

Interleukin-18 as a Potential Biomarker in Alzheimer's Disease: A Scoping Review

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Introduction

Alzheimer's disease (AD) is the most common cause of dementia worldwide and represents a significant global public health burden¹.

Hallmark pathological features of AD include β -amyloid ($A\beta$) plaques and neurofibrillary tangles (NFTs), which actively drive neuroinflammation through microglial and astrocytic activation².

Interleukin-18 (IL-18) is a key pro-inflammatory cytokine with a direct and reciprocal relationship to core AD pathology³.

IL-18 enhances NF- κ B signaling⁴, increases oxidative stress⁵, and promotes tau phosphorylation⁶, exacerbating both $A\beta$ toxicity and tangle formation.

Clinical and preclinical studies demonstrate elevated IL-18 levels in serum and cerebrospinal fluid of individuals with AD, correlating with disease severity^{7,8}.

These findings position IL-18 as a driver of AD-related neuroinflammation and a promising biomarker for early detection, disease staging, and progression.

Objective

This scoping review aimed to evaluate clinical evidence of IL-18 as a diagnostic and prognostic biomarker for Alzheimer's disease.

Methods

Preliminary articles were identified through a search of three peer-reviewed databases (Ovid MEDLINE, EMBASE, and Web of Science) for studies published between 2015 and 2025.

The search strategy combined terms including: "interleukin-18" OR "IL-18" AND "Alzheimer's disease" OR "mild cognitive impairment" OR "neurodegeneration" OR "biomarkers" OR "neuroinflammation."

The search was limited to English-language, human studies that directly measured or evaluated IL-18 in adults with Alzheimer's disease or mild cognitive impairment, using blood, CSF, or tissue.

Duplicates were removed and included articles followed a two-stage title/abstract and full-text review process, with study selection summarized using a PRISMA 2020 flow diagram.

Results

Blood findings: IL-18 frequently elevated in AD, sometimes in MCI; correlated with inflammasome activation, pro-inflammatory cytokines, and poorer cognitive performance.

Brain tissue findings: Most studies showed increased IL-18 mRNA and protein in AD, localized near amyloid plaques and activated glia; mechanistic studies support IL-18's role in neuroinflammation, though some heterogeneity exists.

CSF findings: IL-18 alone showed limited staging value, but panels including IL-18 identified MCI individuals at higher risk for progression to AD.

Overall, IL-18 shows strongest and most consistent associations in blood and brain tissue, supporting its role as a mechanistic contributor and potential biomarker for AD progression.

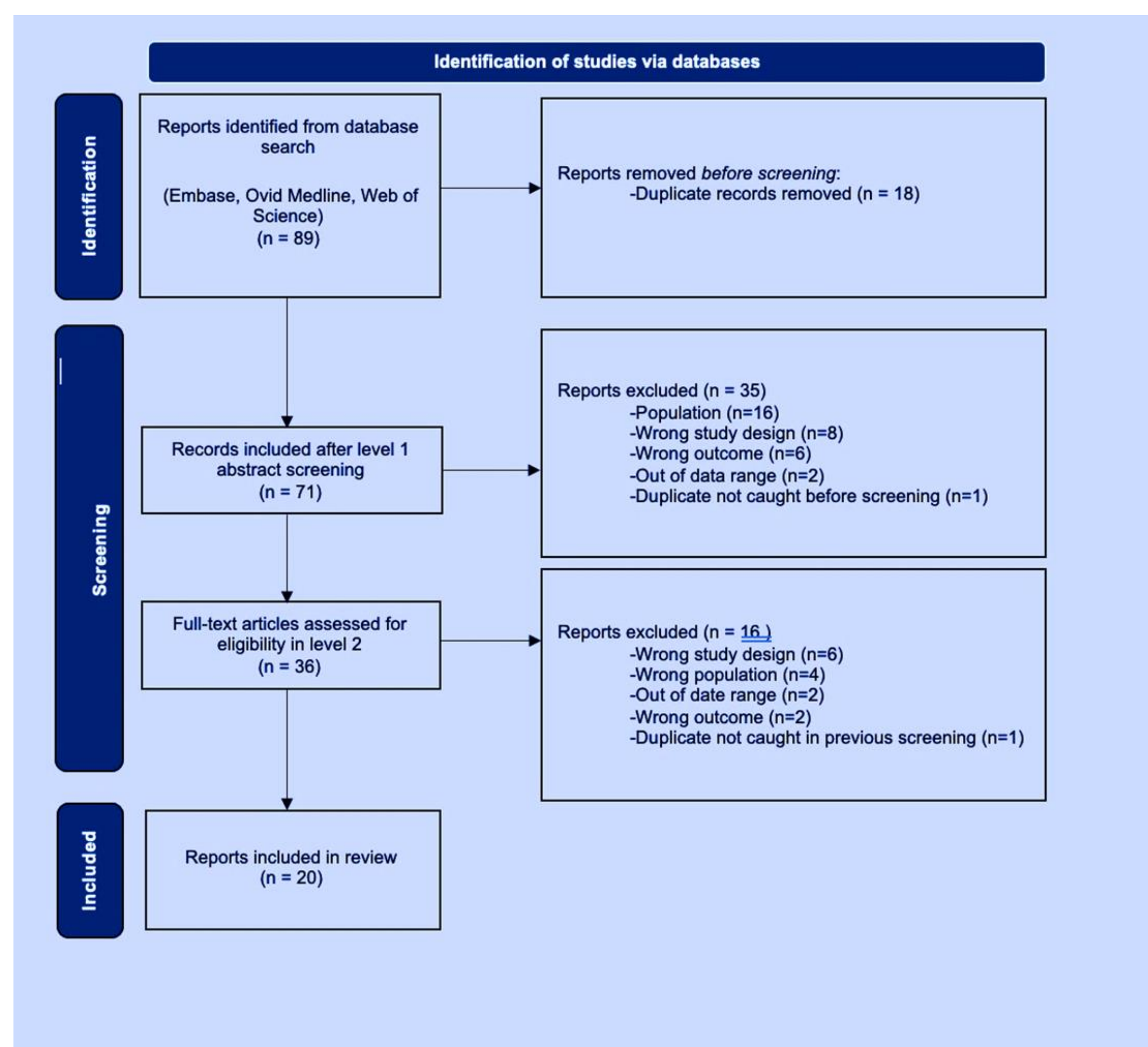


Figure 1. PRISMA Diagram

Conclusion

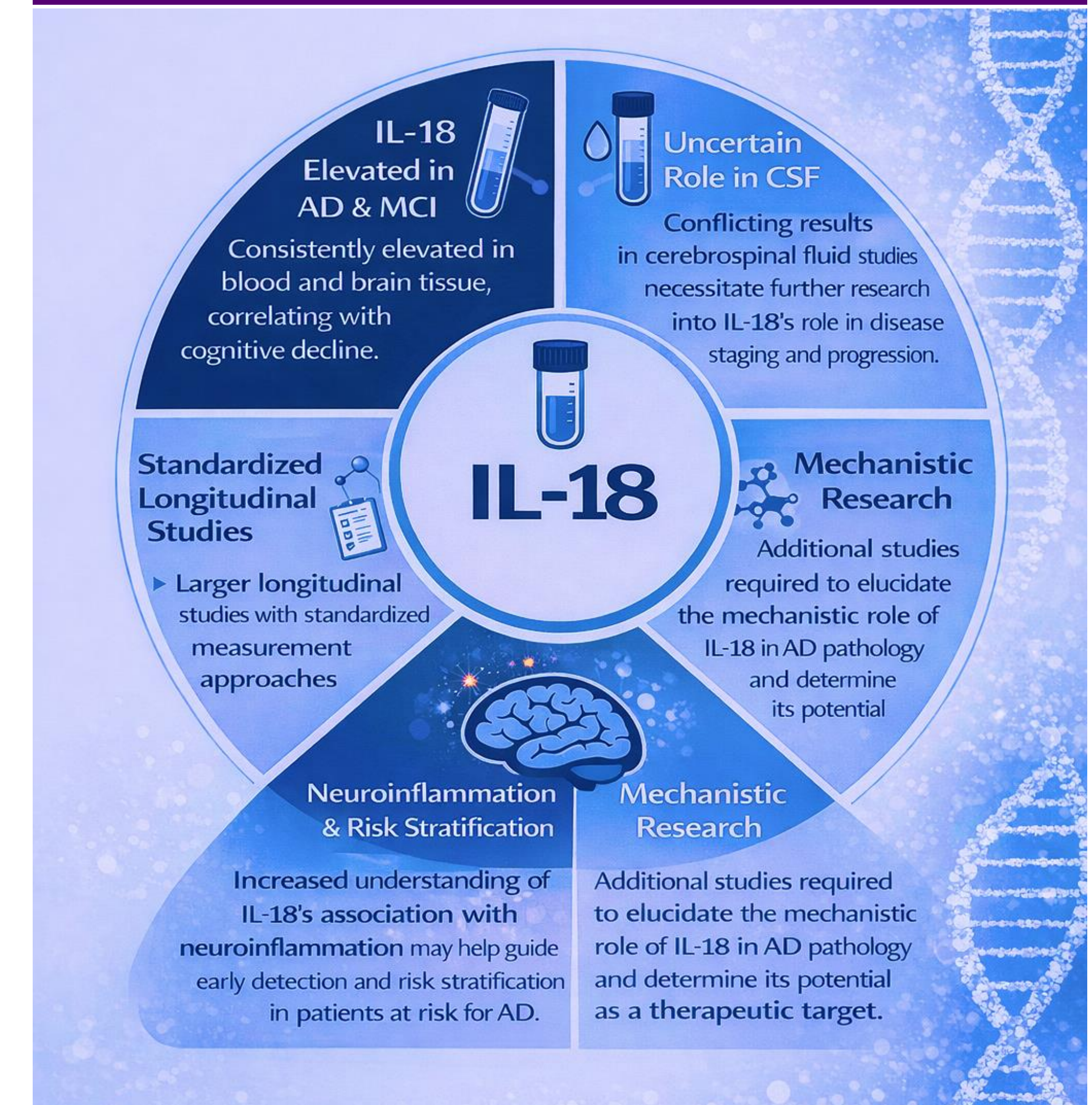


Figure 2. Conclusion Diagram

Findings from this review suggest that IL-18 is consistently elevated in blood and brain tissue of individuals with AD and MCI, correlating with cognitive decline.

Conflicting results in cerebrospinal fluid studies indicate that further research is needed to clarify IL-18's role in disease staging and progression.

Increased understanding of IL-18's association with neuroinflammation may help guide early detection and risk stratification in patients at risk for AD.

Additional studies are required to elucidate the mechanistic role of IL-18 in AD pathology and determine its potential as a therapeutic target.

Larger longitudinal studies with standardized measurement approaches are needed to establish the clinical utility of IL-18 as a biomarker for AD progression and intervention strategies.

References

