

Assessing dementia risk factors in mid-life: comparison to late-life scores and midlife risk factors identified by the Lancet Commission

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1. Background

Midlife (age 40-64 years) represents a critical window for dementia prevention as most of the key modifiable risk factors emerge decades before diagnosis¹. Most dementia risk assessment tools were developed on data from older adults and validated in older cohorts. We comprehensively reviewed midlife risk assessment tools, evaluated length of follow-up, whether tools corresponded with guidelines and the Lancet Commission report ², and compared them to tools that cover mid-late life and late-life.

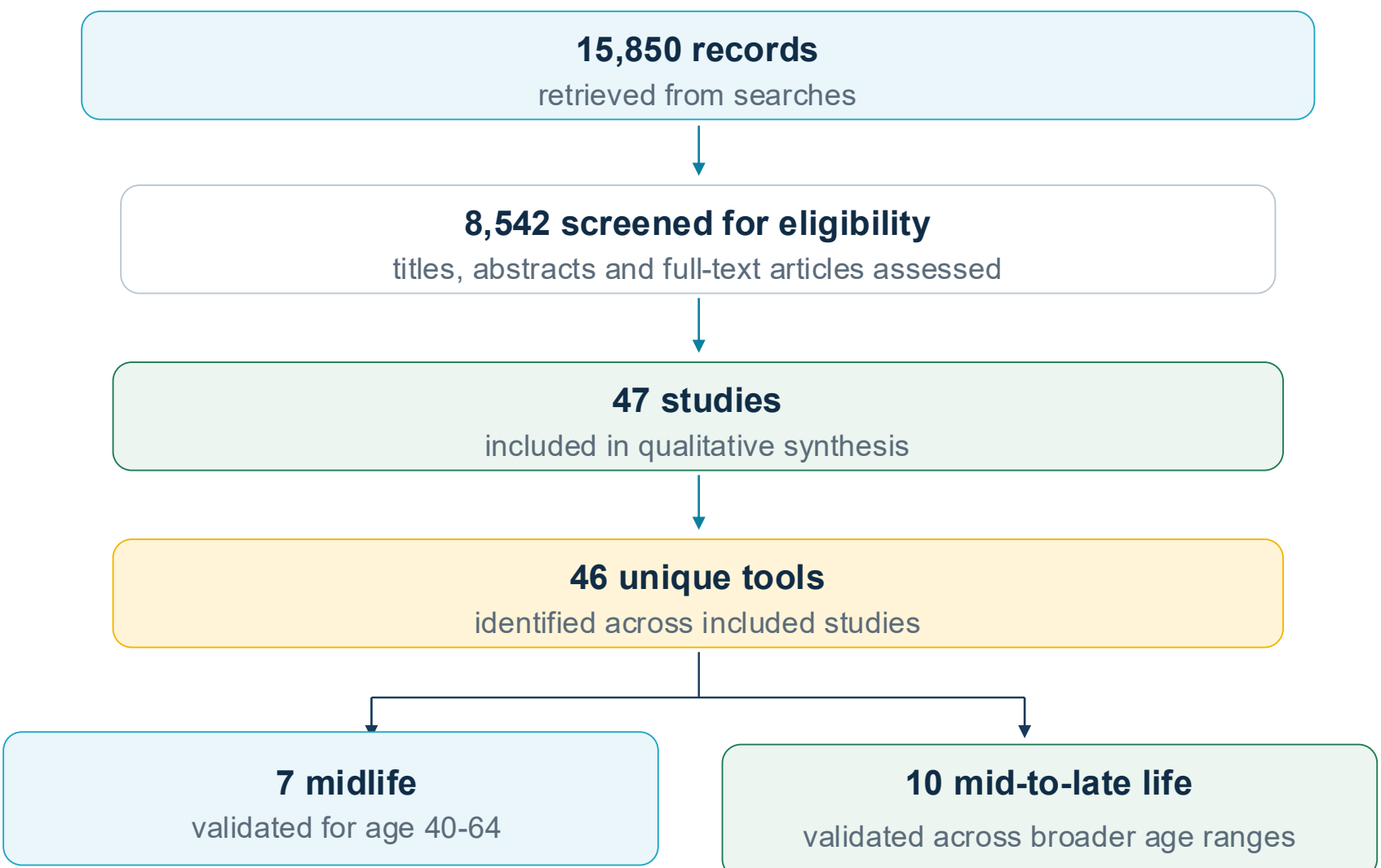
Review objectives

- Synthesise evidence for all-cause dementia, Alzheimer's disease and vascular dementia.
- Classify scores by target population: midlife, mid-to-late life or late-life.
- Evaluate content, cost, validation design and suitability for implementing risk-reduction guidelines.

2. Methods

Based on a registered, published systematic review³(PROSPERO: CRD42023392435), searches identified published risk assessment tools that included modifiable risk factors and reported predictive validity or accuracy. Data were extracted on risk factors, cohort characteristics, follow-up, AUC/C-statistics and validation samples.

Search strategy	Eligibility	Synthesis
Inception - Feb 2025	Published dementia risk tools	Qualitative review and meta-analysis



References

1. Anstey KJ, et al. Dementia risk scores and their role in the implementation of risk reduction guidelines. *Front Neurol.* 2022;12:765454.
2. Livingston G, et al. Dementia prevention, intervention, and care: 2024 report of the Lancet Standing Commission. *Lancet.* 2024;404(10452):572–628.
3. Huque MH, et al. A critical review and classification of dementia risk assessment tools to inform dementia risk reduction. *J Prev Alzheimers Dis.* 2025;12(9):100333.
4. Kivipelto M, et al. Risk score for the prediction of dementia risk in 20 years among middle-aged people: a longitudinal, population-based study. *Lancet Neurol.* 2006;5(9):735–741.
5. Eskelinen MH, et al. Midlife healthy-diet index and late-life dementia and Alzheimer's disease. *Dement Geriatr Cogn Dis Extra.* 2011;1(1):103–112.
6. Vuoksimaa E, et al. Middle-age self-report risk score predicts cognitive functioning and dementia in 20–40 years. *Alzheimers Dement (Amst).* 2016;4:118–125.
7. Jung W, et al. Predicting mid- and late-life dementia risk in primary care: a prognostic study from a national health screening cohort. *Psychiatry Res.* 2024;342:116237.
8. Liang Y, et al. Cardiovascular health metrics from mid- to late-life and risk of dementia: a population-based cohort study in Finland. *PLoS Med.* 2020;17(12):e1003474.
9. Huque MH, et al. Development of a midlife-specific CogDrisk algorithm (CogDrisk-ML) to enable validated implementation of dementia risk assessment from midlife to late life. *Age Ageing.* 2025;54(7):afaf201.
10. Ibarrrondo O, et al. Dementia risk score for a population in Southern Europe calculated using competing risk models. *J Alzheimers Dis.* 2022;86(4):1751–1762.

3. Results at a glance

Of 46 identified dementia risk assessment algorithms, 7 were developed and validated for midlife risk assessment, and a further 10 were validated for assessment of both mid to late life. The majority were developed by identifying risk factors from single cohorts, CogDrisk and ANU-ADRI used evidence synthesis to identify risk factors and risk ratios, and LIBRA and CogDrisk-ML used a combination of approaches for risk factor selection. The median reported length of follow-up for studies reporting development of midlife tools was 8.7yrs (Q1-Q3:5.0-20.9 years), which is not long enough to observe the case of incident dementia in a cohort.

Evidence synthesis

CogDrisk + ANU-ADRI

Combined approaches

LIBRA + CogDrisk-ML

Single-cohort tools

majority of algorithms

3.1. Mid-life risk scores included

Risk score	Risk factors included
CAIDE risk score ⁴	Age, sex, education, SBP, BMI, total cholesterol, physical activity, ApoE ε4.
CAIDE midlife healthy-diet index ⁵	Beneficial components (e.g., vegetables and roots); Unhealthy components (e.g., sausage foods); Alcohol drinking; Use of salt; Type of fats used for cooking
Education & Occupation-based midlife risk ⁶	Age, education, working status, nature of work, work environment, physicality of work
Midlife primary care risk score ⁷	Age, sex, obesity, smoking, alcohol consumption, physical activity, diabetes, hypertension, dyslipidaemia, and Chronic kidney disease.
Cardiovascular Health (CVH) metrics ⁸	Smoking, physical activity, BMI, fasting plasma glucose, total cholesterol, serum total cholesterol and blood pressure
CogDrisk-ML ⁹	Age, sex, education, BMI, smoking, hypertension, high cholesterol/dyslipidaemia, depression, fish intake/diet, physical activity, diabetes, stroke, traumatic brain injury, loneliness/social isolation, sleep problems, and hearing loss
Risk scores for late risk of dementia ¹⁰	Age, sex, physical activity, hypertension, hyperlipemia, diabetes, Cambridge Index, smoking, education, BMI, diet

3.2. Comparison to lancet commission mid-life risk factors

CogDrisk-ML included the most Lancet Commission midlife risk factors

10/11

CogDrisk-ML

5.3

mean factors

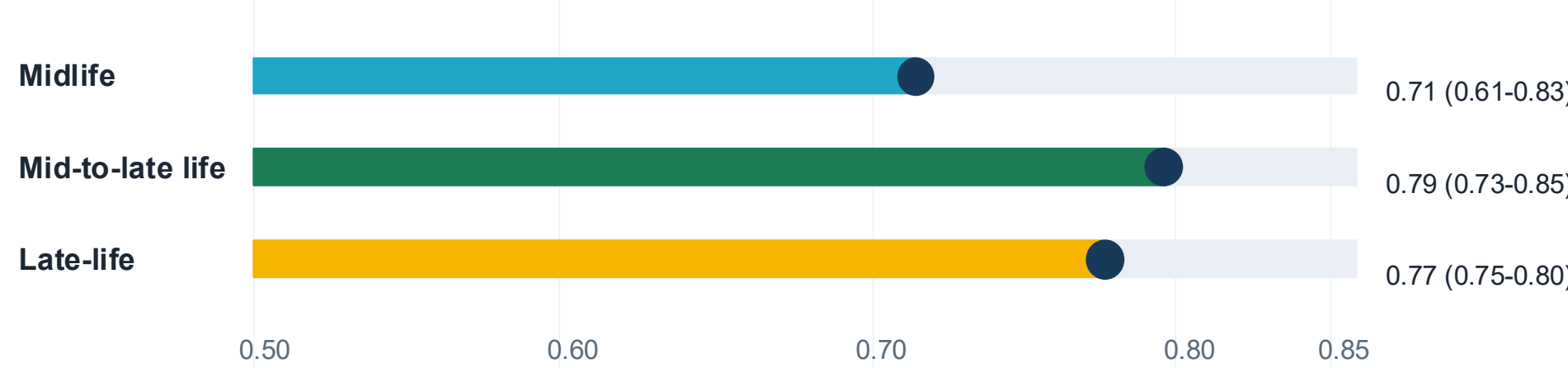
Most common factors

Hypertension | low education | dyslipidaemia

Lancet risk factor	Midlife							Both mid and late life									
	Healthy diet	CAIDE	CVH metrics	Educ/ work	Late risk score	CogDrisk-ML	Primary care	ANU-ADRI	LIBRA score	CogDrisk	CogDrisk-AD	SIAS index	Clinical Dementia risk	MDRS	Neurocog disorders	mCAIDE score	UKBDRS
No. factors covered	1	5	6	1	7	10	7	10	8	9	9	6	6	3	3	4	5
Physical activity		•	•		•	•	•	•	•	•	•						
Smoking			•		•	•	•	•	•	•	•		•				
Alcohol consumption	•					•	•	•	•				•				
Overweight/obese		•	•		•	•	•	•	•	•	•		•			•	
Hypertension		•	•		•	•	•	•	•	•	•	•		•	•		•
Diabetes			•		•	•	•	•	•	•	•	•	•				•
Dyslipidaemia		•	•		•	•	•	•	•	•	•	•				•	
Depression						•	•	•	•	•	•			•	•		•
Hearing loss						•	•			•	•						
Early-life education		•		•	•			•	•	•	•	•	•	•	•	•	•
Head injury						•		•		•	•						

3.2. Predictive accuracy

Pooled C-statistic (95% CI)



Interpret with caution: tools differ in target age, cohort, follow-up length, outcome definitions and predictors.

4. Discussions

- Midlife dementia risk assessment is critical as many modifiable risk factors emerge decades before clinical diagnosis, creating an earlier window for prevention.
- Midlife risk scores showed prediction accuracy comparable to mid-to-late-life and late-life tools, suggesting that risk stratification before older age is feasible.
- However, direct comparison between midlife and late-life tools should be interpreted cautiously because tools differ in target age, follow-up duration, sampling frame, outcome definition, and included predictors.
- Many dementia risk scores still rely on limited sets of cardiometabolic predictors, while psychosocial, sensory, lifestyle, and injury-related risk factors are less consistently included.
- Few midlife tools captured the full breadth of modifiable risk factors identified by the Lancet Commission; CogDrisk-ML showed the strongest coverage of Lancet midlife risk factors.
- Longer follow-up studies beginning in midlife are needed to improve validation, calibration, and generalisability of midlife dementia risk tools.

5. Conclusions

Midlife risk assessment tools have similar accuracy to late-life tools for risk prediction. Currently, tool development appears limited by short lengths of followup as few cohorts are followed for 30-40 years. Other than CogDrisk-ML, few midlife dementia risk assessment tools include the breadth of risk factors identified by the Lancet Commission.

6. Limitation

Few midlife cohorts had follow-up long enough to capture sufficient incident dementia cases, limiting the development and validation of midlife dementia risk assessment tools.

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