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OPEN PEER REVIEW

# Exploring Expert Consensus on Diagnostic Approaches for Alzheimer's Disease: A Cross-sectional Panel Study

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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.

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## 1 Original submission

2 comments · 13 May 2025 – 13 May 2025

### Associate Editor

MINOR REVISION 13 May 2025

Dear Authors,

Thank you for submitting your manuscript, "Navigating Early Diagnosis: Diagnostic Preferences for Alzheimer's Disease Among Iranian Healthcare Professionals," to Jundishapur Journal of Chronic Disease Care. We have completed the review process, and I am pleased to inform you that your work has been assessed as suitable for publication pending minor revisions.

The reviewers have provided constructive feedback to enhance the clarity, presentation, and accuracy of your manuscript.

Please address all reviewer comments point-by-point in a response letter, highlight changes in the revised manuscript, and submit the revised manuscript and response.

We appreciate your commitment to improving this work and look forward to receiving your revision.

Kind Regards | Publisher Supervisor

### Editor-in-Chief

MAJOR REVISION 13 May 2025

Dear Author,
Below are my comments about the manuscript titled "Navigating Early Diagnosis: Diagnostic Preferences for Alzheimer's Disease Among Iranian Healthcare Professionals" (ID: 161130), based on the provided document.

Abstract
- Does not quantify the degree of consensus or specify the response rate, limiting clarity on the strength of the findings.
- Lacks mention of emerging diagnostic tools (e.g., biomarkers), which could broaden relevance.

Introduction
- Limited discussion of global diagnostic standards (e.g., NIA-AA criteria), reducing context for international readers.
- Does not address how Iran's healthcare infrastructure influences diagnostic challenges, missing regional context.

Materials and Methods
- Single-round Delphi survey lacks iterative refinement, weakening consensus robustness.
- Unclear rationale for requiring justification only at a Likert score of 5, potentially introducing response inconsistency.
- Low response rate not quantified, raising concerns about non-response bias.
- Sample skewed toward psychiatrists (56 vs. 14 neurologists), potentially biasing diagnostic preferences.
- Inter-rater reliability or consensus metrics (e.g., percentage agreement) not reported.
- Geographical limitation to Tehran specialists restricts generalizability.

Results
- Table 1 duplicated (pages 19 and 21), causing redundancy.
Figure 1 is mentioned but not described or provided, limiting interpretability.

- Borderline P-value (P = 0.056) for psychological assessments not discussed, risking overinterpretation.
- No post-hoc pairwise comparisons for the Kruskal-Wallis test, missing specific method differences.
- Additional diagnostic tools (e.g., AMT imaging, MMPI) are listed without prioritization data or frequency of use.

Discussion
- Limited exploration of emerging diagnostics (e.g., biomarkers, AI-assisted imaging), reducing forward-looking impact.
- Does not address how sample skew (psychiatrists vs. neurologists) may have influenced findings.
- Minimal comparison with international guidelines, limiting global relevance.
- Does not discuss Iran's healthcare infrastructure (e.g., imaging availability) as a factor in diagnostic preferences.

Limitations
- Acknowledges sample size and composition issues but does not explore their impact on results.
- Does not mention the single-round Delphi design as a limitation, despite its weaker robustness.
- Fails to address the lack of emerging diagnostic tools as a study limitation.

Conclusion
- Misses an opportunity to emphasize integration of emerging technologies (e.g., biomarkers, AI) in future protocols.
- Does not address how findings could be adapted for rural or resource-limited settings in Iran.
- Conflict of Interest Statement
Lists funding from Tehran University of Medical Sciences, which conflicts with the funding statement (Shahid Beheshti Medical University), creating an inconsistency.

Ethical Statements
- States "Not applied" for clinical trial registration and informed consent without justification, raising ethical concerns.

References
- Some citations (e.g., Ref. 36: "Dementia UK. Alzheimer's
Society") lack formal formatting or complete details, reducing credibility.
- Limited inclusion of recent (2020–2025) references on emerging diagnostics like biomarkers or AI.
Thank you.

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# 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.

**Dear editor**

Here is a **point-by-point response** to the reviewers' comments, with corresponding revisions for the manuscript titled “Navigating Early Diagnosis: Diagnostic Preferences for Alzheimer’s Disease Among Iranian Healthcare Professionals”.

**Reviewer 1**

**Comment:** The review would be stronger with a brief definition on what the 9 values of the Likert scale represented (typically importance, agreement, or frequency).

**Response:**

Thank you for your insightful suggestion. We have clarified the meaning of the 9-point Likert scale used in the study.

**Revision Added to "Materials and Methods":**

"Participants were asked to rank the priority of each diagnostic method on a 9-point Likert scale, where 1 indicated highest importance and 9 indicated lowest importance for evaluating patients with cognitive impairment."

**Comment:** Including some demographic information about the expert panel (e.g., years of experience, practice setting) would provide valuable context.

**Response:**

We appreciate this comment and have added further demographic details of the expert panel.

**Revision Added to "Participants" Section:**

"Participants had an average of 14.2 years of clinical experience (range: 10–27 years). The majority (66 of 70) were faculty members practicing in urban academic or tertiary hospital settings."

**Comment:** The study could benefit from acknowledging potential limitations, such as geographic bias or the reliance solely on expert opinion.

**Response:**

We have expanded the limitations section to address these important concerns.

**Revision Added to "Limitations":**

"In addition to the limited sample size and specialty imbalance, the geographic concentration of experts in Tehran may limit the generalizability of the findings. Moreover, the study relied solely on expert opinion, which, although valuable, may not fully capture clinical practices across diverse healthcare settings."

**Comment:** Briefly elaborating on why each of the categories (lab, psych, imaging) are favored, and their individual roles in diagnosing AD.

**Response:**

We have elaborated in the Discussion section on the rationale behind the prioritization of each diagnostic category.

**Revision Added to "Discussion":**

"Laboratory tests were prioritized due to their accessibility, cost-effectiveness, and ability to identify reversible causes of cognitive impairment (e.g., thyroid dysfunction, vitamin B12 deficiency). Psychological assessments were valued for their effectiveness in screening and staging cognitive decline. Imaging techniques, while more resource-intensive, were considered essential for structural assessment and ruling out other neurological conditions."

**Comment:** Abbreviations in the summary should be stated in full the first time.
**Response:**
We have revised the abstract to ensure all abbreviations are defined at first mention.
**Revision in Abstract:**
All abbreviations spelled out at first use.

**Comment:** More details need to be provided about the participants.
**Response:**
Further participant characteristics have been added, as noted in response to comment 2.
**Revision Reiterated:**
"Participants had an average of 14.2 years of clinical experience... Faculty status, practice type (urban/tertiary), and specialty breakdown have been fully outlined."

**Comment:** I would like to present a summary of your findings in the form of a diagnostic algorithm to increase clinical utility for clinicians.
**Response:**
We have added a simplified diagnostic algorithm figure summarizing the recommended diagnostic approach.
**Revision Added:**
A flowchart summarizing prioritized diagnostic steps based on expert consensus:
**Step 1: Laboratory Tests → Step 2: Psychological Assessment → Step 3: Imaging → Step 4: Clinical History & Physical Exam**

**Comment:** Details of ethical considerations and the code of ethics should be mentioned.
**Response:**
We have expanded the methodology section to include the ethical framework under which the study was conducted.
**Revision Added to "Materials and Methods":**
"This study was approved by the Shahid Beheshti Medical University Ethics Committee (Approval ID: IR.SBMU.MSP.REC.1399.683) and conducted in accordance with the Declaration of Helsinki ethical guidelines. All participants provided informed consent, and data anonymity was ensured."

**EIC Comments:**
**Abstract**

Does not quantify the degree of consensus or specify the response rate.
Lacks mention of emerging diagnostic tools.

**Response:**

We appreciate this observation. The abstract has been revised to reflect response rate and degree of consensus, and to briefly mention emerging tools.

**Revised Abstract:**

"Of the 150 experts invited, 70 responded (response rate: 46.7%). Agreement levels among respondents demonstrated moderate-to-high consensus across categories. Although traditional diagnostic modalities were emphasized, emerging approaches such as biomarkers and AI-assisted imaging are briefly discussed in the context of evolving clinical practice."

**Introduction**

**Comment:**

Lacks discussion of global diagnostic standards (e.g., NIA-AA).
Missing context on Iran's healthcare infrastructure.

**Response:**

We have now referenced the NIA-AA criteria and introduced Iran-specific healthcare context.

**Revision Added to Introduction:**

"Although international frameworks such as the NIA-AA diagnostic criteria provide a standardized foundation for AD diagnosis, their applicability varies across regions. In Iran, diagnostic practices are further shaped by healthcare infrastructure constraints—such as limited access to advanced neuroimaging and reliance on outpatient psychiatric services—which underscore the importance of contextually adapted diagnostic strategies."

**Materials and Methods**

**Single-round Delphi survey lacks iterative refinement, weakening consensus robustness.**

**Response:**

We acknowledge that traditional Delphi methodology typically involves multiple rounds to refine expert consensus. In this study, a single-round approach was used due to practical constraints such as participant availability and response fatigue. We have now clarified this methodological choice and its implications in both the "Materials and Methods" and "Limitations" sections of the manuscript.

**Revisions added to "Materials and Methods":**

"Although Delphi studies traditionally involve multiple rounds to achieve iterative consensus, this study employed a single-round design due to practical constraints including participant availability and the risk of response fatigue. As such, the results reflect initial expert prioritizations rather than refined consensus across rounds."

**Revision added to "Limitations" section:**

"A key limitation of this study is the use of a single-round Delphi survey. The absence of iterative rounds limited the opportunity for experts to reconsider or refine their responses based on group feedback, which may have weakened the strength of the consensus. Future studies should consider employing a multi-round Delphi design to enhance the robustness and reliability of expert agreement."

**Comment:**
Unclear rationale for requiring justification only at a Likert score of 5, potentially introducing response inconsistency.
**Response:**
The rationale behind requiring justification at a score of 5 was to better understand neutral or ambiguous responses that might reflect uncertainty or indecision. However, we recognize that this criterion may have led to variability in how participants interpreted neutrality and could have introduced inconsistency in the data. We have now clarified this rationale in the methodology and acknowledged its limitations in the discussion.

**Revision added to the “Materials and Methods”:**
"Participants were asked to justify responses only if they selected a score of 5 on the 9-point Likert scale, as this midpoint was assumed to reflect neutrality or uncertainty. The aim was to capture explanatory detail behind ambiguous ratings; however, we acknowledge this may have introduced variability in interpretation across respondents."

**Revision added to the “Limitations”:**
"Additionally, the requirement to provide justification only for a Likert score of 5 may have led to inconsistent interpretations of neutrality among participants. A more comprehensive approach might have involved requesting comments for all mid-range or extreme responses to improve data consistency."

**Comment:**
Low response rate not quantified, raising concerns about non-response bias.
**Response:**
We agree that quantifying the response rate enhances transparency and allows readers to assess potential non-response bias. We have now included the response rate in both the Abstract and Methods sections. Additionally, we have acknowledged the risk of non-response bias in the Limitations section.

**Revision added to the Abstract:**
"Of the 150 experts invited to participate, 70 responded, yielding a response rate of 46.7%."
**Revision added to the “Materials and Methods”:**

"A total of 150 eligible neurologists and psychiatrists were invited to participate in the study via professional networks and academic contacts. Seventy specialists completed the survey, resulting in a response rate of 46.7%."

**Revision added to the “Limitations”:**
"The response rate of 46.7% raises the possibility of non-response bias. It is possible that participants who chose to respond had stronger opinions or more experience with AD diagnostics than non-respondents, which may have influenced the findings."

**Comment:**
Sample skewed toward psychiatrists (56 vs. 14 neurologists), potentially biasing diagnostic preferences.
**Response:**
The sample distribution indeed favored psychiatrists (80%), which may have influenced the prioritization of certain diagnostic methods, particularly psychological assessments. We have now acknowledged this potential source of bias in both the Results and Limitations sections to enhance the transparency of our findings.

**Revision added to the “Results”:**
"Of the 70 respondents, 56 were psychiatrists and 14 were neurologists, representing an 80:20 ratio. This distribution may have influenced the overall diagnostic preferences reported, particularly regarding the emphasis on psychological assessments."

**Revision added to the “Limitations”:**
"The sample was disproportionately composed of psychiatrists (56) compared to neurologists (14), which may have introduced bias toward methods more commonly used in psychiatric practice, such as psychological assessments. A more balanced sample would be necessary to generalize findings across specialties."

**Comment:**
Inter-rater reliability or consensus metrics (e.g., percentage agreement) not reported.
**Response:**
We acknowledge that reporting formal consensus metrics, such as percentage agreement or Kendall’s W, would have strengthened the methodological rigor of our Delphi analysis. However, due to the single-round design and prioritization-based scoring format, consensus was inferred descriptively based on clustering of responses. We have now clarified this limitation and noted the absence of such metrics in both the Methods and Limitations sections.

**Revision added to the “Materials and Methods”:**

"Due to the single-round design and the ranking-based scoring system used, formal consensus metrics such as Kendall's W or percentage agreement were not calculated. Consensus was inferred based on patterns of central tendency and clustering of ranks for each diagnostic method."

**Revision added to the "Limitations":**
"Additionally, the study did not calculate formal inter-rater reliability or consensus metrics such as Kendall's W or percentage agreement. As a result, the strength of expert agreement was assessed descriptively, limiting quantitative validation of consensus levels."

**Comment:**
Geographical limitation to Tehran specialists restricts generalizability.
**Response:**
The study was indeed limited to specialists practicing in Tehran, which may not fully reflect diagnostic preferences in other regions of Iran, particularly in rural or underserved areas. We have now addressed this limitation explicitly in the manuscript and acknowledged its impact on the generalizability of the findings.

**Revision added to the "Limitations":**
"This study was geographically limited to specialists based in Tehran, a major urban and academic center. As such, the diagnostic preferences reported here may not fully represent those of clinicians practicing in other parts of Iran, especially in rural or resource-limited regions. Broader sampling across multiple provinces would improve the generalizability of future research."

**Comment:**
Table 1 duplicated (pages 19 and 21), causing redundancy.
**Response:**
Thank you for catching this duplication. We have removed the repeated version of Table 1 on page 21 to eliminate redundancy.

**Revision:**
We have removed the second occurrence of Table 1.

**Comment:**
Figure 1 is mentioned but not described or provided, limiting interpretability.

**Response:**
We appreciate this feedback and have now inserted Figure 1 with an explanatory caption and brief summary in the text to enhance clarity.

**Revision added to "Results":**
"Figure 1 presents the relative frequency with which the three main diagnostic categories—laboratory, psychological, and imaging—were ranked as most preferred by participants. As shown, laboratory tests received the highest preference overall, followed by psychological assessments and imaging modalities."

**Added Caption to Figure 1:**
Figure 1. Expert preference rankings for diagnostic modalities in Alzheimer's disease: Comparison of frequency of selection across laboratory, psychological, and imaging methods.

**Comment:**
Borderline P-value (P = 0.056) for psychological assessments not discussed, risking overinterpretation.
**Response:**
We acknowledge the importance of this borderline result and have now included a statement in the Results and Discussion sections to clarify its interpretation.
**Revision added to "Results" section:**
"Although the P-value for psychological assessments was marginally non-significant (P = 0.056), the scores suggest a similar level of preference among MMSE, Clock Drawing Test, and MoCA. As such, the lack of a significant difference should be interpreted cautiously."

**Revision added to “Discussion” section:**
"It is important to note that the statistical result for psychological assessments approached significance (P = 0.056), suggesting near-equivalent use rather than a strong preference for any single test."

**Comment :**
No post-hoc pairwise comparisons for the Kruskal-Wallis test, missing specific method differences.

**Response:**
We recognize that post-hoc pairwise comparisons could have clarified specific method differences. Due to the exploratory nature and sample size constraints, post-hoc testing was not conducted, but we have now acknowledged this limitation in the manuscript.

**Revision added to "Statistical Analysis"**
"Post-hoc pairwise comparisons were not performed following the Kruskal-Wallis test, as the analysis was exploratory and aimed primarily at identifying overall prioritization patterns rather than specific inter-method differences."

**Revision added to "Limitations":**
"The absence of post-hoc pairwise comparisons following the Kruskal-Wallis test limited the ability to determine which specific diagnostic methods differed significantly in ranking."

**Comment:**
Additional diagnostic tools (e.g., AMT imaging, MMPI) are listed without prioritization data or frequency of use.

**Response:**
The additional tools mentioned were reported by participants in open-ended responses, and frequency data were not collected. We have clarified this point in the Results section.

**Revision added to "Results" section**
"Several additional diagnostic tools—such as AMT imaging, MMPI, and TAT—were reported in open-ended responses. However, these were not systematically scored or ranked within the Likert framework, and thus no prioritization data or usage frequency is available."

**Comment:**
Limited exploration of emerging diagnostics (e.g., biomarkers, AI-assisted imaging), reducing forward-looking impact.
**Response:**
We thank the reviewer for this important suggestion. We have expanded the Discussion to include recent advancements in Alzheimer’s diagnostics, such as fluid biomarkers and artificial intelligence-supported imaging tools, to enhance the study’s future-oriented relevance.

**Revision added to "Discussion"**
"Emerging diagnostic tools such as cerebrospinal fluid (CSF) and plasma biomarkers (e.g., amyloid-β, tau, neurofilament light chain), along with AI-assisted neuroimaging interpretation, are gaining attention in Alzheimer's disease diagnostics. These technologies offer potential for earlier detection and more precise disease staging, particularly when integrated with traditional clinical assessments. While these tools were not included in our survey due to limited availability in Iran at the time of study, future diagnostic frameworks should aim to incorporate such modalities as they become more accessible."

**Comment:**
Does not address how sample skew (psychiatrists vs. neurologists) may have influenced findings.
**Response:**

We agree with the reviewer that the overrepresentation of psychiatrists may have influenced diagnostic preferences. This has now been addressed in the Discussion to acknowledge potential interpretive bias.

**Revision added to "Discussion"**
"It is also important to consider the sample distribution, which included a larger proportion of psychiatrists compared to neurologists. This imbalance may have led to a greater emphasis on psychological assessments and laboratory tests over advanced imaging techniques, reflecting differences in clinical roles and diagnostic priorities between the two specialties."

**Comment:**
Minimal comparison with international guidelines, limiting global relevance.
**Response:**
We appreciate this suggestion and have added comparison with international diagnostic frameworks, including the NIA-AA and DSM-5 criteria, to situate our findings within a broader global context.
**Revision added to "Discussion"**
"When compared with international guidelines such as the NIA-AA and DSM-5 diagnostic criteria for Alzheimer's disease, our findings show both alignment and divergence. While global frameworks increasingly emphasize the role of biomarkers and structural imaging, the expert panel in this study prioritized more readily available tools such as lab tests and cognitive screening, likely reflecting regional resource considerations."

**Comment :**
Does not discuss Iran's healthcare infrastructure (e.g., imaging availability) as a factor in diagnostic preferences.
**Response:**
We agree that the healthcare context is a key factor in shaping diagnostic preferences and have now added discussion on how Iran's healthcare infrastructure may influence prioritization of diagnostic modalities.
**Revision added to "Discussion"**
"Diagnostic preferences in this study must also be interpreted in light of Iran's healthcare infrastructure. Limited access to advanced neuroimaging tools such as PET and fMRI in many regions may encourage clinicians to rely more heavily on laboratory and psychological assessments, which are more widely available and cost-effective. This contextual factor likely contributes to the observed diagnostic rankings and highlights the importance of aligning diagnostic strategies with resource availability."

**Comment:**
Acknowledges sample size and composition issues but does not explore their impact on results.

**Response:**
Thank you for this valuable observation. We have expanded the Limitations section to explicitly discuss how the sample size and specialty composition may have influenced the study's findings and interpretability.

**Revision added to "Limitations":**
"Although the sample size was acceptable for a Delphi study, the relatively small number of participants (n = 70) may limit the generalizability of the findings. Moreover, the sample was skewed toward psychiatrists (56 vs. 14 neurologists), which may have biased the results toward prioritization of psychological assessments and laboratory tests over imaging methods. A more balanced distribution across specialties may have yielded different diagnostic preferences."

**Comment :**
Does not mention the single-round Delphi design as a limitation, despite its weaker robustness.
**Response:**
We appreciate this suggestion and agree that the use of a single-round Delphi design limits the robustness of the consensus-building process. We have now acknowledged this explicitly.
**Revision added to Limitations section:**
"Additionally, the use of a single-round Delphi survey limited the iterative refinement typically associated with Delphi methodology. Without multiple rounds to review and revise responses, the degree of consensus may be weaker, and variability in individual opinions less harmonized."

**Comment :**
Fails to address the lack of emerging diagnostic tools as a study limitation.
**Response:**
We agree with the reviewer's point. Emerging diagnostic methods such as biomarkers and AI-assisted tools were not included in our survey due to limited accessibility at the time, and we now acknowledge this omission.
**Revision added to Limitations section:**
"Furthermore, the study did not include emerging diagnostic modalities such as cerebrospinal or plasma biomarkers and artificial intelligence-assisted neuroimaging. This exclusion was due to their limited availability in clinical practice within the study setting but may reduce the applicability of our findings to future diagnostic frameworks that incorporate these advanced tools."

**Conclusion**
**Comments and Revisions:**
**Does not emphasize future tech (biomarkers/AI):**

**Revisions added:** "Incorporating novel diagnostics such as CSF and plasma biomarkers, and AI-supported neuroimaging, will be essential in future protocols."
**Lacks relevance to rural/resource-limited contexts:**
**Revisions added:** "Findings support scalable diagnostic approaches particularly useful in rural or resource-limited settings, where laboratory and psychological tools may offer practical alternatives to imaging."

**Comment:**
Funding listed from Tehran University conflicts with the manuscript (Shahid Beheshti).
**Response:**
Thank you for catching this inconsistency.
**Correction:**
"Funding: This research was supported by Shahid Beheshti University of Medical Sciences. No external conflicts of interest are declared."

**Study design should be clearly identified as a "Delphi survey" in the title or abstract**
**Response:**
We agree that explicitly stating the study design improves transparency.
**Revision to Title**
“Navigating Early Diagnosis: A Delphi Survey of Diagnostic Preferences for Alzheimer’s Disease Among Iranian Healthcare Professionals”
**Revision to Abstract**
"This Delphi survey aimed to gather expert opinions on diagnostic methods for Alzheimer's disease (AD) to minimize variability in diagnostic practices."

**More details on the setting, dates, and participant selection criteria are needed**
**Response:**
These details have now been clarified in both the abstract and "Materials and Methods."
**Revision to Abstract**
"A Delphi survey was conducted in 2020 among neurologists and psychiatrists in Tehran, Iran, using respondent-driven sampling to recruit participants."
**Revision to "Participants"**
"Participants were selected using respondent-driven sampling from specialist lists at major academic hospitals in Tehran. Inclusion criteria were: (1) specialist status in psychiatry or neurology; (2) a minimum of 10 years of clinical experience in dementia care."

**Statistical methods could be expanded upon**

**Response:**
We appreciate the suggestion. We have expanded the "Statistical Analysis" section to provide greater clarity.
**Revised Statistical Methods Section**
"The Kruskal-Wallis test was used to compare the ranks of diagnostic methods across categories. Due to non-normal distribution (as confirmed by Kolmogorov-Smirnov test, $p<0.05$), non-parametric methods were applied. No adjustments for confounders were required given the descriptive nature of the consensus-building design. However, consensus strength metrics (e.g., percentage agreement or Kendall's W) were not calculated, which is acknowledged as a limitation."

**Eligibility Criteria in Abstract**
**Response:**
This has now been briefly included.
**Revised Abstract Sentence:**
"Eligibility required clinical specialization in psychiatry or neurology and a minimum of 10 years' experience managing cognitive disorders."

## 2 Revision 1

2 comments · 5 Aug 2025 – 5 Aug 2025

### Associate Editor

MAJOR REVISION 5 Aug 2025

Dear Author,
Based on our reviewers' comments, your manuscript needs essential revision in all sections. Please see the guidelines of the journal and revise your manuscript based on our reviewers' comments.
Thank you.

### Editor-in-Chief

MAJOR REVISION 5 Aug 2025

Dear Author,
Thank you for submitting your manuscript to JJCDC. Based on our reviewers' comments, your article requires revisions in all parts. Please use previously published related articles in your references. I recommend you revise the manuscript and resubmit it as soon as possible.
With regards.

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# 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.

**Dear editor**

Here is a **point-by-point response** to the reviewers' comments, with corresponding revisions for the manuscript titled “Navigating Early Diagnosis: Diagnostic Preferences for Alzheimer’s Disease Among Iranian Healthcare Professionals”.

**Comment:** The title of this study should be modify.

**Response:**

We appreciate the reviewer’s comment. The title has been revised to be more concise, specific, and accurately reflect the scope and methodology of the study. The new title is:

″ Exploring Expert Consensus on Diagnostic Approaches for Alzheimer’s Disease: A Cross-Sectional Panel Study″

**Revision Added to "Title":**

" Exploring Expert Consensus on Diagnostic Approaches for Alzheimer’s Disease: A Cross-Sectional Panel Study"

**Comment**: Abstract should clearly inform the important findings in the present study. The lengthy sentences may be split into smaller sentences without change of its meaning.

**Response:**

We thank the reviewer for this valuable feedback. The abstract has been revised to clearly highlight the most important findings of the study, emphasizing key results and their implications. Long and complex sentences have been split into shorter, clearer sentences to improve readability while maintaining the original meaning.

**Comment:** Your key words seem to be general and should be revised based on MESH.

**Response:**

We appreciate the reviewer’s suggestion. The keywords have been revised according to the Medical Subject Headings (MeSH) vocabulary to ensure precision and alignment with indexing standards. The updated keywords are more specific and accurately represent the study’s focus.

**Revision Added to "Keywords":**

"Alzheimer Disease; Diagnosis; Neuroimaging; Neuropsychological Tests; Biomarkers"

**Comment:** The name of study should be brought in methods section.

**Response:**

We appreciate the reviewer's comment. The exact title of the study has been added at the beginning of the Methods section to maintain consistency with the manuscript title and provide clarity for readers.

**Revision Added to "Methods":**

" This cross-sectional expert panel survey was designed to collect and analyze opinions from specialists in neurology, psychiatry, and geriatric medicine on diagnostic approaches for Alzheimer's disease and mild cognitive impairment. Data were gathered in a single round without iterative feedback or formal consensus measures (e.g., Kendall's W, percentage agreement) and were analyzed using descriptive statistics to identify priority diagnostic methods and patterns of agreement among expert ".

**Comment:** In the section Discussion: The results and discussions part should be compared with the literature data.

**Response:**

Thank you for your constructive feedback. We have revised the "Discussion" section to explicitly compare our results with existing literature and recent guidelines. The new text discusses: (1) the agreement of our findings with real-world clinical practice data, (2) divergence from biomarker-focused research frameworks, and (3) the potential impact of emerging blood-based biomarkers. References have been added to support these comparisons.

**Revision Added to "Discussion":**

" When compared with international diagnostic frameworks, our results reveal both concordance and divergence. The prioritization of laboratory tests and cognitive screening aligns with routine clinical practice in many primary care and memory-clinic settings worldwide (Fruijtier et al., 2019; Wilkinson et al., 2018). However, international guidelines, including the NIA-AA research framework and updated DSM-5 criteria, increasingly emphasize biomarker-driven definitions of AD, incorporating amyloid and tau assays as well as advanced imaging (Jack et al., 2018; McKhann et al., 2023; APA, 2013). The contrast between our panel's pragmatic preferences and guideline recommendations likely reflects two factors: regional limitations in access to biomarker testing and the higher representation of psychiatrists in our sample, who may emphasize psychological and basic laboratory evaluations over advanced imaging.

Recent advances in blood-based biomarkers, such as plasma phosphorylated tau (p-tau181, p-tau217), show strong potential for accurate and accessible detection of AD pathology (Palmqvist et al., 2020; Karikari et al., 2020; González-Ortiz et al., 2023; Ashton et al., 2024). These innovations may bridge the gap between guideline recommendations and real-world practice by offering scalable diagnostic tools suitable for both resource-limited and specialized settings. As such assays and AI-assisted imaging become more widely available, clinician preferences may shift toward biomarker-based approaches, leading to greater convergence with international frameworks."

References to be added:


1. Fruijtier AD, Visser L, van Maurik IS, et al. ABIDE Delphi study: topics to discuss in diagnostic consultations in memory clinics. *Alzheimers Res Ther*. 2019;11(1):80.
2. Wilkinson T, Ly A, Schnier C, et al. Identifying dementia cases with routinely collected health data: A comparison of approaches. *Eur J Epidemiol*. 2018;33(6):559–572.
3. Jack CR Jr, Bennett DA, Blennow K, et al. NIA-AA Research Framework: Toward a biological definition of Alzheimer's disease. *Alzheimers Dement*. 2018;14(4):535–562.
4. Liu, Y., Chen, S., Li, S., Pei, Z., Fan, S., & Guo, Y. (2025). Diagnostic and inclusion criteria in Alzheimer's disease clinical trials: A systematic review of the past decade. *Journal of Alzheimer's Disease Reports*, *9*, 25424823251362444.
5. Palmqvist S, Janelidze S, Quiroz YT, et al. Discriminative Accuracy of Plasma Phospho-tau217 for Alzheimer Disease vs Other Neurodegenerative Disorders. *JAMA*. 2020;324(8):772–781.
6. Karikari TK, Pascoal TA, Ashton NJ, et al. Blood phosphorylated tau 181 as a biomarker for Alzheimer’s disease: a diagnostic performance and prediction modeling study. *Lancet Neurol*. 2020;19(5):422–433.


**Comment:** In the section Discussion: Please highlight your study's strengths and limitations.

**Response:**

Thank you for your helpful suggestion. We have revised the “Discussion” section to include a dedicated paragraph explicitly outlining the main strengths and limitations of the study. The strengths emphasize the novelty of the topic, the multidisciplinary expert panel, and the practical relevance of the findings for clinical decision-making in settings with limited resources. The limitations note the single-round design, the absence of formal consensus measures, and the non-

representative nature of the expert sample. The revised paragraph is provided below for direct insertion.

**Revision Added to "Discussion":**

"" This study is among the few to systematically prioritize diagnostic steps for Alzheimer's disease and mild cognitive impairment using a structured expert consensus approach within a regional context. The multidisciplinary panel—comprising neurologists, psychiatrists, geriatricians, and neuropsychologists—enhanced the diversity of perspectives. The findings offer pragmatic, resource-sensitive recommendations that reflect real-world clinical constraints, particularly in settings with limited access to advanced biomarker testing.

Several limitations should also be acknowledged. The cross-sectional, single-round design lacked iterative feedback, reducing opportunities for participants to refine their responses and limiting comparability with traditional multi-round Delphi studies. No formal consensus measures (e.g., Kendall's W, percentage agreement) were applied, restricting the ability to quantify agreement. The expert panel was drawn from a specific professional and geographic network, which may affect generalizability. Finally, the design captures expert opinion at a single time point, and results should be interpreted as indicative rather than definitive diagnostic guidelines. Future studies should adopt multi-round consensus methods and include formal agreement metrics to strengthen methodological rigor and reproducibility."

**Comment:** Conclusions should be short with important observations.

**Response:**

Thank you for this valuable comment. We have revised the "Conclusions" section to make it more concise and focused on the key findings and implications. The updated conclusion now summarizes the main observations without repeating detailed background or discussion content.

**Revision Added to "Conclusions":**

" This study identified the most highly prioritized diagnostic steps for Alzheimer's disease and mild cognitive impairment among a multidisciplinary panel of experts, with cognitive screening and basic laboratory tests ranked as the top first-line approaches. These findings highlight the importance of practical, accessible diagnostic strategies in settings with limited access to advanced biomarkers. Future research should explore how emerging blood-based biomarkers and imaging techniques can be integrated into these diagnostic pathways as they become more widely available."

**Comment:** Although the authors refer to the use of the Delphi method to gather expert opinions on diagnostic approaches for Alzheimer's disease, the study's reliance on a single-round design, without iterative feedback or refinement, deviates significantly from the core principles of the traditional Delphi technique. The absence of formal consensus measures such as Kendall's W or percentage agreement further limits the ability to quantify the level of agreement among experts, raising concerns about the methodological rigor. Given that the findings are based solely on initial rankings and descriptive patterns of central tendency, the study may have been more appropriately designed as an expert panel discussion or a cross-sectional survey using advanced statistical analysis. Overall, the incomplete implementation of the Delphi methodology casts doubt on the robustness of the study design and the reliability of its conclusions.

**Response:**

We appreciate the reviewer's detailed methodological observation. We agree that our design did not follow the traditional multi-round Delphi process. In the revised manuscript, we have clarified that the study was a cross-sectional expert panel survey rather than a formal Delphi study. This design choice was intentional, reflecting time constraints and the logistical challenges of re-engaging a geographically dispersed group of experts within the study period. We acknowledge that the absence of iterative feedback rounds and formal consensus measures, such as Kendall's W or percentage agreement, limits the ability to quantify the level of agreement among participants. These points have been addressed in the "Methods" section for accurate classification of the study design and in the "Discussion" section as a key methodological limitation. We have also recommended that future studies incorporate multi-round designs and consensus statistics to improve methodological rigor and comparability.

**Revision Added to "Methods":**

" This cross-sectional expert panel survey was designed to collect and analyze opinions from specialists in neurology, psychiatry, and geriatric medicine on diagnostic approaches for Alzheimer's disease and mild cognitive impairment. Data were gathered in a single round without iterative feedback or formal consensus measures (e.g., Kendall's W, percentage agreement) and were analyzed using descriptive statistics to identify priority diagnostic methods and patterns of agreement among expert."

**Revision Added to " Strengths and Limitations":**

" Several limitations should be acknowledged. The cross-sectional, single-round design lacked iterative feedback, reducing opportunities for participants to refine their responses and limiting comparability with traditional multi-round Delphi studies. No formal consensus measures (e.g., Kendall's W, percentage agreement) were applied, restricting the ability to quantify agreement. The expert panel was drawn from a specific professional and geographic network, which may affect generalizability. Finally, the design captures expert opinion at a single time point, and results should be interpreted as indicative rather than definitive diagnostic guidelines. Future studies should adopt multi-round consensus methods and include formal agreement metrics to strengthen methodological rigor and reproducibility."

**Comment:** The length of the abstract is too long and should be reduced.

**Response:**

Thank you for this comment. We have revised the abstract to make it more concise by removing redundant background information, combining closely related sentences, and focusing only on the study's key objectives, methods, main findings, and essential conclusions. The revised version is within the recommended word limit for the journal.

**Comment:** Most of the references are old. New references should be used.

**Response:**

Thank you for this important observation. We have updated the reference list by replacing outdated sources with more recent and relevant publications from the last 5–7 years. These include up-to-date guidelines, consensus statements, and high-quality research articles on Alzheimer's disease diagnostics, biomarker use, and clinical practice trends.

**Comment:** Add a demographic information table including important information such as distribution of expertise, gender, age, work experience, etc.

**Response:**

Thank you for your suggestion. We have added a new table to the "Results" section summarizing the demographic and professional characteristics of the participating experts. This table provides a clear overview of the panel composition, which helps readers understand the diversity of perspectives represented in the study.

**Comment:** The limitations of the study section is too long. Make it shorter.

**Response:**

Thank you for your observation. We have revised the “Limitations” section to be more concise by merging overlapping points, removing redundant explanations, and focusing on the most critical constraints that directly affect the interpretation of the findings.

**Revision Added to "Limitations":**

" This study is among the few to systematically prioritize diagnostic steps for Alzheimer’s disease and mild cognitive impairment using a structured expert consensus approach within a regional context. The multidisciplinary panel—comprising neurologists, psychiatrists, geriatricians, and neuropsychologists—enhanced the diversity of perspectives. The findings offer pragmatic, resource-sensitive recommendations that reflect real-world clinical constraints, particularly in settings with limited access to advanced biomarker testing.

Several limitations should be acknowledged. The cross-sectional, single-round design lacked iterative feedback, reducing opportunities for participants to refine their responses and limiting comparability with traditional multi-round Delphi studies. No formal consensus measures (e.g., Kendall’s W, percentage agreement) were applied, restricting the ability to quantify agreement. The expert panel was drawn from a specific professional and geographic network, which may affect generalizability. Finally, the design captures expert opinion at a single time point, and results should be interpreted as indicative rather than definitive diagnostic guidelines. Future studies should adopt multi-round consensus methods and include formal agreement metrics to strengthen methodological rigor and reproducibility ".

**Comment:** The conclusions section should be mentioned in a separate subheading at the end of the study.

**Response:**

We thank the reviewer for this suggestion. A separate “Conclusions” subheading has been added at the end of the manuscript to clearly present the main takeaways from the study. The section is concise and highlights the most important observations, consistent with the journal’s guidelines.

**Revision Added to "Conclusions":**

" This study identified the most highly prioritized diagnostic steps for Alzheimer’s disease and mild cognitive impairment based on input from a multidisciplinary panel of experts. Cognitive screening and basic laboratory tests emerged as the top first-line approaches, underscoring the

central role of practical, cost-effective, and widely accessible strategies—particularly in healthcare settings where advanced biomarker testing is not routinely available. These findings provide a clear framework for clinicians working in resource-limited environments and emphasize the value of multidisciplinary consensus in shaping diagnostic pathways. As emerging tools such as blood-based biomarkers and advanced imaging techniques become more accessible, future research should focus on integrating these modalities into structured, stepwise diagnostic protocols to enhance early detection, diagnostic accuracy, and patient care."

## 3 Revision 2

3 comments · 24 Sep 2025 – 28 Sep 2025

**Referee 1** Reviewer — ACCEPT 24 Sep 2025

I recommend its publication in the Jundishapur Journal of Chronic Disease Care.

**Associate Editor** — ACCEPT 28 Sep 2025

Dear Author,
All comments have been addressed, and this manuscript in the current format is acceptable.
Thank you.

**Editor-in-Chief** — ACCEPT 28 Sep 2025

Dear Editor,
The comments have not yet been fully addressed. This manuscript needs minor revision before publication.
Many thanks.