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Lifestyle Factors and Non-Pharmacological Interventions in Mild Cognitive Impairment: Implications for Cognitive Health

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ABSTRACT

Background. Mild Cognitive Impairment (MCI) is a heterogeneous clinical syndrome associated with an increased risk of progression to dementia, although individual trajectories vary substantially. Growing evidence indicates that modifiable vascular-metabolic, lifestyle, nutritional, and psychosocial factors influence cognitive outcomes in MCI, and that non-pharmacological interventions (NPIs) may support cognitive performance.

Aim. To synthesize current evidence on modifiable risk factors associated with progression from MCI to dementia and to evaluate the effectiveness of NPIs targeting cognitive outcomes in patients with MCI.

Material and methods. This structured narrative review was based on a targeted search of the PubMed database. Systematic reviews, meta-analyses, longitudinal cohort studies, and randomized controlled trials examining modifiable risk factors and NPIs in MCI were included. Twenty-eight peer-reviewed articles met predefined eligibility criteria and were synthesized narratively.

Results. Cardiometabolic conditions, physical inactivity, depressive symptoms, and suboptimal dietary patterns were consistently associated with increased risk of cognitive decline in MCI. Biomarker-informed studies suggest that modifiable factors remain relevant even in patients with underlying Alzheimer's disease (AD) pathology. Randomized trials and systematic reviews indicate that structured exercise, cognitive training, dietary interventions, and multidomain lifestyle programs are associated with improved cognitive performance, with evidence of dose-response effects.

Conclusions. An integrated clinical approach combining assessment of modifiable risk factors with targeted NPIs may support cognitive outcomes in patients with MCI and represents a relevant strategy for early preventive care.

Keywords: mild cognitive impairment, dementia, cognitive decline prevention, lifestyle-related risk factors, physical activity, exercise interventions, non-pharmacological interventions, multidomain lifestyle program

1. Introduction

MCI is a clinically defined syndrome characterized by measurable cognitive decline with relative preservation of functional independence, representing an intermediate stage between normal ageing and dementia. Foundational descriptions and contemporary guidelines emphasize its heterogeneity, prognostic variability, and relevance for identifying patients at increased risk of neurodegenerative progression.^{1,2} Although patients with MCI exhibit a higher likelihood of developing dementia, particularly AD, longitudinal data consistently demonstrate substantial heterogeneity: some patients transition to dementia, others remain cognitively stable for extended periods, and a meaningful proportion may even revert to normal cognitive status.^{3–6}

An expanding body of evidence indicates that this variability in disease trajectory is shaped in part by modifiable determinants spanning vascular, metabolic, lifestyle, nutritional, and psychosocial domains. Systematic reviews and umbrella analyses highlight hypertension, diabetes, physical inactivity, unhealthy dietary patterns, and neuropsychiatric symptoms as important contributors to increased dementia risk among patients with MCI.^{7–9} Further cohort-based investigations demonstrate that these factors interact with demographic characteristics, sociocultural context, and disease-specific features to influence cognitive trajectories and progression risk.^{3,10,11} More recent findings incorporating amyloid and tau biomarkers suggest that modifiable exposures may modulate progression risk even within biologically defined AD, supporting an interdisciplinary clinical–pathological approach for understanding MCI outcomes.¹² Alongside research describing modifiable risk factors, there has been growing interest in the role of NPIs in attenuating cognitive decline in MCI. Evidence from systematic reviews and network meta-analyses supports beneficial effects of structured exercise programs,

cognitive training protocols, dietary approaches, and multidomain lifestyle interventions on cognitive performance and related outcomes.^{13–15} RCTs corroborate these findings, demonstrating that aerobic and resistance exercise, combined behavioural and cognitive interventions, Mediterranean-style dietary patterns, intensive lifestyle-modification programs, and digital multidomain interventions can support cognitive health and functional maintenance in MCI.^{16–22} Collectively, these data indicate that progression from MCI to dementia is not exclusively determined by underlying neurobiology but is meaningfully influenced by modifiable exposures.^{7–9,12} *In parallel, evidence from systematic reviews and randomized trials demonstrates that appropriately targeted NPIs can improve cognitive outcomes and functional trajectories in patients with MCI.*^{5,15–23} The objective of this review is to synthesize evidence on modifiable risk factors influencing progression from MCI to dementia.^{7–9,11,12,24} It also evaluates non-pharmacological interventions supported by systematic reviews and randomized controlled trials in MCI.^{13–22} By integrating these complementary domains, this review seeks to inform clinical decision-making and support individualized preventive strategies in patients at risk for cognitive decline.^{1,2,11,12}

2. Modifiable Risk Factors for Progression from MCI to Dementia

A large body of research indicates that progression from MCI to dementia is associated with multiple modifiable factors that influence vulnerability to cognitive decline.^{7–9,24} Systematic reviews and umbrella analyses consistently show that vascular-metabolic risk factors, lifestyle behaviours, nutritional patterns, and psychosocial determinants are associated with increased likelihood of conversion to dementia among patients with MCI.^{7–9,24} *Across observational studies and meta-analyses, vascular and metabolic factors are the most consistently associated modifiable predictors of progression, whereas lifestyle and psychosocial factors are also linked to progression risk.*^{7–9,24} Longitudinal cohort studies further confirm that these factors operate across diverse settings and populations, reinforcing their prognostic significance.^{3,4,10,11}

2.1. Vascular and Metabolic Factors

Vascular and metabolic conditions represent some of the most consistently identified modifiable contributors to progression from MCI to dementia.^{7–9,24} Systematic reviews have demonstrated that hypertension, diabetes, dyslipidaemia, obesity, and cardiovascular disease are associated with elevated risk of cognitive decline and dementia.^{7–9} Umbrella analyses further indicate that the co-occurrence of metabolic and vascular risk factors is associated with a higher probability of cognitive deterioration. These findings highlight the importance of

cardiometabolic health in shaping disease trajectories.²⁴ Longitudinal cohort studies extend these observations by documenting that patients with greater vascular-metabolic burden are more likely to convert from MCI to dementia over time.^{3,4} In a large multi-year cohort, cardiometabolic factors were significant predictors of progression to AD, demonstrating the enduring influence of vascular health on long-term cognitive outcomes.⁴ Additional evidence from primary care populations shows that metabolic comorbidities are linked to cognitive vulnerability in older adults, reinforcing the relevance of vascular-metabolic risk modification across healthcare settings.¹⁰ Cohort data from large population studies further demonstrate that combinations of modifiable vascular and metabolic factors exert cumulative effects on dementia risk among people with MCI.¹¹

2.2. Lifestyle Behaviours and Physical Activity

Lifestyle behaviours, including physical activity, sedentary patterns, and social engagement, play an important role in shaping progression risk. Systematic evidence shows that insufficient physical activity is associated with increased risk of cognitive decline, whereas participation in regular physical activity corresponds with improved cognitive outcomes. These associations are consistent with proposed neuroprotective mechanisms of physical activity, including improvements in vascular function, inflammatory profiles, and cognitive reserve.⁷⁻⁹ Observational studies support these conclusions by demonstrating that older adults with healthier lifestyle patterns, including regular exercise and greater behavioural engagement, exhibit a lower likelihood of cognitive deterioration.¹⁰ Cohort findings from population-based screening and monitoring programs further confirm that lifestyle risk profiles significantly influence long-term cognitive trajectories in patients with MCI.¹¹

2.3. Nutritional Factors and Dietary Patterns

Dietary quality represents another meaningful behavioural factor associated with cognitive outcomes in MCI. Evidence from systematic reviews demonstrates that unhealthy dietary patterns contribute to accelerated cognitive decline, whereas adherence to dietary approaches emphasising high-quality fats, plant-rich foods, and antioxidant-rich components, such as Mediterranean-style diets, is associated with more favourable cognitive outcomes.^{8,9} Findings from cohorts examining Mediterranean diet adherence and probiotic supplementation in older adults with MCI highlight the potential relevance of dietary composition and metabolic-nutritional factors in cognitive vulnerability.²³

2.4. Psychosocial and Neuropsychiatric Factors

Psychosocial determinants contribute meaningfully to progression risk. Systematic reviews identify depressive symptoms as a robust and modifiable risk factor for cognitive decline in patients with MCI, underscoring the influence of neuropsychiatric status on disease trajectory.^{7–9} Additional evidence from primary care settings indicates that psychosocial context, including mental health and social functioning, affects cognitive performance and may alter the risk of progression to dementia within diverse populations.¹⁰

2.5. Biomarker-Linked Modifiable Risk Interactions

Emerging evidence integrates modifiable risk factors with amyloid and tau biomarkers to clarify how behavioural and vascular exposures interact with underlying AD pathology. Studies demonstrate that cardiovascular and lifestyle-related risk factors continue to predict progression in biomarker-positive patients, indicating that modifiable exposures influence clinical trajectories even in the presence of established AD pathology. These findings indicate that modifiable factors remain associated with progression risk alongside biological disease processes.¹²

2.6. Heterogeneity of Progression and Predictive Modelling

Multiple longitudinal studies highlight substantial variability in the progression of MCI, showing that patients may convert to dementia, remain stable, or revert to normal cognition.^{3–5,25} This variability has driven the development of predictive models incorporating modifiable factors, cognitive profiles, and biological data to improve identification of patients at risk for progression. Machine-learning approaches using routinely collected clinical data or cortical morphometry have demonstrated enhanced capacity to classify high-risk patients, offering support for precision risk stratification models.^{25,26} Cohort studies also confirm that combinations of modifiable determinants contribute to individual and population-level risk profiles.¹¹

3. Non-Pharmacological Interventions in Mild Cognitive Impairment

NPIs represent a key area of research in the management of MCI, reflecting growing evidence that behavioural and lifestyle approaches can influence cognitive trajectories in at-risk patients.^{13–15} Evidence from randomized and intervention-focused studies further supports cognitive benefits of selected NPIs in patients with MCI.^{16–20}

3.1. Evidence from Systematic Reviews and Network Meta-Analyses

Systematic reviews indicate that several categories of non-pharmacological interventions are associated with improvements in global cognition, memory, and executive function in patients with MCI.^{13,14} Network meta-analytic findings indicate that both single-component and multicomponent interventions, such as aerobic exercise, cognitive training, and multimodal behavioural programs, produce measurable cognitive gains, though the magnitude varies across intervention types.¹⁴ Meta-analytic evidence further demonstrates a dose–response relationship, with higher intervention intensity, frequency, and duration associated with greater improvements in cognitive outcomes.¹⁵ Together, these findings from aggregated analyses establish NPIs as evidence-based strategies capable of supporting cognitive performance in MCI.^{13–15}

3.2. Exercise-Based Interventions

Exercise interventions are among the most consistently validated NPIs for MCI.^{13–15} The EXERT study, a large and rigorously designed RCT, demonstrated that structured aerobic and stretching-toning exercise programs produced cognitive benefits and favourable changes in Alzheimer’s-related biomarkers among older adults with MCI. These results highlight the potential biological mechanisms through which exercise may support neuronal health, including effects on neurotrophic factors and cerebrovascular function.¹⁶ Another RCT found that exercise alone, or combined with cognitive training and vitamin D supplementation, supported cognitive outcomes and contributed to maintenance of cognitive function in patients with MCI.¹⁷ A peer-supported exercise intervention also demonstrated cognitive and functional benefits, indicating that structured and socially facilitated physical activity is feasible and effective in real-world settings.¹⁸ Taken together, these randomized trials support exercise as a beneficial behavioural intervention for mitigating cognitive decline in patients with MCI.^{16–18}

3.3. Cognitive Training and Digital Interventions

Cognitive training has shown positive effects across multiple cognitive domains in systematic reviews of interventions for patients with MCI. Improvements in memory, attention, and executive function have been documented across studies using structured cognitive training protocols.^{13,14} Digital delivery platforms are emerging as a complementary approach, with a pilot study demonstrating that a digital multidomain lifestyle and cognitive intervention was feasible and associated with cognitive benefits in patients with MCI. These findings suggest

that technology-assisted interventions may broaden access to cognitive rehabilitation and enable personalized training programs.²²

3.4. Multidomain Lifestyle Interventions

Multidomain lifestyle interventions that simultaneously target several behavioural strategies have shown strong potential to sustain or improve cognitive outcomes in patients with MCI.^{13–15} A randomized clinical trial involving intensive lifestyle modification, including dietary changes, physical activity, stress management, and psychosocial support, demonstrated favourable cognitive effects and slowed clinical progression among participants with MCI or early AD.¹⁹ Another large RCT applying a 52-week multimodal intervention combining exercise, cognitive training, and behavioural strategies showed maintenance of global cognition in patients with MCI.²⁰ These findings highlight the importance of addressing multiple behavioural determinants of cognitive health in a coordinated manner.^{19,20}

3.5. Nutritional and Dietary Interventions

Dietary interventions have also been studied as strategies to support cognitive outcomes in MCI.^{8,9} A randomized pilot trial found that consumption of high-phenolic early harvest extra virgin olive oil improved cognitive performance compared with standard dietary oils, suggesting that bioactive nutritional components may exert neuroprotective effects.²¹ Findings from a Mediterranean diet and probiotic supplementation cohort further support the relevance of dietary patterns, metabolic–nutritional interactions, and gut-related mechanisms in shaping cognitive trajectories in patients with MCI.²³ Together, these studies reinforce the potential of dietary modification as a viable NPI for cognitive support in MCI.^{21,23}

3.6. Mechanisms and Preventive Potential

Evidence from systematic reviews and randomized controlled trials indicates that NPIs influence cognitive outcomes in patients with MCI through several complementary mechanisms.^{13–15} Exercise-based interventions are consistently associated with improvements in cognitive performance in patients with MCI.^{16,17} In selected trials, exercise has also been associated with changes in Alzheimer’s disease–related biomarkers, suggesting an influence on vascular and metabolic mechanisms relevant to neurodegeneration.¹⁶ Structured physical activity has been shown to improve cardiovascular fitness and metabolic health, factors that are strongly associated with cognitive trajectories in MCI, thereby linking improvements in

vascular and metabolic health with more favourable cognitive outcomes.^{16–18} Cognitive training interventions, in turn, primarily target domain-specific cognitive functions such as memory and executive processes, supporting the role of sustained cognitive engagement in maintaining functional performance.^{13,14}

Multidomain lifestyle interventions, combining exercise, diet, stress management, and cognitive or psychosocial support, have demonstrated favourable cognitive outcomes in randomized trials, supporting the value of comprehensive behavioural approaches in MCI management.^{19,20} Future research should further examine how modifiable exposures interact with AD pathology, building on emerging evidence showing that cardiovascular and lifestyle-related factors influence progression even among biomarker-positive patients.¹² Dietary composition and nutritional modification have been associated with metabolic and inflammatory factors implicated in cognitive decline. Evidence from dietary intervention studies in MCI supports the concept that nutritional composition may influence cognitive outcomes, although the magnitude and durability of these effects remain incompletely defined.^{21,23} Across intervention types, individual responses to NPIs vary substantially, reflecting heterogeneity in baseline risk profiles, disease stage, and adherence.^{13–15} Nevertheless, the convergence of findings across systematic reviews and randomized trials supports the potential role of NPIs in slowing cognitive decline and modifying trajectories associated with increased risk of progression to dementia, particularly when interventions are tailored to individual risk profiles and implemented in a multidomain context.^{13–20}

4. Integrating Modifiable Risk Profiles with Non-Pharmacological Interventions

Understanding how modifiable risk factors interact with NPIs may help clinicians tailor preventive strategies for patients with MCI. Evidence indicates that vascular-metabolic, lifestyle, nutritional, and psychosocial factors influence cognitive trajectories in MCI and may represent modifiable targets addressed by NPIs.^{7–9,24} Longitudinal cohort studies further show that combinations of modifiable factors are associated with distinct progression patterns across populations, supporting the rationale for integrated, risk-informed intervention approaches.^{3,4,10,11} Vascular and metabolic factors are strongly associated with increased probability of conversion to dementia, and these same domains are modifiable through behavioural interventions, including physical activity, dietary modification, and multidomain lifestyle programs.^{7,8,10,24} RCTs show that exercise-based and lifestyle interventions are associated with improvements in cognitive outcomes and, in some cases, AD-related

biomarkers, indicating overlap between modifiable risk profiles and intervention effects.^{16,17} Evidence that high-phenolic nutritional interventions and Mediterranean dietary patterns support cognitive outcomes in patients with MCI further highlights the potential to target metabolic and inflammatory factors implicated in progression risk.^{21,23} Lifestyle behaviours, including physical activity and cognitive engagement, constitute domains in which both risk modification and intervention strategies overlap.^{7–9} Reviews consistently show that physical inactivity increases progression risk, whereas structured exercise improves cognitive outcomes, indicating that NPIs may directly counteract modifiable behavioural vulnerabilities.^{13–15} Cognitive training interventions also support functions that decline early in MCI, and digital platforms provide scalable means of reinforcing cognitively stimulating behaviours associated with reduced progression risk.²² Psychosocial factors are also relevant to the effectiveness of NPIs in MCI.^{7–9} Depressive symptoms constitute a modifiable risk factor for adverse cognitive outcomes, and multidomain lifestyle interventions incorporating stress management and psychosocial support have demonstrated cognitive benefits, underscoring the relevance of addressing emotional and behavioural health within intervention strategies.¹⁹ These findings support the rationale for integrated approaches that simultaneously target psychological, behavioural, and biological contributors to cognitive decline. Recent studies combining amyloid and tau biomarkers with clinical data indicate that behavioural and lifestyle factors remain associated with cognitive outcomes even in biologically defined AD.¹² These findings suggest that NPIs may remain relevant across different pathological contexts by addressing vascular, metabolic, and behavioural factors associated with cognitive decline.^{12–22} Predictive modelling studies using routine clinical data, cortical morphological features, and multivariable risk profiling further support the feasibility of stratifying patients by modifiable risk burden to align them with tailored intervention strategies.^{25,26} Cohort research demonstrating strong associations between risk-factor clusters and progression patterns reinforces the value of such personalized approaches.¹¹ Taken together, current evidence supports an integrated clinical approach in which vascular-metabolic, lifestyle, nutritional, and psychosocial risk domains are jointly considered when assessing progression risk in MCI.^{7–9,11,24} Within this strategy, NPIs supported by systematic reviews and randomized trials provide actionable strategies that may attenuate cognitive decline in patients with MCI.^{13–22} *Available data suggest that modifiable risk factors remain associated with progression risk even in selected biomarker-defined patient groups.¹²*

5. Clinical Implications and Future Directions

Current evidence indicates that modifiable risk factors and NPIs influence cognitive outcomes in patients with MCI and may be incorporated into early preventive clinical care.^{7–9,24} Because vascular and metabolic risk factors, lifestyle behaviours, dietary patterns, and psychosocial factors are strongly associated with progression to dementia, routine clinical assessment and targeted modification of these factors should be considered an integral component of MCI management.^{7–9,24} Cohort findings showing long-term associations between cardiometabolic burden, lifestyle patterns, and progression risk further support the relevance of risk-factor monitoring across different clinical settings.^{3,4,10,11} Findings from RCTs reinforce the potential value of recommending structured physical activity programs as part of standard MCI management.^{16–18} Exercise interventions have demonstrated cognitive benefits as well as favourable effects on biomarkers associated with AD, suggesting that physical activity may influence both functional outcomes and selected biological markers associated with disease progression.¹⁶ Cognitive training interventions also represent a feasible clinical option, with systematic reviews showing improvements across multiple cognitive domains.^{13,14} Digital behavioural platforms may improve access to such interventions, particularly for patients with limited mobility or geographic constraints, with pilot studies supporting their feasibility.²² Dietary interventions represent an additional, non-pharmacological component of MCI management.^{8,9} Evidence showing cognitive improvement following consumption of high-phenolic olive oil and supporting the role of Mediterranean-style dietary patterns supports consideration of nutritional counselling as part of MCI care.^{21,23} Multidomain lifestyle interventions, combining exercise, diet, stress management, and cognitive or psychosocial support, have demonstrated favourable cognitive outcomes in randomized trials, supporting their inclusion in MCI management strategies. Future research should further examine how modifiable exposures interact with AD pathology, building on emerging evidence showing that cardiovascular and lifestyle-related factors influence progression even among biomarker-positive patients.¹² Advances in predictive modelling using clinical data and neuroimaging-derived morphological features support improved identification of patients at higher risk of progression, enabling clinicians to align patients with personalized, risk-targeted interventions.^{25,26} Large-scale cohort studies show that the combined assessment of multiple modifiable risk factors improves identification of individuals at higher risk of progression and may inform more targeted preventive strategies in clinical practice.¹¹ *Overall, the available evidence supports an integrated clinical approach in which assessment and modification of*

vascular, metabolic, behavioural, and psychosocial factors are paired with structured NPIs to support cognitive trajectories and functional outcomes in patients with MCI.^{7,8,11–22} Continued integration of risk profiling, biomarker assessment, and personalized intervention strategies remains an important consideration for future clinical practice and research in dementia prevention.^{11,12,25,26}

6. Limitations

This review has several important limitations that should be considered when interpreting its findings. First, although the included literature encompasses systematic reviews, meta-analyses, large cohort studies, and randomized controlled trials, substantial heterogeneity exists across study designs, study populations, outcome measures, and follow-up durations. Such variability limits direct comparability of results and precludes precise quantification of the relative contribution of individual modifiable risk factors or non-pharmacological interventions. Second, the definition and operationalization of mild cognitive impairment vary across studies, reflecting differences in diagnostic criteria, cognitive assessment tools, and thresholds for impairment. This heterogeneity may influence estimates of progression risk and intervention effectiveness and complicates the generalizability of findings across different clinical settings. Third, many observational studies are subject to residual confounding and cannot fully disentangle causal relationships between modifiable risk factors and cognitive outcomes. Lifestyle, vascular, and psychosocial exposures are often interrelated, and their independent effects may be difficult to isolate despite multivariable statistical adjustment. Similarly, reverse causality cannot be entirely excluded, particularly in studies with shorter follow-up periods. Fourth, evidence supporting non-pharmacological interventions is limited by variability in intervention intensity, duration, adherence, and outcome selection. While randomized trials demonstrate cognitive benefits, long-term effects on dementia incidence and sustained functional outcomes remain insufficiently characterized. In addition, some intervention studies rely on relatively small sample sizes or pilot designs, which may limit statistical power. Finally, emerging approaches integrating biomarkers and predictive modelling are promising but remain constrained by limited external validation and restricted availability in routine clinical practice. Further large-scale, longitudinal studies are required to clarify how biomarker-informed risk stratification can be effectively combined with targeted non-pharmacological interventions. Despite these limitations, the convergence of evidence across multiple methodological approaches strengthens the overall conclusions of this review and supports the

relevance of modifiable risk factors and non-pharmacological strategies in the management of mild cognitive impairment.

7. Conclusion

MCI represents a critical window for preventive strategies aimed at reducing the risk of progression to dementia. Available evidence indicates that modifiable vascular-metabolic, lifestyle, nutritional, and psychosocial factors are associated with cognitive trajectories in patients with MCI. These findings highlight the clinical relevance of systematic assessment and targeted modification of these risk domains in routine practice. NPIs, including structured physical activity, cognitive training, dietary modification, and multidomain lifestyle programs, have consistently demonstrated beneficial effects on cognitive performance in patients with MCI. In selected studies, these interventions have also been associated with changes in biomarkers related to AD, suggesting effects beyond purely functional outcomes. Digital intervention platforms may support the delivery of cognitive and lifestyle programs and contribute to more individualized preventive approaches. Recent evidence suggests that integrating modifiable risk factors with biomarker-based and predictive models may improve the clinical utility of risk stratification. These findings contribute to understanding the interactions between behavioural, metabolic, and biological factors involved in cognitive decline. Overall, the accumulated evidence supports a comprehensive and individualized approach to MCI management. By combining risk-factor identification with targeted non-pharmacological interventions, clinicians may be able to support cognitive function and potentially reduce the likelihood of progression to dementia. Further refinement of predictive tools and evaluation of multimodal interventions remain priorities for future research and clinical application. MCI should be viewed as an actionable clinical state rather than a passive diagnosis.

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Conceptualization: NMK, WP, BP;

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Data curation: BP, JP, WP;

Writing-rough preparation: MMT;

Writing -review and editing: NMK, BP, JAW, AG;

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