

Harmonization and pooling of information about modifiable risk factors for Alzheimer and other dementias: a systematic review of the Italian clinical Cohorts.



Giuseppe Salemi, M. Lodico, D. Tarantino, C. Migliazzo, P. Allegra, L. Maniscalco, T. Piccoli, N. Vanacore, D. Matranga.

Department of Diagnostic and Interventional Radiology and Stroke - Azienda Ospedaliera Universitaria - Paolo Giaccone - Palermo.

Department of Diagnostic, Interventional and Stroke Radiology. UOC Neurology. - A.OUP 'P.Giaccone' - Palermo.

Department of Diagnostic, Interventional and Stroke Radiology. UOC Neurology. - A.OUP 'P.Giaccone' - Palermo.

Department of Diagnostic, Interventional and Stroke Radiology. UOC Neurology. - A.OUP 'P.Giaccone' - Palermo.

Department of Health Promotion, Mother and Child Care, Internal Medicine and Medical Specialties - PROMISE - University of Palermo - Palermo.

Department of Health Promotion, Mother and Child Care, Internal Medicine and Medical Specialties - PROMISE - University of Palermo - Palermo.

Department of Biomedicine, Neuroscience and Advanced Diagnostics (BIND) - University of Palermo - Palermo.

National Center for Disease Prevention and Health Promotion - Italian National Institute of Health - Rome.

Department of Health Promotion, Mother and Child Care, Internal Medicine and Medical Specialties - PROMISE - University of Palermo - Palermo.

INTRODUCTION

Alzheimer's disease (AD) and other dementias are the leading cause of cognitive decline and disability, affecting >57 million people worldwide, including ~8 million in the EU and 1.2 million in Italy (~600,000 AD). AD represents 53.7% of cases, followed by vascular dementia (15.8%). About 40% of dementia cases are attributable to 14 modifiable risk factors (e.g., hypertension, diabetes, obesity, smoking, depression, social isolation), while genetics, biomarkers, and neuroimaging remain key non-modifiable predictors [1]. International cohort networks (e.g., GAAIN, CONCORD-AD) [2,3] advance early diagnosis and risk factor research, though Italian participation is limited to initiatives such as I-ADNI [4], WMH-AD, and CONFORT age. This study systematically reviewed Italian dementia cohorts (2019–2024) to evaluate definitions of modifiable risk factors, assess harmonization with international standards, and propose standardized data collection, aiming to improve comparability and integration of Italian cohorts into global research networks.

MATERIALS AND METODES

This systematic review followed PRISMA (figure 1) guidelines and was registered in PROSPERO (ID: 1089977) [5]. MEDLINE, Embase, and Scopus were searched (2019–2024) for observational cohort studies on Alzheimer's disease (AD) or other dementias in Italian populations, focusing on modifiable risk factors. Eligible studies were peer-reviewed, in English, full-text, and included ≥5 exposed participants; reviews, case reports, animal studies, and those lacking exposure data were excluded. Data extraction captured study characteristics and eight key variables: BMI, hypertension, diabetes, diet, alcohol consumption, smoking, depression, and physical activity, with details on measurement tools, categorizations, and coding. Harmonization was based on WHO and international definitions (e.g., BMI cut-offs, GDS/CES-D, IPAQ, ADA/WHO criteria, FFQ, standardized alcohol units). Variable comparability was assessed using the DataSHaPER framework, classifying harmonization as complete, partial, or impossible. This standardized approach supports cross-study integration and strengthens the contribution of Italian dementia cohorts to international research networks.

RESULTS

From 365 records, 18 Italian studies published between 2019 and 2024 were included. These studies, using cross-sectional, longitudinal, cohort, or case-control designs, examined modifiable risk factors—hypertension, diabetes, obesity, smoking, depression, physical inactivity, diet, and alcohol consumption—in relation to AD, dementia, or MCI, with sample sizes ranging from <100 to >5000 participants. Harmonization analysis showed highest compatibility for obesity (BMI: 44% complete, 22% not assessable) and diet (44% complete, 55% not assessable). Physical inactivity and diabetes reached 33% harmonization, while smoking achieved 28% complete and 17% partial, with 55% not feasible. Depression and hypertension had the lowest harmonization (22% complete; 78% impossible). Alcohol consumption was considered in six studies, only 17% fully harmonizable. Overall, obesity and diet were the most harmonizable factors, whereas depression, hypertension, and alcohol showed the greatest variability. Across all risk factors, 62% of assessments were not harmonizable.

CONCLUSION AND DISCUSSION

This review reveals high heterogeneity in assessing modifiable dementia risk factors in Italian cohorts, limiting data integration. BMI and diabetes, with greater harmonization potential, demonstrate the feasibility of pooled analyses and confirm their impact in the Italian population. Standardized, internationally validated data collection protocols are urgently needed to improve research quality and enable integration of Italian cohorts into global networks, advancing dementia prevention and understanding.

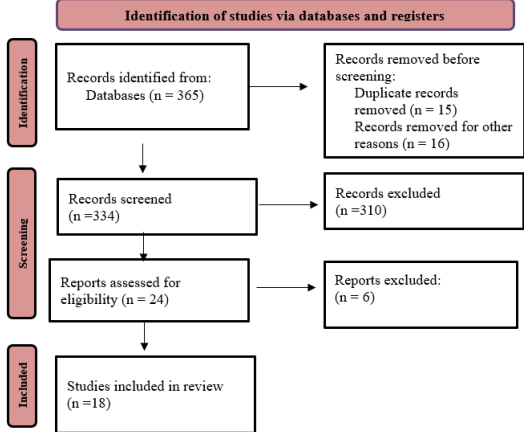


Figure 1. PRISMA Flow Diagram

REFERENCES.

- Livingston G, Huntley J, Liu KY, Costafreda SG, Selbaek G, Alallat S, Ames D, Banerjee S, Burns A, Brayne C, Fox NC, Ferri CP, Gitlin LN, Howard R, Kales HC, Kivimäki M, Larson EB, Nakasujia N, Rockwood K, Samus Q, Shirai K, Singh-Manoux A, Schneider LS, Walsh S, Yao Y, Sommerlad A, Mukadam N. Dementia prevention, intervention, and care: 2024 report of the Lancet standing Commission. *Lancet*. 2024 Aug 10;404(10452):572-628. doi: 10.1016/S0140-6736(24)01296-0. Epub 2024 Jul 31. PMID: 39096926.
- The Global Alzheimer's Association Interaction Network Arthur W. Toga, Scott C. Neu, Priya Bhatt, Karen L. Crawford, Naveen Ashish First published: 25 August 2015 <https://doi.org/10.1016/j.jalz.2015.06.1896>.
- Pavlik VN, Burnham SC, Kass JS, Helmer C, Palmqvist S, Vassilaki M, Dartigues JF, Hansson O, Masters CL, Pérès K, Petersen RC, Stomrud E, Butler L, Coloma PM, Teisma XM, Doody R, Sano M; CONCORD-AD investigators. Connecting Cohorts to Diminish Alzheimer's Disease (CONCORD-AD): A Report of an International Research Collaboration Network. *J Alzheimers Dis*. 2022;85(1):31-45. doi: 10.3233/JAD-210525. PMID: 34776434; PMCID: PMC8842789.
- Cavedo E, Redolfi A, Angeloni F, Babiloni C, Lizio R, Chiapparini L, Bruzzone MG, Aquino D, Sabatini U, Alesiani M, Cherubini A, Salvatore E, Soricelli A, Vernieri F, Scarscia F, Sinforiani E, Chiarati P, Bastianello S, Montella P, Corbo D, Tedeschi G, Marino S, Baglieri A, De Salvo S, Carducci F, Quattrocchi CC, Cobelli M, Frisoni GB. The Italian Alzheimer's Disease Neuroimaging Initiative (I-ADNI): validation of structural MR imaging. *J Alzheimers Dis*. 2014;40(4):941-52. doi: 10.3233/JAD-132666. PMID: 24577455.
- Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, Shamseer L, Tetzlaff JM, Moher D. Updating guidance for reporting systematic reviews: the development of the PRISMA 2020 statement. *J Clin Epidemiol*. 2021 Jun;134:103-112. doi: 10.1016/j.jclinepi.2021.02.003. Epub 2021 Feb 9. PMID: 33577987.



Finanziato dall'Unione europea NextGenerationEU

Funding: This research was funded by European Union-Next Generation EU-"PNRR M6C2-Investimento 2.1 Valorizzazione e potenziamento della ricerca biomedica del SSN", grant number PNRRMAD-2022-12375822, CUP derivato: I75E22000550006- CUP Master ISS I55E22000560006.

24-28 Ottobre 2025 Padova Congress

55° CONGRESSO SOCIETÀ ITALIANA DI NEUROLOGIA