Baseline Vitamin B12 as a Prognostic Marker of Cognitive Progression in Mild Cognitive Impairment: A Systematic Review

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BACKGROUND

Mild cognitive impairment (MCI) represents an intermediate stage between normal aging and dementia, particularly Alzheimer's disease.

Vitamin B12 deficiency is frequently evaluated in patients presenting with cognitive complaints and is routinely measured in memory clinics.

However, it remains unclear whether baseline vitamin B12 levels predict cognitive decline or conversion to dementia among individuals with MCI.

Understanding the prognostic role of vitamin B12 may improve risk stratification and inform biomarker interpretation in clinical practice.

STUDY OBJECTIVE

To evaluate whether baseline serum vitamin B12 levels predict longitudinal cognitive decline or conversion to dementia in individuals with mild cognitive impairment.

METHODS

Study Design

Systematic review conducted according to PRISMA 2020 guidelines.

Databases Searched

• PubMed • Embase • PsycINFO • Scopus

Search Period: 2005 – 2025

Inclusion Criteria

- Adults with clinician-diagnosed MCI
- Baseline serum vitamin B12 measurement
- Longitudinal follow-up
- Outcomes reporting:
  - Cognitive decline on standardized testing
  - Conversion from MCI to dementia

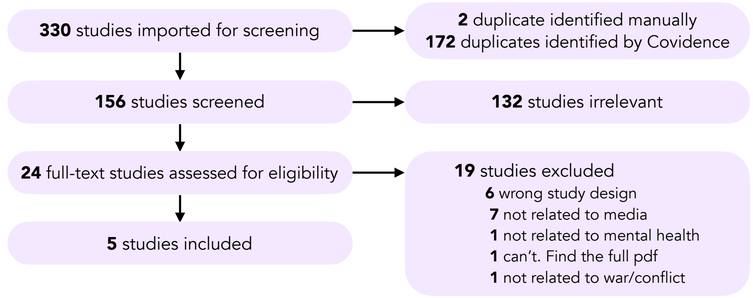
Screening

- Title/abstract and full-text screening performed in Covidence

Data Synthesis

Due to heterogeneity in study design and outcome measures, findings were narratively synthesized.

Study Selection



Characteristics of Included Studies

STUDY	DESIGN	POPULATION	FOLLOW-UP	KEY FINDING
Rawtaer 2014	Community cohort	MCI	3.5 yrs	No biomarker prediction
Lipczyńska-Łojkowska 2009	Prospective cohort	MCI	24 mo	No association
Quadri 2004	Prospective cohort	MCI elderly	Multi-year	Association attenuated after adjustment
Blasko 2008	Longitudinal biomarker study	MCI	Longitudinal	Weak association
Blasko 2012	Biomarker cohort	MCI	Longitudinal	No independent association

RESULTS

Across the five longitudinal cohort studies, findings were inconsistent.

Studies reporting association

Two studies observed an association between lower baseline vitamin B12 levels and greater cognitive decline.

However:

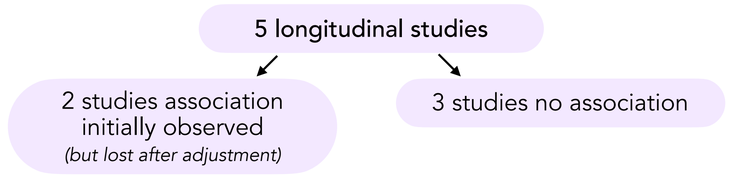
- Associations were attenuated after multivariable adjustment
- Some cohorts included mixed MCI and early Alzheimer's disease populations

Studies reporting no association

Three studies, including the largest and most methodologically robust cohort, found no significant relationship between baseline vitamin B12 levels and:

• Cognitive decline • Conversion from MCI to dementia

Evidence Summary Graphic



Key Interpretation

Current longitudinal evidence does not consistently support baseline serum vitamin B12 as an independent prognostic marker of cognitive progression in MCI.

CLINICAL IMPLICATIONS

Routine measurement of serum vitamin B12 alone may have limited prognostic value for predicting disease progression in MCI.

Future research should focus on:

- Functional biomarkers of B12 metabolism
- Combined biomarker panels
- Standardized cognitive progression endpoints

LIMITATIONS

- Small number of eligible longitudinal studies
- Heterogeneity in study design and outcome definitions
- Two studies available only as conference abstracts, limiting methodological detail
- Variation in biomarker measurement methods

CONCLUSIONS

Current longitudinal evidence does not support baseline vitamin B12 as a reliable predictor of cognitive progression in mild cognitive impairment.

Further studies incorporating functional B12 biomarkers and standardized longitudinal outcomes are needed.

REFERENCES: