

Please peer review this manuscript for a reputable periodic. Insert date.

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As a computational neuroscientist, I'll provide a comprehensive peer review of this systematic review manuscript. The review is dated 26 June 2025, as noted at the top of the document.

Key Strengths:

1. Comprehensive Approach
 - Rigorous systematic review following PRISMA 2020 guidelines
 - Broad search strategy across multiple databases
 - Extensive inclusion of studies (187 from 1,847 initial records)
2. Novel Conceptual Framework
 - Introduces "final common pathway" hypothesis for delirium
 - Integrates pathophysiological mechanisms with artificial intelligence applications
 - Provides a unified framework for understanding delirium's complex etiology
3. Methodological Rigor
 - Transparent methodology with clear inclusion/exclusion criteria
 - Used multiple quality assessment tools
 - Employed modified GRADE approach for evidence synthesis
4. Innovative AI Integration
 - Demonstrates AI's potential in delirium detection and prediction
 - Critically examines implementation challenges
 - Provides real-world example from Mount Sinai Health System

Potential Improvements:

1. Limitations Section
 - Appropriately acknowledges study heterogeneity and potential biases
 - Could benefit from more detailed discussion of generalizability concerns
2. Future Research Directions

- Comprehensive suggestions for precision medicine and therapeutic development
 - Could elaborate on specific computational approaches for personalized interventions
3. Implementation Challenges
- Insightful discussion of AI deployment
 - Recommend more detailed cost-effectiveness analysis across different healthcare settings

Overall Recommendation: Accept with Minor Revisions

The manuscript offers a significant contribution to understanding delirium's pathophysiology and presents an innovative approach to detection and potential prevention. The integration of neuroinflammation research with computational methods represents a promising direction in clinical neuroscience.

Suggested Minor Revisions:

1. Expand on potential limitations of the "final common pathway" hypothesis
2. Provide more detailed economic modeling for AI implementation
3. Include a more nuanced discussion of cultural factors in delirium presentation

Significance: High - Represents a paradigm-shifting approach to understanding and managing delirium. 26/06/25