

Dementia biomarkers in Very Late Onset Psychosis: a systematic review

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KEY TAKE AWAY: There is renewed interest in the use of dementia biomarkers in VLOP: two recent uncontrolled cohort studies, one using amyloid PET and CSF p-tau¹ and one using FP-CIT and MIBG SPECT², reporting high rates of positivity in keeping with neurodegenerative disease. Controlled, prospective, longitudinal dementia biomarker studies in VLOP are needed to establish rates of biomarker abnormality in VLOP to guide clinical practice and future research.

RESEARCH NEED

Very late onset psychosis (VLOP) is an umbrella term for functional psychotic disorders with first onset over age 60.³

Population-based studies indicate that ~20% of VLOP patients develop dementia with long-term follow-up.^{3,4,5}

However, the rate of dementia biomarker abnormality, in VLOP, remains unclear.

High rates of dementia biomarker abnormality in VLOP would have significant implications for its clinical management and future research, including clinical trials of disease modifying dementia therapies.

STUDY AIM

This systematic review aims to produce an up-to-date evidence synthesis for use of dementia biomarkers in VLOP, including markers of amyloid and p-tau burden, alpha-synuclein assays, FP-CIT SPECT and MRI, as well as other biomarkers with published evidence in VLOP.

METHODS

We searched PubMed, MEDLINE, PsychINFO & EMBASE for studies reporting data in VLOP (any affective or non-affective psychosis presenting over age 60).

Studies with data for >5 VLOP subjects were included, when reporting use of:

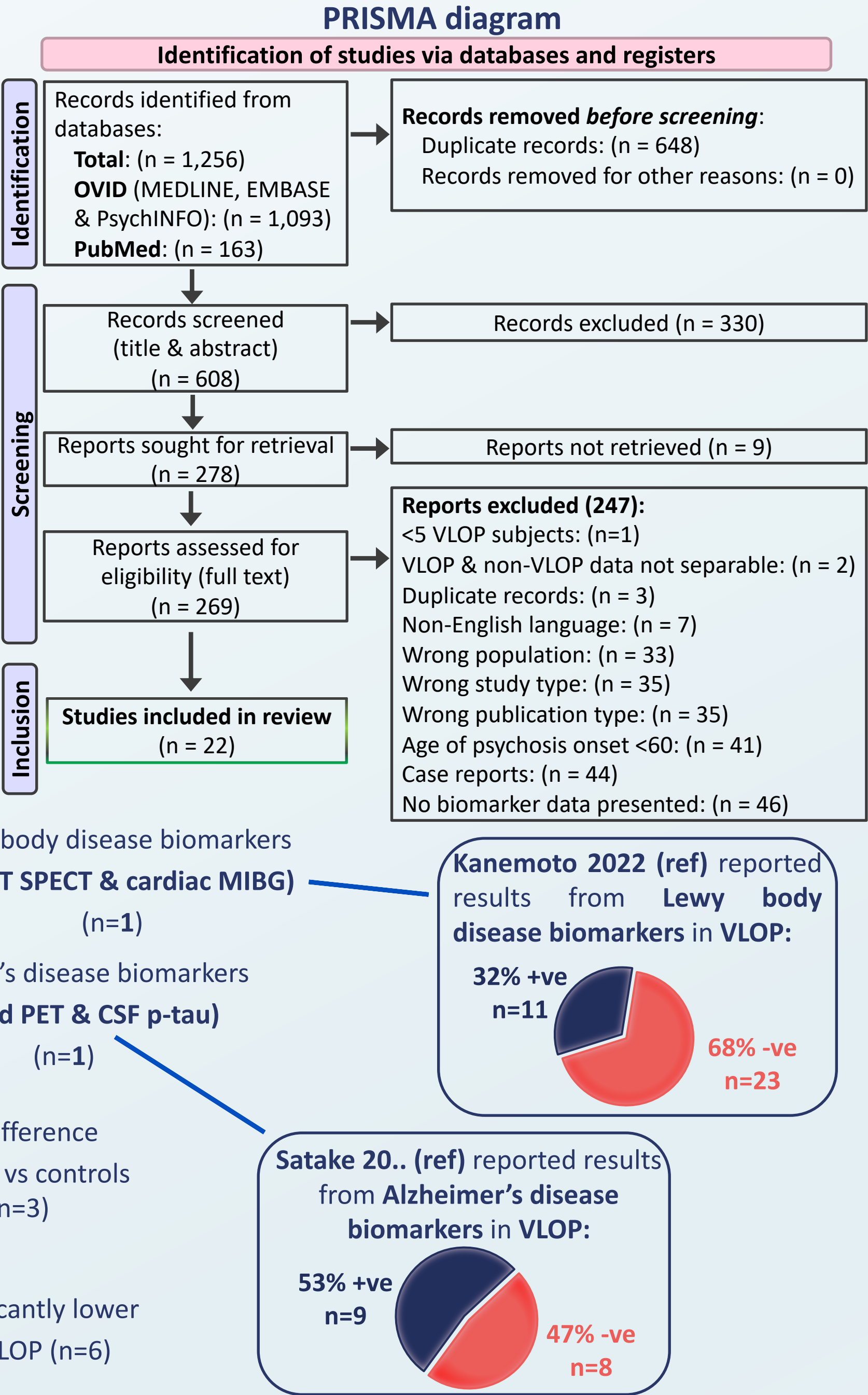
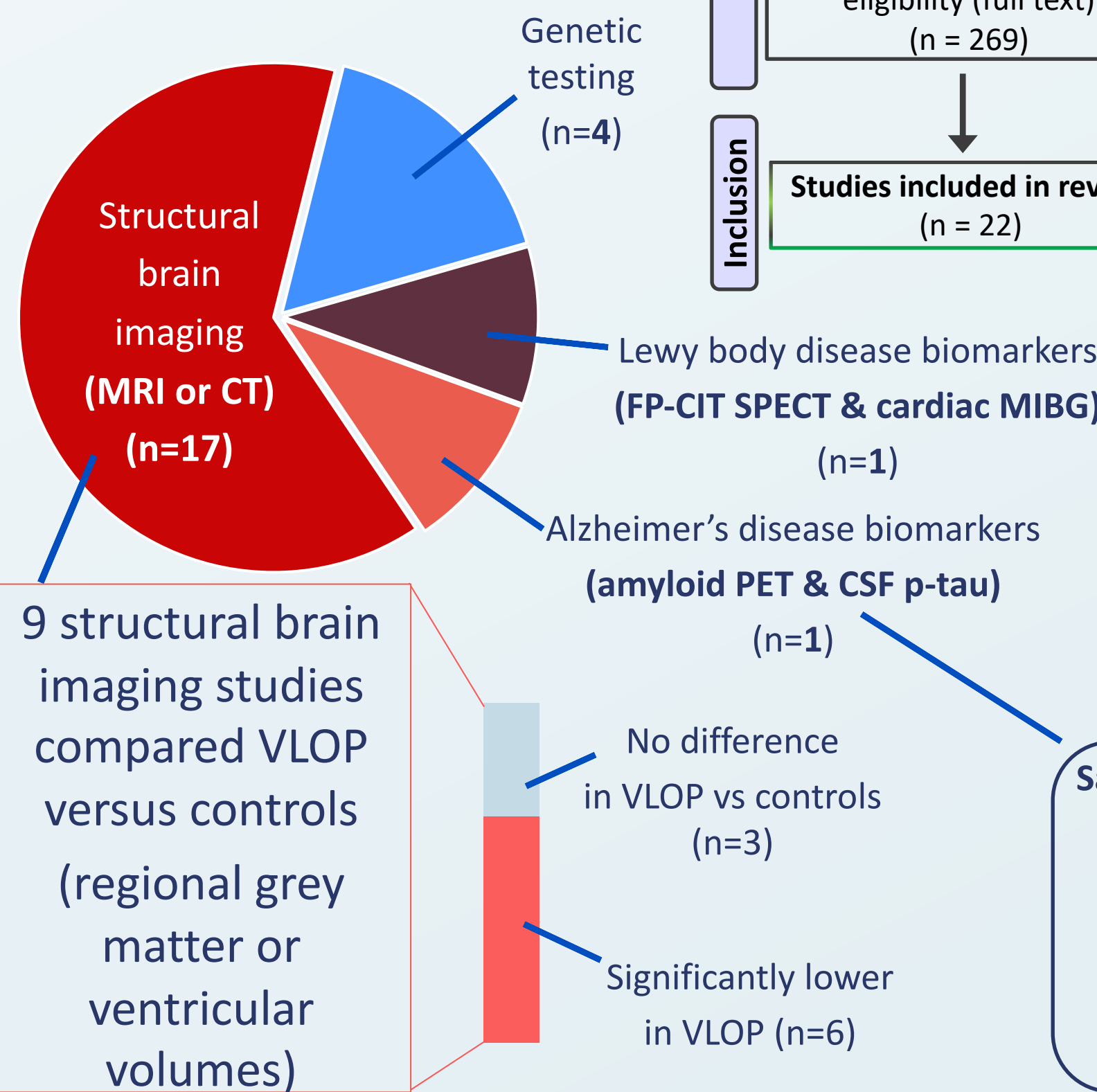
- fluid biomarkers (including blood and cerebrospinal fluid)
- imaging biomarkers (including MRI, PET, SPECT)
- Tissue, EEG or retinal biomarkers

Narrative synthesis was conducted.

RESULTS

We screened 608 published reports and included **22 papers** reporting the use of biomarker measurement in VLOP.

No retained studies described use of blood-based biomarkers, alpha-synuclein assays, other tissue-based or retinal biomarkers.



CONCLUSION & FUTURE DIRECTION

- This study finds few studies examining dementia biomarkers in VLOP but also finds an uptick in recent interest in application of dementia biomarkers in VLOP.
- While overall, structural imaging findings appeared equivocal, two recent MRI studies identified lower volumes in VLOP cohorts.
- Early evidence indicates high rates positivity in AD and LBD biomarkers in VLOP.
- Further prospective and longitudinal studies are needed to test clinically relevant dementia biomarkers in VLOP, including blood-based biomarkers and alpha-synuclein seeding assays
- The rate of biomarker abnormality and rate of conversion to dementia will be of significant interest to the clinical care of VLOP patients.

REFERENCES

1. Characteristics of very late-onset schizophrenia-like psychosis classified with the biomarkers for Alzheimer's disease: a retrospective cross-sectional study. Y Satake *et al.* 2024
2. Characteristics of very late-onset schizophrenia-like psychosis as prodromal dementia with Lewy bodies: a cross-sectional study. H Kanemoto *et al.* 2022
3. Characteristics associated with progression to probable dementia with Lewy bodies in a cohort with very late-onset psychosis. L Gibson *et al.* 2024
4. Association between risk of dementia and very late-onset schizophrenia-like psychosis: a Swedish population-based cohort study. J Stafford *et al.* 2023
5. Severe psychiatric disorders are associated with increased risk of dementia. J Stevenson-Hoare *et al.* 2024

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