

Motoric Cognitive Risk Syndrome As A Predictive Factor of Cognitive Impairment and Dementia – A Systematic Review and Meta-Analysis

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ABSTRACT

Background: Motoric cognitive risk syndrome (MCR) is defined as the presence of slow gait-speed and subjective cognitive decline in older individuals without mobility disability or dementia. Evidence of MCR as a pre-dementia syndrome that may help predict the risk of cognitive impairment and dementia is inconsistent. The objective of this study is to comprehensively analyse this association between MCR and development of cognitive impairment and dementia.

Methods: PubMed, Embase, and The Cochrane Library were systematically searched from inception to 19 August 2024 for relevant studies. Maximally adjusted hazards and odds ratios to determine the longitudinal and cross-sectional risk of cognitive impairment and dementia were favoured. Potential sources of heterogeneity were investigated, and sensitivity and subgroup analyses were conducted. The quality of evidence was assessed using the Newcastle-Ottawa Scale (NOS) and the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) framework.

Results: We included 20 studies comprising a combined cohort of 1,206,782 participants, of which 17 studies were included in the quantitative analysis. The pooled analysis outlined that individuals with MCR exhibited 2.20-fold higher risk of cognitive impairment and dementia, compared to controls (RR=2.20; 95%CI=1.91-2.53). These findings remained robust across all subgroup analyses, sensitivity analyses and assessments of publication bias.

Conclusion: MCR may be considered a predictive factor for long-term cognitive impairment and dementia. This should be taken into consideration when clinically evaluating the risk of cognitive impairment and dementia, but further research is required to lend greater clarity to this association.

Key Words: Motoric Cognitive Risk Syndrome; Cognitive Impairment; Cognitive Decline; Dementia; Alzheimer's Disease

INTRODUCTION

Background:

- According to the Lancet Commission, 57.4 million cases of dementia worldwide in 2019, and this is expected to increase to 152.8 million by 2050¹
- Dementia is a debilitating disease with physical, psychological, and economic burden not only on persons living with dementia but their caregivers
- Early identification of risk groups prior to symptom onset is essential in ensuring robust management of the growing prevalence and negative impact of dementia²

Dementia and Cognitive Impairment and MCR:

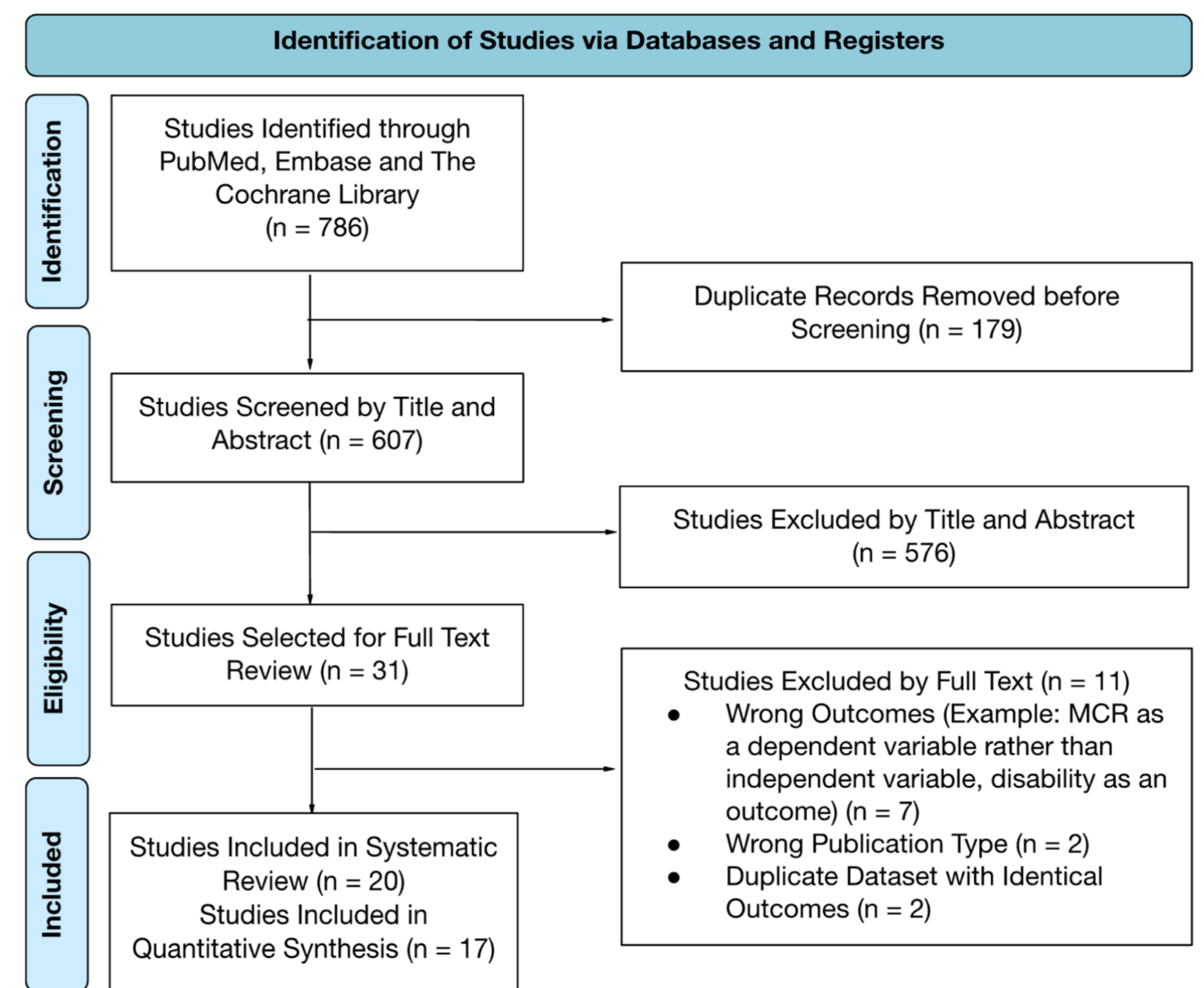
- MCR is the presence of slow gait-speed and subjective cognitive decline in older individuals without mobility disability or dementia³
- Multiple reviews have concluded the strong relationship between slowed gait-speed and the incidence of cognitive impairment and dementia⁴⁻⁶
- MCR is reliable and easily measured without expensive or complicated investigations²
- MCR still lacks practical clinical utility in risk assessments for cognitive impairment and dementia a decade after it was first described

Current Evidence:

- Verghese et al. reported significantly higher hazards of dementia in MCR patients, ranging from 1.61 to 3.54 compared to healthy controls in various cohorts worldwide³
- However, not all literature concur with this conclusion
- Bortone et al. 2021 reported no significant association between MCR and decreased global cognition or decreased immediate/delayed free recall of verbal memory, instead suggesting its association with motor-related aspects like low muscle strength⁷

Given the lack of therapeutic options, growing prevalence, health and social care cost due to dementia in today's context, a comprehensive review of existing literature regarding its predictive factors is both timely and clinically important. We performed this study to provide clarity on the association between MCR and the risk of cognitive impairment and dementia. It is our hypothesis that MCR is cross-sectionally and longitudinally associated with both cognitive impairment and dementia.

METHODS

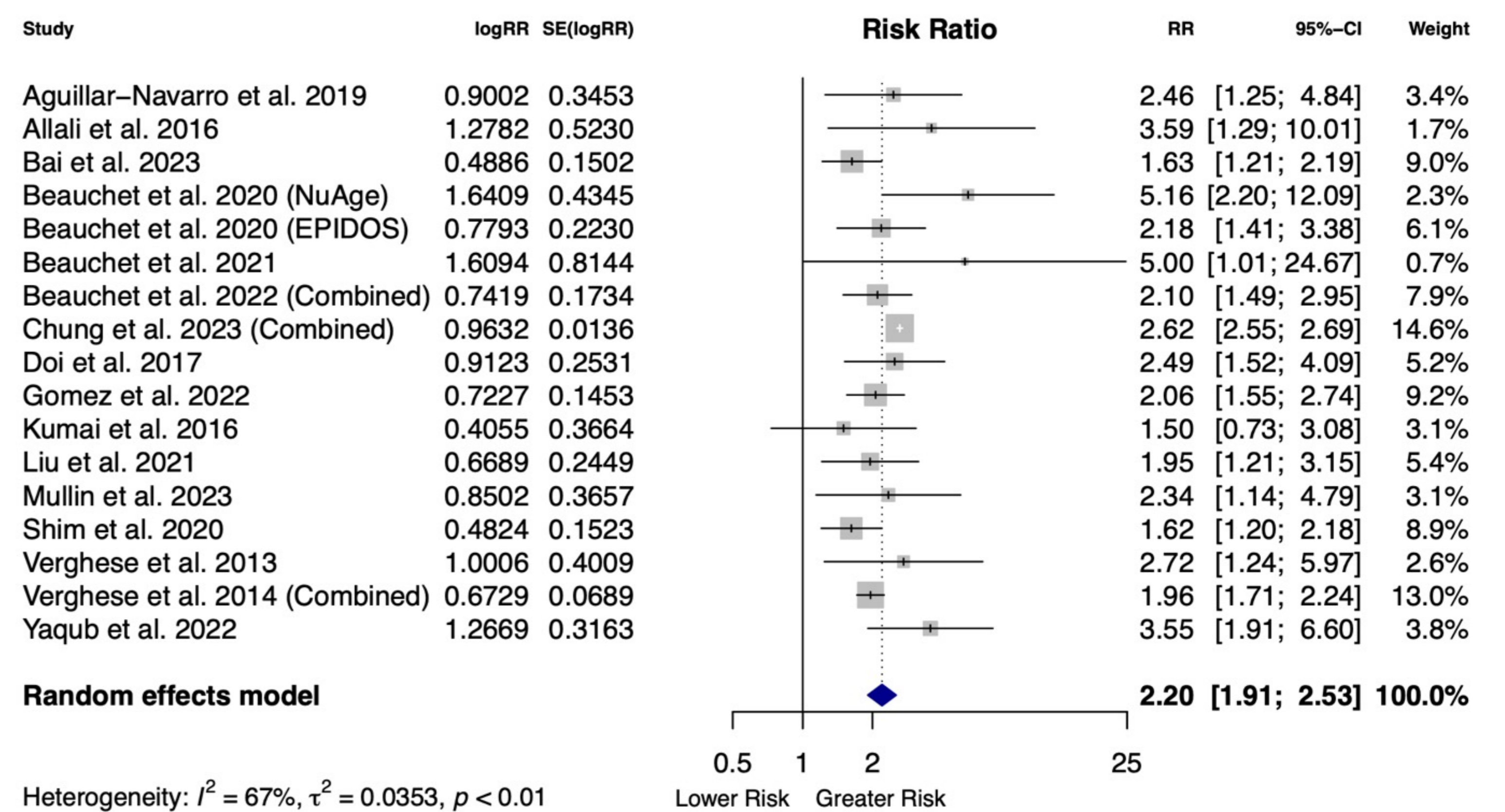


Inclusion: Cohort studies published as full-length articles in peer-reviewed journals, adults aged 18 years or older, outcomes for 1) diagnosis of major neurocognitive disorders (i.e. dementia and its various subtypes, cognitive impairment) based on accepted clinical diagnostic criteria; or 2) measurement of general cognitive function via validated cognitive test scores

Exclusion: Case reports, reviews, letters, abstracts, conference proceedings, articles published in a language other than English and studies with duplicate datasets.

Data Extraction: First author, publication year, study design, country, sample size, mean/median age, number of male and female participants, definition of cognitive impairment or dementia, HR and OR of cognitive impairment or dementia in individuals with MCR as opposed to those without MCR, and specific covariates adjusted for in maximally-adjusted ratios.

RESULTS



This systematic review and meta-analysis of 20 studies with 1,206,782 participants found a 2.20-fold increase in risk of cognitive impairment and dementia, among individuals with MCR, compared to healthy controls without MCR. This association remained significant in various subgroup analyses including the type of cognitive outcome assessed and continent. These findings were also robust to various sensitivity analyses and publication bias assessments.

CONCLUSION

This study adds valuable evidence to the growing base of studies surrounding MCR as a pre-dementia syndrome. Early detection of MCR prior to onset of cognitive impairment and dementia would allow for greater outcomes for such individuals. However, more studies are required to confirm this association.

References:

1. Estimation of the global prevalence of dementia in 2019 and forecasted prevalence in 2050: an analysis for the Global Burden of Disease Study 2019. *Lancet Public Health*. Feb 2022;7(2):e105-e125. doi:10.1016/s2468-2667(21)00249-8
2. Borson S, Frank L, Bayley PJ, et al. Improving dementia care: the role of screening and detection of cognitive impairment. *Alzheimers Dement*. Mar 2013;9(2):151-9. doi:10.1016/j.jalz.2012.08.008
3. Verghese J, Ayers E, Barzilai N, et al. Motoric cognitive risk syndrome: Multicenter incidence study. *Neurology*. Dec 9 2014;83(24):2278-84.
4. Sekhon H, Allali G, Launay CP, et al. Motoric cognitive risk syndrome, incident cognitive impairment and morphological brain abnormalities: Systematic review and meta-analysis. *Maturitas*. May 2019;123:45-54. doi:10.1016/j.maturitas.2019.02.006
5. Mullin DS, Cockburn A, Welstead M, Luciano M, Russ TC, Muniz-Terrera G. Mechanisms of motoric cognitive risk-Hypotheses based on a systematic review and meta-analysis of longitudinal cohort studies of older adults. *Alzheimers Dement*. Dec 2022;18(12):2413-2427. doi:10.1002/alz.12547
6. Huang C, Wu B, Zhang C, et al. Motoric Cognitive Risk Syndrome as a Predictor of Adverse Health Outcomes: A Systematic Review and Meta-Analysis. *Review. Gerontology*. 2024;70(7):669-688. doi:10.1159/000538314
7. Bortone I, Griseta C, Battista P, et al. Physical and cognitive profiles in motoric cognitive risk syndrome in an older population from Southern Italy. *Eur J Neurol*. Aug 2021;28(8):2565-2573. doi:10.1111/ene.14882