REVIEWER'S REPORT

Manuscript No.: IJAR-56366

Title: Prevalence and Predictors of Potentially Inappropriate Medications (PIMs) in Saudi Older Adults with Mood and Anxiety Disorders: A Systematic Review and Meta-analysis,

Recommendation:

Accept as it is ………………………………

Accept after minor revision………………

Accept after major revision ……YES…………

Do not accept (*Reasons below*) ………

Rating	Excel.	Good	Fair	Poor
Originality		√		
Techn. Quality			√	
Clarity			√	
Significance		√		

Detailed Reviewer's Report

STRENGTHS

1.1 Topical and Clinical Relevance

The manuscript addresses an important geriatric psychiatry safety issue: potentially inappropriate medications (PIMs) in older adults.

Focus on Saudi Arabia fills a regional evidence gap.

The emphasis on mood and anxiety disorders is clinically meaningful given psychotropic polypharmacy risk.

1.2 Clear Use of Established Criteria

Incorporates recognized tools such as:

American Geriatrics Society Beers Criteria (2015/2019/2023)

STOPP/START criteria

These enhance methodological credibility.

1.3 Registration and Reporting Framework

Protocol registered in PROSPERO.

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Alignment with PRISMA 2020 strengthens transparency.

1.4 Quantitative Synthesis Attempt

Use of random-effects meta-analysis (logit transformation) is statistically appropriate for pooling proportions.

Heterogeneity acknowledged and interpreted cautiously.

1.5 Policy-Oriented Discussion

Strong translational focus (pharmacist-led review, deprescribing pathways, decision support).

Integration with global frameworks including World Health Organization medication safety initiatives.

WEAKNESSES

2.1 Major Methodological Concerns

A. Incomplete Reporting of Search Strategy

Database search dates are not finalized.

Full electronic search syntax not provided.

PRISMA flow diagram not included.

B. Very Small Evidence Base

Only two eligible studies:

Saudi Pharmaceutical Journal (Meraya et al., 2021)

Frontiers in Medicine (Alsultan et al., 2025)

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Pooling two studies severely limits meta-analytic validity.

C. High Heterogeneity

Psychotropic-only PIPM vs overall PIM definitions pooled together.

Beers 2015 vs Beers 2019 versions differ substantially.

Conceptual heterogeneity weakens pooled estimate interpretability.

D. Risk-of-Bias Assessment Not Completed

JBI tool mentioned but item-level judgments not reported.

No risk-of-bias table presented.

E. Certainty of Evidence Not Graded

GRADE mentioned but not applied.

2.2 Structural and Writing Issues

Numerous grammatical errors and sentence fragmentation.

Repetition throughout discussion.

Some sections read like methodological notes rather than finalized manuscript.

Inconsistent formatting and citation style.

Conclusion section is incomplete and truncated.

2.3 Conceptual Concerns

The title suggests "predictors," but predictor synthesis is minimal.

Predictors are not meta-analyzed.

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No structured synthesis of adjusted effect sizes.

Overinterpretation risk given only two studies.

SIGNIFICANCE

Scientific Significance: Moderate

First focused Saudi geriatric psychiatry PIM synthesis.

Contributes regional evidence to global literature.

Clinical Significance: High

~60% pooled prevalence suggests major patient safety implications.

Strong relevance to geriatric psychopharmacology.

Policy Significance: High (National Level)

Supports development of:

Pharmacist-led deprescribing programs

CNS polypharmacy monitoring

National quality indicators

However, evidence strength is limited by small study base.

KEY POINTS FOR REVISION

Major Revisions Required

Provide complete search strategies (all databases, dates, syntax).

Add PRISMA flow diagram.

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Include full risk-of-bias table (JBI).

Conduct sensitivity analysis (psychotropic-only vs overall PIM).

Avoid overinterpretation of pooled estimate.

Apply GRADE certainty framework.

Strengthen predictor synthesis (structured table of effect estimates).

Revise entire manuscript for English clarity and grammar.

Complete and refine conclusion section.

Ensure consistency between protocol and final methods.

Minor Revisions

Standardize terminology (PIM vs PIPM).

Improve forest plot clarity.

Remove drafting language ("to be provided," "planned to…").

Reduce redundancy in discussion.

OVERALL RECOMMENDATION

Recommendation: MAJOR REVISION

The manuscript addresses a highly relevant clinical and public health issue and has potential for publication. However:

Methodological reporting is incomplete.

Statistical pooling is based on extremely limited data.

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Risk-of-bias and certainty assessments are missing.

Substantial language revision is required.

With rigorous methodological completion and careful interpretation, the paper could become a valuable regional contribution to geriatric psychopharmacology literature.

WHY "MAJOR REVISION" — DETAILED JUSTIFICATION

A **major revision** is recommended when:

The study question is relevant,

The manuscript has publishable potential,

BUT core methodological and reporting components are incomplete or insufficiently transparent.

Your manuscript meets that definition.

A. Incomplete Search Strategy Reporting

What is missing:

Exact search dates

Full Boolean search strings

Database-specific syntax

Supplementary search methods

PRISMA flow diagram

Why this is MAJOR (not minor):

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According to PRISMA 2020:

Item 7: Full search strategy must be reproducible.

Item 16: Flow diagram is mandatory.

Without this:

Review cannot be replicated.

Risk of selection bias cannot be evaluated.

Editors cannot judge comprehensiveness.

This affects **internal validity** → therefore MAJOR.

B. Only Two Included Studies

Included:

Saudi Pharmaceutical Journal (Meraya et al., 2021)

Frontiers in Medicine (Alsultan et al., 2025)

Why this is MAJOR:

Meta-analysis with only two studies:

No reliable heterogeneity estimation

No publication bias assessment

Unstable pooled estimates

Wide confidence intervals

Statistically:

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Between-study variance (τ^2) unreliable

I^2 unstable

Pooling may be methodologically questionable.

 This affects **statistical robustness and interpretability** → MAJOR.

C. Conceptual Heterogeneity

You pooled:

Psychotropic-only PIPM

Overall PIM

Beers 2015 vs Beers 2019

But:

The American Geriatrics Society Beers 2015 and 2019 criteria differ in:

Drug classifications

Added/removed medications

Strength of recommendations

Thus:

Different operational definitions

Different outcome constructs

Pooling conceptually different endpoints weakens validity.

 This affects **construct validity** → MAJOR.

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D. Risk-of-Bias Not Reported in Detail

You mention JBI tool but:

> No item-level table

> No judgment summary

> No graphical presentation

According to PRISMA:

> Risk-of-bias must be transparently presented.

Without this:

> Readers cannot judge credibility of included studies.

> Meta-analysis may combine high-bias studies unknowingly.

This affects **credibility and interpretability** → MAJOR.

E. GRADE Not Applied

You state GRADE was planned but:

> No certainty table

> No downgrade justification

The GRADE Working Group requires:

Downgrading for:

> Risk of bias

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Inconsistency

Imprecision

Indirectness

Publication bias

With only two heterogeneous studies:

Evidence certainty is likely LOW or VERY LOW.

Without grading:

Policymakers may overinterpret findings.

This affects strength-of-evidence communication → MAJOR.

STRUCTURAL & WRITING ISSUES (Why Also Major)

You have:

Incomplete sentences

Draft wording ("to be provided")

Repetition

Truncated conclusion

This is not stylistic polishing.

It indicates:

Manuscript not finalized.

Sections still in protocol phase.

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Possible deviation from registered protocol not clarified.

This affects **professional quality and editorial readiness** → MAJOR.

CONCEPTUAL ISSUE: "Predictors" Not Fully Addressed

Title includes:

> "Prevalence and Predictors"

But:

Predictors not meta-analyzed.

No structured synthesis table.

No pooled odds ratios.

No separate model analysis.

This is a scope misalignment.

If predictors are in title:
They must be rigorously analyzed.

This affects **conceptual completeness and title accuracy** → MAJOR.

OVERINTERPRETATION RISK

You report ~60% pooled prevalence.

But:

Based on 2 studies

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High heterogeneity

Different definitions

Strong policy statements may not be proportionate to evidence certainty.

This risks:

Editorial concern

Request for downgrading claims

This affects **interpretation validity** → MAJOR.

WHY NOT REJECTION?

Because:

Topic is important
Regional gap addressed
PROSPERO registration exists
Statistical attempt appropriate
Potential for publication after correction

The study is salvageable.

Therefore:

Not reject → Major Revision.

WHY NOT MINOR REVISION?

Minor revision is appropriate when:

Methods are complete

Analyses are correct

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Only small clarifications needed

Here:

Core reporting elements missing

Evidence grading absent

Conceptual heterogeneity unresolved

Predictor analysis incomplete

These are structural and methodological issues, not cosmetic.

Therefore:

Not minor → Major Revision.

SUMMARY TABLE

Issue	Type	Impact Level	Revision Category
Search strategy incomplete	Reporting validity	High	Major
Only 2 studies pooled	Statistical validity	High	Major
Conceptual heterogeneity	Construct validity	High	Major
Risk-of-bias not shown	Credibility	High	Major
GRADE absent	Evidence strength	High	Major
Predictors inadequately analyzed	Conceptual scope	High	Major
Language issues	Presentation	Moderate	Major

FINAL JUSTIFICATION STATEMENT

The recommendation of **MAJOR REVISION** is justified because:

Core PRISMA reporting elents are missing.

Statistical pooling is based on extremely limited and heterogeneous data.

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Risk-of-bias and certainty assessment are incomplete.

Predictor analysis does not match the stated objectives.

Interpretation currently exceeds evidentiary strength.

However, the study remains publishable with substantial methodological strengthening.