

Comparative Performance of Externally Validated  
Dementia Risk Prediction Models in General  
Populations: A Systematic Review

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Age-only or age-and-sex baselines matched or exceeded multivariable model performance in the majority of paired comparisons (11 studies, 41 pairs). No current model has demonstrated the calibration or clinical utility evidence needed to support routine deployment in general population settings. Current models are best suited to prevention trial stratification.

| INTRODUCTION                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | METHODS                                                                                                 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| <p>Over 100 dementia risk prediction models have been developed in the last two decades, yet evidence on their external validity in general populations remains limited.</p> <p>Prior systematic reviews (Hou 2019; Cochrane 2023; Stephan 2026) identified limited external validity but did not examine whether models add discriminative value beyond simple age-based baselines.</p> <p>No review has systematically quantified the calibration and clinical utility evidence gap across the external validation literature.</p> <p><b>Aims</b></p> <ul style="list-style-type: none"><li>• Characterise externally validated models for incident dementia in general population cohorts</li><li>• Describe discrimination against age-only and age-and-sex baseline comparators</li><li>• Quantify calibration and clinical utility reporting</li><li>• Appraise risk of bias and applicability using PROBAST</li></ul> | <p><b>Registration</b></p> <p>PROSPERO: CRD42024561858</p> <p><b>Search Strategy</b></p> <ul style="list-style-type: none"><li>• MEDLINE, Embase, Cochrane Library, PsycINFO (Inception to 20 August 2024)</li><li>• 17,973 database records identified + 6 citation records</li></ul> <p><b>Eligibility Criteria</b></p> <ul style="list-style-type: none"><li>• Studies externally validating multivariable prognostic models for incident dementia</li><li>• General population cohorts using demographic, clinical, and lifestyle predictors</li><li>• Excluded: models where &gt;50% predictors were neuroimaging, fluid biomarkers, metabolomic, or polygenic panel markers</li></ul> <p><b>Data Extraction &amp; Appraisal</b></p> <ul style="list-style-type: none"><li>• CHARMS checklist guided extraction. PROBAST for risk of bias and applicability</li><li>• Heterogeneity precluded meta-analysis; findings summarised descriptively</li></ul> <p>Note: Numbers presented reflect final analysis and supersede submitted abstract (based on a preliminary extraction).</p> | <p><b>Study Selection:</b> 29 studies included; 28 unique risk prediction models; 93 model-level validations</p> <p><b>Discrimination by Model Type:</b> Midlife vascular/lifestyle scores showed marked context-dependence:</p> <p>CAIDE: C=0.66-0.75 in midlife cohorts vs 0.51-0.56 in late-life settings</p> <p>Late-life multidomain models: ANU-ADRI 0.59-0.75; BDSI 0.68-0.78; CogDrisk 0.65-0.77</p> <p>EHR-derived models: AUC 0.79-0.84 over short horizons; declined on external validation</p> <p>Cognitive test models: AUC 0.86-0.93 (structural ceiling identified)</p> <p><b>Comparator Analysis (Novel):</b> Age-only or age-and-sex benchmarks reported in 11 of 29 studies (41 paired comparisons)</p> <p>Simple baselines matched or exceeded multivariable performance in majority of pairs</p> <p>UK Biobank: age-only C=0.79 exceeded ANU-ADRI (0.59), BDSI (0.68), CAIDE (0.66)</p> <p><b>Calibration &amp; Clinical Utility:</b> Quantitative calibration: 9 of 29 studies only</p> <p>Decision curve analysis: 0 of 29 studies</p> <p>Competing risk of death formally modelled: 7 of 29 studies</p> <p><b>PROBAST Risk of Bias</b></p> <p>Low RoB: 2 studies. Some concerns: 23. High RoB: 4</p> <p>Most common domain concern: Analysis (competing risks, calibration handling)</p> | <p>No dementia risk prediction model demonstrated the combination of discrimination, calibration, and clinical utility required for routine general population deployment</p> <ul style="list-style-type: none"><li>• Age-based baselines often matched or exceeded multivariable performance - a structural ceiling exists for purely clinical and lifestyle models</li><li>• Vonk 2021: every model with C≥0.76 included cognitive testing; every model without cognitive predictors reached C≤0.75</li></ul> <p><b>Clinical Implications</b></p> <ul style="list-style-type: none"><li>• Current models best suited for prevention trial stratification, not population screening</li><li>• As plasma biomarker testing advances, these findings establish the performance baseline against which biomarker-enriched models must be evaluated</li></ul> <p>Future validation must treat comparator benchmarking, quantitative calibration, decision curve analysis, and competing risk modelling as standard requirements</p> <p>Increased validation in low- and middle-income country populations is needed</p> | <div><div><div>1. Hou XH et al. J Neurol Neurosurg Psychiatry. 2019;90:373-379</div><div>2. Geethadevi GM et al. Cochrane Database Syst Rev. 2023;6:CD014885</div><div>3. Stephan BCM et al. BMC Med. 2026;24:132</div><div>4. Fayosse A et al. BMC Med. 2020;18:107</div><div>5. Kivimaki M et al. JAMA Netw Open. 2023;6:e2318132</div><div>6. Wolff RF et al. Ann Intern Med. 2019;170:51-58</div><div>7. Livingston G et al. Lancet. 2024;404:572-628</div></div><div>Full reference list: PROSPERO CRD42024561858</div></div> <div>CONTACT</div> <div><div>Dr Zain Hussain.<br/>Clinical Lecturer in<br/>Psychiatry<br/>University of Glasgow<br/><a href="mailto:zain.hussain@glasgow.ac.uk">zain.hussain@glasgow.ac.uk</a></div><div><div>ALZHEIMER'S<br/>ASSOCIATION</div><div>AAIC&gt;26</div></div></div> |