability of the findings.

  Thanks a lot, We concur with the reviewer's assessment. The abstract will be revised to briefly mention the limitations associated with the cross-sectional design and the potential challenges in generalizing the findings beyond the specific geographic region (Rasht). A more comprehensive discussion of these limitations will be included in the full text.

Minor Comments:

- The abstract could benefit from a more detailed description of the statistical methods used. We agree. The abstract will be revised to mention the key statistical tests used, including the Kolmogorov-Smirnov test (for normality assessment) and the Chi-square test (for analyzing associations between categorical variables).
- Providing confidence intervals or adjusted estimates would enhance the clarity of the results. I didn't understand the meaning of this question.
- Including a discussion on the comparison with similar studies would strengthen the interpretation of the findings. We acknowledge the importance of contextualizing our findings within the existing literature. The discussion section will be expanded to include a more thorough comparison of our results with those of similar studies conducted in Iran and other regions, highlighting both consistencies and discrepancies.

3 Revision 2

1 comment · 18 Mar 2025

Associate Editor

MINOR REVISION 18 Mar 2025

Question: Indicate the study's design with a commonly used term in the title or the abstract.
Peer Review: The abstract clearly identifies the study as a "cross-sectional study" in the methods section.

Abstract
Question: Provide in the abstract an informative and balanced summary of what was done and what was found.
Peer Review: The abstract provides a summary of the study's background, methods, results, and conclusions. It mentions the frequency of methadone and opium syrup use and highlights the need for gender-specific interventions.

Introduction
Question: Explain the scientific background and rationale for the investigation being reported.
Peer Review: The background section briefly mentions the limited studies on methadone and opium syrup use in the Iranian population, providing a rationale for the study.

Objectives
Question: State specific objectives including any prespecified hypotheses.
Peer Review: The objective is to examine the frequency of methadone and opium syrup use in treating drug abuse.

Methods
Question: Present key elements of study design early in the paper.
Peer Review: The methods section describes the study as a cross-sectional study conducted on patients with a history of methadone and opium syrup consumption.

Setting
Question: Describe the setting, locations, and relevant dates including periods of recruitment, exposure, follow-up, and data collection.
Peer Review: The study was conducted in Rasht from 2018 to 2022.

Eligibility Criteria
Question: Give the eligibility criteria and the sources and methods of selection of participants.
Peer Review: The study included patients with a history of methadone and opium syrup consumption, using a convenience sampling method.

Data Sources/Measurement
Question: For each variable of interest, give sources of data and details of methods of assessment (measurement).
Peer Review: Data were collected using a checklist from patient records, including demographic characteristics.

Bias
Question: Describe any efforts to address potential sources of bias.
Peer Review: The abstract does not mention any efforts to address potential sources of bias.

Study Size
Question: Explain how the study size was arrived at.

Peer Review: The abstract does not provide information on how the study size was determined.

Quantitative Variables
Question: Explain how quantitative variables were handled in the analyses.
Peer Review: The abstract mentions the average age and the statistical significance of the difference in age based on substance type.

Statistical Methods
Question: Describe all statistical methods including those used to control for confounding.
Peer Review: The abstract mentions a statistically significant difference in age with a p-value but does not detail the statistical methods used.

Results
Question: Report numbers of individuals at each stage of the study.
Peer Review: The abstract provides percentages of participants using methadone and opium syrup but does not report the total number of participants.

Descriptive Data
Question: Give characteristics of study participants and information on exposures and potential confounders.
Peer Review: The abstract provides the average age and percentages of substance use but lacks detailed demographic data.

Outcome Data
Question: Report numbers of outcome events or summary measures.
Peer Review: The abstract reports the percentage of participants using each substance.

Main Results
Question: Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision.
Peer Review: The abstract provides a p-value for the age difference but does not include confidence intervals or adjusted estimates.

Discussion
Question: Summarize key results with reference to study objectives.
Peer Review: The conclusions highlight the need for gender-specific interventions, aligning with the study's objectives.

Limitations
Question: Discuss limitations of the study taking into account sources of potential bias or imprecision.
Peer Review: The abstract does not discuss any limitations of the study.

Interpretation
Question: Give a cautious overall interpretation considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence.
Peer Review: The abstract provides a general interpretation but lacks a discussion on limitations or comparisons with similar studies.

Generalisability
Question: Discuss the generalizability (external validity) of the study results.
Peer Review: The abstract does not discuss the generalizability of the findings.

Major Comments:

The abstract lacks detailed information on the study size and how it was determined.
There is no mention of efforts to address potential sources of bias.
The abstract does not discuss the limitations of the study or the generalizability of the findings.

Minor Comments:

The abstract could benefit from a more detailed description of the statistical methods used.
Providing confidence intervals or adjusted estimates would enhance the clarity of the results.
Including a discussion on the comparison with similar studies would strengthen the interpretation of the findings.

Revision: 2

Based on the abstract provided, the study design is a cross-sectional study. Therefore, I will use the STROBE-cross-sectional checklist to conduct the peer review.
Peer Review Using STROBE-Cross-Sectional Checklist

Title and Abstract
Question: Indicate the study's design with a commonly used term in the title or the abstract.
Review: The abstract mentions that the study is a "cross-sectional study," which is appropriate.

Abstract
Question: Provide in the abstract an informative and balanced summary of what was done and what was found.
Review: The abstract provides a clear summary of the study's background, methods, results, and conclusions.

Introduction
Background/Rationale: Explain the scientific background and rationale for the investigation being reported.
Review: The background is briefly mentioned, highlighting the limited studies on methadone and opium syrup use in Iran.

Objectives
Question: State specific objectives including any prespecified hypotheses.
Review: The objective is clearly stated as examining the frequency of methadone and opium syrup use in treating drug abuse.

Methods
Study Design: Present key elements of study design early in the paper.
Review: The study design is mentioned as cross-sectional.

Setting
Question: Describe the setting, locations, and relevant dates including periods of recruitment, exposure, follow-up, and data collection.
Review: The study was conducted in Rasht from 2018 to 2022.

Eligibility Criteria
Question: Give the eligibility criteria and the sources and methods of selection of participants.
Review: Participants were selected based on a history of methadone and opium syrup consumption.

Variables
Question: Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria if applicable.
Review: The abstract does not explicitly define these elements.

Data Sources/Measurement
Question: For each variable of interest, give sources of data and details of methods of assessment (measurement).
Review: Data were collected using a checklist from patient records.

Bias
Question: Describe any efforts to address potential sources of bias.
Review: The abstract does not mention efforts to address bias.

Study Size
Question: Explain how the study size was arrived at.
Review: The study size of 149 patients is mentioned, but the rationale is not provided.

Quantitative Variables
Question: Explain how quantitative variables were handled in the analyses.
Review: The abstract mentions statistical tests used, including the Kolmogorov-Smirnov test and Chi-square test.

Statistical Methods
Question: Describe all statistical methods including those used to control for confounding.
Review: Statistical methods are described, but there is no mention of controlling for confounding.

Results
Participants: Report numbers of individuals at each stage of the study.
Review: The number of participants is reported as 149.

Descriptive Data
Question: Give characteristics of study participants (e.g., demographic, clinical, social) and information on exposures and potential confounders.
Review: Demographic characteristics such as age, sex, marital status, occupation, place of residence, and education level are included.

Outcome Data
Question: Report numbers of outcome events or summary measures.
Review: The results include the percentage of participants abusing methadone and opium syrup.

Main Results
Question: Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision.
Review: A statistically significant difference in age based on substance type is reported.

Discussion
Key Results: Summarize key results with reference to study objectives.
Review: The conclusion emphasizes the need for gender-specific and geographical interventions.

Limitations
Question: Discuss limitations of the study taking into account sources of potential bias or imprecision.
Review: Limitations are not discussed in the abstract.

Interpretation
Question: Give a cautious overall interpretation considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence.
Review: The interpretation is focused on the need for interventions but lacks a discussion of limitations.

Generalisability
Question: Discuss the generalizability (external validity) of the study results.

Review: Generalizability is not discussed.

Funding
Question: Give the source of funding and the role of the funders for the present study.
Review: Funding is not mentioned.

Categorization of Comments

Major Comments:

Lack of discussion on potential sources of bias and limitations.
No mention of controlling for confounding variables.

Minor Comments:

The rationale for the study size is not provided.
Generalizability and funding are not discussed.

This review highlights areas where the abstract could be improved to align more closely with the STROBE-cross-sectional checklist.

4

Revision 3

AUTHORS' RESPONSE TO REVIEWERS

Authors' reply to reviewers

The next pages contain the authors' point-by-point reply to the comments of this revision round, as submitted with the revised manuscript. It is published as the authors wrote it.

Categorization of Comments

Major Comments:

- Lack of discussion on potential sources of bias and limitations.

Thank you for pointing out the need for an explicit discussion of potential sources of bias and limitations. We have now addressed the following biases and limitations in the revised manuscript:

Selection Bias: We acknowledge that this study used convenience sampling from a single city (Rasht), which may not fully represent substance abuse patterns across other regions of Iran.

Cross-Sectional Design: The study's cross-sectional nature limits its ability to identify causal relationships or observe trends over time.

Exclusion Criteria Impact: Patients with concurrent psychiatric disorders and those using multiple substances other than methadone or opium syrup were excluded. This may have underestimated the diversity of substance abuse patterns.

- No mention of controlling for confounding variables.

We agree that controlling for confounding variables is crucial in observational studies. While this study aimed to explore basic associations rather than causations, variables such as age, gender, and residence type were analyzed to assess their relationship with substance abuse patterns. In future studies, we plan to use multivariate analyses to control for confounding factors. A note has been added in the Discussion section specifying this limitation and the need for more robust analyses in further research.

Minor Comments:

- The rationale for the study size is not provided.

We appreciate your feedback regarding the lack of rationale for the study size. The sample of 149 patient records was selected as a full census of all eligible cases available during the study period (2018–2022). This reflects the total number of records meeting the inclusion and exclusion criteria in this specific region. This rationale has been clarified in the Methods section to ensure transparency. However, we acknowledge that the sample size limits the generalizability of results and have mentioned this as a limitation in the revised manuscript.

- Generalisability and funding are not discussed.

Thank you for pointing out the need to address generalizability and funding.

Generalisability: The study was conducted in Rasht, focusing on a specific geographic and demographic group. While the insights are valuable for local healthcare planning, the findings may not translate to other regions or countries with different social, economic, and healthcare contexts. A note highlighting this limitation has been added to the Discussion section.

Funding: The study was conducted without external funding or financial support. This has now been mentioned in the Funding section of the manuscript to ensure full transparency.

4 Revision 3

2 comments · 1 May 2025 – 16 May 2025

Associate Editor

MAJOR REVISION 1 May 2025

Revision: 1

Based on the information provided, the study design is a cross-sectional study. Therefore, I will use the STROBE-cross-sectional checklist to perform the peer review of the abstract. Here are the results:

Title and Abstract
Question: Indicate the study's design with a commonly used term in the title or the abstract.
Peer Review: The abstract clearly identifies the study as a "cross-sectional study" in the methods section.

Abstract
Question: Provide in the abstract an informative and balanced summary of what was done and what was found.
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Peer Review: The study was conducted in Rasht from 2018 to 2022.

Eligibility Criteria
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Peer Review: The study included patients with a history of methadone and opium syrup consumption, using a convenience sampling method.

Data Sources/Measurement
Question: For each variable of interest, give sources of data and details of methods of assessment (measurement).
Peer Review: Data, including demographic characteristics, were collected from patient records using a checklist.

Bias
Question: Describe any efforts to address potential sources of bias.
Peer Review: The abstract does not mention any efforts to address potential sources of bias.

Study Size
Question: Explain how the study size was arrived at.
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Major Comments:

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Minor Comments:

The abstract could benefit from a more detailed description of the statistical methods used.
Providing confidence intervals or adjusted estimates would enhance the clarity of the results.
Including a discussion on the comparison with similar studies would strengthen the interpretation of the findings.

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Categorization of Comments

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No mention of controlling for confounding variables.

Minor Comments:

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Editor-in-Chief MAJOR REVISION 16 May 2025

In response to the review of
the manuscript titled “Patterns of Methadone and Opium Syrup Use in Drug Abuse treatment: A Study in Rasht City”:
1. The title needs editing. Usually, after “ : ” it is better to state the type of study rather than the location of the study. Thanks for your insightful comment. It has been corrected: “ Patterns of Methadone and Opium Syrup Use in Drug Abuse Treatment in Rasht ”
2. In the Methods section of the abstract, state that you collected the information from patients or their records, as mentioned in the Methods section of the article. The sampling method should also be mentioned. Thanks for your insightful comment. It has been corrected: “ Data were collected using a checklist from patient records included demographic characteristics such as age, sex, marital status, occupation, place of residence, and education level. The sampling method was convenience”
3. Considering that men are mentioned in the conclusion, it is better to state the ratio of women to men in the results. It has been corrected: “ These findings underscore the need for gender-specific interventions and preventive strategies to address the unique challenges faced by men compared to women in substance abuse contexts.”
4. The inclusion and exclusion criteria for the study should be mentioned in the methods.
Inclusion criteria included patients diagnosed with Methadone or Opium Syrup abuse and individuals aged 18 years and older. Exclusion criteria included incomplete or partially completed patient records. Additionally, patients with concurrent psychiatric disorders and those who were simultaneously using multiple substances other than methadone or opium syrup were excluded from the study.

5. Please check your keywords with Mesh. It has been corrected.
Keywords: Methadone, Opium, Substance-Related Disorders
6. It is not recommended to use subject pronouns in the text of articles. It is better to rewrite these sentences. It has been corrected.

7. The introduction is not structured and only presents relevant statistics. There is no explanation of what the gap in studies in this field is and why the authors want to do this. The purpose of the introduction is to answer the question: What will the results of this study contribute to science in this field? The last paragraph also needs to be revised.
Thanks for your insightful comment. It has been corrected.
Iran's substance abuse research landscape has undergone substantial transformation, paralleling socioeconomic transitions and urbanization trends. While retrospective investigations have suggested correlations between opium consumption and diverse health complications, a notable absence of comprehensive prospective studies exists regarding mortality implications (16).
This research aimed to provide a comprehensive assessment of substance abuse patterns in Rasht county. It generated empirical data on methadone and opium syrup usage. It also developed evidence-based insights for targeted intervention strategies.

8. The references are written twice. It has been corrected.

9. It is recommended that the entire text be re-edited by an English-language editor. It has been corrected.

Please highlight all the amendments in your manuscript or indicate them by using tracked changes. It has been corrected.
Reviewer 2:
Greetings and regards
The writing of the article is at an acceptable level, but the value of its findings is low.
Inclusion and exclusion criteria should be mentioned in the article's methodology. It has been corrected.
Inclusion criteria included patients diagnosed with Methadone or Opium Syrup abuse and individuals aged 18 years and older. Exclusion criteria included incomplete or partially completed patient records. Additionally, patients with concurrent psychiatric disorders and those who were simultaneously using multiple substances other than methadone or opium syrup were excluded from the study.

5

Revision 4

AUTHORS' RESPONSE TO REVIEWERS

Authors' reply to reviewers

The next pages contain the authors' point-by-point reply to the comments of this revision round, as submitted with the revised manuscript. It is published as the authors wrote it.

Revision : 1

Major Comments:

The abstract lacks detailed information on the study size and how it was determined. Thanks a lot , Data collection was done through a census., selecting patient records that met the inclusion criteria. Ultimately, 149 records were included in the study as a full census of eligible cases.

There is no mention of efforts to address potential sources of bias. This sentence" Yet limitations should also be noted. Firstly, due to its cross-sectional design, it was conducted exclusively in Rasht, uncertain whether our results can be generalized to other country patients." is mentioned at the end of the discussion in the limitation.

The abstract does not discuss the limitations of the study or the generalisability of the findings. Thank you for your helpful comment regarding the absence of a discussion on study limitations and generalisability in the abstract. We agree with your observation and have revised the abstract to briefly address both points. Specifically, we now mention that the cross-sectional design and the single-center setting in Rasht may limit the generalisability of the findings to other populations or regions. Additionally, we note that the study's retrospective data collection and focus on basic associations, rather than causation, represent important limitations. These changes aim to provide readers with a more balanced and transparent summary of the study's scope and applicability.

Thank you again for your constructive feedback, which has improved the clarity and completeness of our abstract.

Minor Comments:

The abstract could benefit from a more detailed description of the statistical methods used. All statistical analyses were carried out by using SPSS (version 26.0). statistical tests used, including the Kolmogorov-Smirnov test (for normality assessment) and the Chi-square test (for analyzing associations between categorical variables). A two-tailed $P < 0.05$ was considered to be of statistical significance.

Providing confidence intervals or adjusted estimates would enhance the clarity of the results. It was not our goal.

Including a discussion on the comparison with similar studies would strengthen the interpretation of the findings. Thank you for this valuable suggestion. We agree that contextualizing our findings within the broader literature enhances the interpretation and relevance of the results. In the revised manuscript, we have expanded the Discussion section to include comparisons with key regional and national studies on methadone and opioid use patterns in Iran.

Revision : 2

Major Comments:

Lack of discussion on potential sources of bias and limitations.it was highlighted.it was corrected. Several limitations should be considered when interpreting these results. First, the cross-sectional design limits the ability to infer causality between demographic factors and substance abuse patterns. Second, the study was conducted exclusively in Rasht, which may restrict the generalisability of the findings to other regions with different socio-economic or healthcare contexts. Third, the reliance on patient records may introduce information bias due to incomplete or inaccurate documentation. Additionally, confounding

factors such as psychiatric comorbidities and concurrent use of other substances were excluded, which may affect the observed associations.

No mention of controlling for confounding variables. It was not our goal.

Minor Comments:

The rationale for the study size is not provided. Data collection was done through a census., selecting patient records that met the inclusion criteria. Ultimately, 149 records were included in the study as a full census of eligible cases.

Generalisability and funding are not discussed. Thank you for your helpful comment regarding the absence of a discussion on study limitations and generalisability in the abstract. We agree with your observation and have revised the abstract to briefly address both points. Specifically, we now mention that the cross-sectional design and the single-center setting in Rasht may limit the generalisability of the findings to other populations or regions. Additionally, we note that the study's retrospective data collection and focus on basic associations, rather than causation, represent important limitations. These changes aim to provide readers with a more balanced and transparent summary of the study's scope and applicability.

Thank you again for your constructive feedback, which has improved the clarity and completeness of our abstract.

5 Revision 4

2 comments · 25 May 2025 – 26 May 2025

Associate Editor

MINOR REVISION 25 May 2025

Based on the provided abstract, the study design is cross-sectional. Therefore, I will use the STROBE-cross-sectional checklist to conduct the peer review.

Here are the questions from the STROBE-cross-sectional checklist along with the corresponding answers from the abstract:

Title and Abstract: Indicate the study's design with a commonly used term in the title or the abstract.
Peer Review: The abstract clearly states that the study is a "cross-sectional study."

Abstract: Provide in the abstract an informative and balanced summary of what was done and what was found.
Peer Review: The abstract provides a summary of the study's background, methods, results, and conclusions. It mentions the study's aim, the methods used, the main findings, and the implications of the results.

Background/Rationale: Explain the scientific background and rationale for the investigation being reported.
Peer Review: The background section highlights the limited number of studies on methadone and opium syrup use in the Iranian population, providing a rationale for the investigation.

Objectives: State specific objectives including any prespecified hypotheses.
Peer Review: The objective is to examine the frequency of methadone and opium syrup use in treating drug abuse in Rasht.

Study Design: Present key elements of study design early in the paper.
Peer Review: The study design is identified as cross-sectional, and it is mentioned early in the methods section.

Setting: Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection.
Peer Review: The study was conducted in Rasht, Iran, from 2018 to 2022.

Eligibility Criteria: Give the eligibility criteria and the sources and methods of selection of participants.
Peer Review: Participants were selected based on a history of methadone and opium syrup consumption, with records meeting inclusion criteria included in the study.

Data Sources/Measurement: For each variable of interest, give sources of data and details of methods of assessment (measurement).
Peer Review: Data were collected from patient records, including demographic characteristics and substance use details.

Bias: Describe any efforts to address potential sources of bias.
Peer Review: The abstract does not explicitly mention efforts to address potential sources of bias.

Study Size: Explain how the study size was arrived at.
Peer Review: The study included 149 records as a full census of eligible cases.

Quantitative Variables: Explain how quantitative variables were handled in the analyses.
Peer Review: Statistical analyses were performed using SPSS, and tests such as the Kolmogorov-Smirnov test and Chi-square test were used.

Statistical Methods: Describe all statistical methods, including those used to control for confounding.
Peer Review: Statistical methods are described, including the use of SPSS and specific tests for analysis.

Participants: Report numbers of individuals at each stage of study.
Peer Review: The study included 149 records of patients with a history of methadone and opium syrup consumption.

Descriptive Data: Give characteristics of study participants.
Peer Review: The average age of participants is reported, along with the percentage of methadone and opium syrup users.

Outcome Data: Report numbers of outcome events or summary measures.
Peer Review: The abstract reports the percentage of participants using methadone and opium syrup and the significance of age differences.

Main Results: Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision.
Peer Review: The results include the percentage of substance use and a significant age difference with a p-value.

Key Results: Summarize key results with reference to study objectives.
Peer Review: The key results are summarized, indicating the prevalence of methadone and opium syrup use and age differences.

Limitations: Discuss limitations of the study.
Peer Review: The abstract does not explicitly discuss the limitations of the study.

Interpretation: Give a cautious overall interpretation considering objectives, limitations, and other relevant evidence.
Peer Review: The conclusion suggests the need for gender-specific and geographical interventions but does not discuss limitations.

Generalizability: Discuss the generalizability of the study results.
Peer Review: The abstract does not explicitly discuss the generalizability of the results.

Minor Comments:

The abstract provides a clear summary of the study design, methods, and results.
Statistical methods and participant characteristics are adequately described.

Editor-in-Chief MINOR REVISION 26 May 2025

Public Comment:
Based on the provided abstract, the study design is a cross-sectional study. Therefore, I will use the STROBE-cross-sectional checklist to conduct the peer review.
Here are the questions from the STROBE-cross-sectional checklist along with the corresponding answers from the abstract:
Title and Abstract: Indicate the study's design with a commonly used term in the title or the abstract.
Peer Review: The abstract clearly states that the study is a "cross-sectional study."
Abstract: Provide in the abstract an informative and balanced summary of what was done and what was found.
Peer Review: The abstract provides a summary of the study's background, methods, results, and conclusions. It mentions the study's aim, the methods used, the main findings, and the implications of the results.

Background/Rationale: Explain the scientific background and rationale for the investigation being reported.
Peer Review: The background section highlights the limited number of studies on methadone and opium syrup use in the Iranian population, providing a rationale for the investigation.
Objectives: State specific objectives, including any prespecified hypotheses.
Peer Review: The objective is to examine the frequency of methadone and opium syrup use in treating drug abuse in Rasht.
Study Design: Present key elements of the study design early in the paper.
Peer Review: The study design is identified as cross-sectional, and it is mentioned early in the methods section.
Setting: Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection.
Peer Review: The study was conducted in Rasht, Iran, from 2018 to 2022.
Eligibility Criteria: Give the eligibility criteria and the sources and methods of selection of participants.
Peer Review: Participants were selected based on a history of methadone and opium syrup consumption, with records meeting inclusion criteria included in the study.
Data Sources/Measurement: For each variable of interest, give sources of data and details of methods of assessment (measurement).
Peer Review: Data were collected from patient records, including demographic characteristics and substance use details.
Bias: Describe any efforts to address potential sources of bias.
Peer Review: The abstract does not explicitly mention efforts to address potential sources of bias.
Study Size: Explain how the study size was arrived at.
Peer Review: The study included 149 records as a full census of eligible cases.
Quantitative Variables: Explain how quantitative variables were handled in the analyses.
Peer Review: Statistical analyses were performed using SPSS, and tests such as the Kolmogorov-Smirnov test and Chi-square test were used.
Statistical Methods: Describe all statistical methods, including those used to control for confounding.
Peer Review: Statistical methods are described, including the use of SPSS and specific tests for analysis.
Participants: Report numbers of individuals at each stage of the study.
Peer Review: The study included 149 records of patients with a history of methadone and opium syrup consumption.
Descriptive Data: Give characteristics of study participants.
Peer Review: The average age of participants is reported, along with the percentage of methadone and opium syrup users.
Outcome Data: Report numbers of outcome events or summary measures.
Peer Review: The abstract reports the percentage of participants using methadone and opium syrup and the significance of age differences.
Main Results: Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision.
Peer Review: The results include the percentage of substance use and a significant age difference with a p-value.
Key Results: Summarize key results with reference to study objectives.
Peer Review: The key results are summarized, indicating the prevalence of methadone and opium syrup use and age differences.
Limitations: Discuss limitations of the study.
Peer Review: The abstract does not explicitly discuss the limitations of the study.

Interpretation: Give a cautious overall interpretation considering objectives, limitations, and other relevant evidence.
Peer Review: The conclusion suggests the need for gender-specific and geographical interventions but does not discuss limitations.
Generalizability: Discuss the generalizability of the study results.
Peer Review: The abstract does not explicitly discuss the generalizability of the results.
Minor Comments:
The abstract provides a clear summary of the study design, methods, and results.
Statistical methods and participant characteristics are adequately described.

Decision:
Minor revision

6

Revision 5

AUTHORS' RESPONSE TO REVIEWERS

Authors' reply to reviewers

The next pages contain the authors' point-by-point reply to the comments of this revision round, as submitted with the revised manuscript. It is published as the authors wrote it.

Major Comments:

The abstract does not explicitly mention efforts to address potential sources of bias.

Response: Thank you for this important observation. We have revised the abstract to briefly mention that the study utilized a census sampling method and excluded incomplete records and those with psychiatric comorbidities or poly-substance abuse, in order to minimize selection and information bias. We have also acknowledged the potential for residual bias due to the retrospective nature of data collection from patient records.

Limitations of the study are not discussed in the abstract.

Response: We appreciate this suggestion. The abstract has been updated to include key limitations, specifically noting the cross-sectional design, the single-center setting, and the reliance on retrospective patient records, all of which may affect the interpretation and strength of our findings.

The generalisability of the study results is not addressed.

Response: Thank you for highlighting this omission. We have now added a statement to the abstract indicating that the findings may not be generalisable to other populations or regions due to the study's focus on a single city (Rasht) and the specific characteristics of the sample.

Minor Comments:
The abstract provides a clear summary of the study design, methods, and results. Statistical methods and participant characteristics are adequately described.

Response: We thank the reviewer for these positive remarks and are glad that the clarity and comprehensiveness of the abstract were appreciated.

6 Revision 5

2 comments · 31 Jul 2025 – 2 Aug 2025

Associate Editor

ACCEPT 31 Jul 2025

The article is acceptable.

Editor-in-Chief

ACCEPT 2 Aug 2025

Accept