International Platform of Registered Systematic Review and Meta-analysis Protocols

INPLASY

Design of Trials for Cerebral Small Vessel Disease and Vascular Cognitive Impairment

INPLASY202590013
doi: 10.37766/inplasy2025.9.0013
Received: 5 September 2025
Published: 5 September 2025

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ADMINISTRATIVE INFORMATION

Support - No external funding.

Review Stage at time of this submission - Completed but not published.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202590013

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 5 September 2025 and was last updated on 5 September 2025.

INTRODUCTION

Review question / Objective To review and descriptively synthesize the included and excluded populations, interventions studied and methods used to assess treatment effects in clinical trials of cerebral small vessel disease (cSVD) and vascular cognitive impairment (VCI).

Condition being studied Cerebral small vessel disease (cSVD), Vascular cognitive impairment (VCI).

METHODS

Participant or population Patients with all subtypes and severities of non-amyloidal sporadic cerebral small vessel disease (cSVD) and vascular cognitive impairment (VCI).

Intervention All interventions studied in the included clinical trials.

Comparator Not applicable.

Study designs to be included Clinical trials (randomised and/or non-randomised).

Eligibility criteria
Inclusion criteria:
1. Randomized and non-randomized clinical trials, completed and ongoing clinical trials
2. Trials involving adult human participants of any age with any non-amyloidal sporadic cSVD presentation (including lacunar stroke and neuroimaging features)
3. Trials involving adult human participants of any age with VCI (subtypes may include vascular dementia, post-stroke cognitive impairment and cognitive impairment resulting from cSVD)
4. Trials studying any pharmacological and/or non-pharmacological interventions to treat or prevent non-amyloidal sporadic cSVD or VCI

Exclusion criteria:
1. Any non-interventional designs (such as observational studies, systematic reviews, test accuracy studies)
2. Conference abstracts
3. Secondary and subgroup analyses (if the primary focus of the paper was not cSVD or VCI)
4. Duplicate titles
5. Non-English studies without a suitable translation or equivalent English text
6. Trials involving mixed or non-lacunar stroke pathologies
7. Trials involving genetic or amyloidal cSVD types
8. Trials involving dementia types other than vascular dementia, such as Alzheimer's disease, frontotemporal dementia and 'mixed dementia'.

Information sources Ovid MEDLINE; Ovid EMBASE; PsycInfo (EBSCO); Clinicaltrials.gov; International Clinical Trials Registry Platform (ICTRP); European Union Clinical Trials Register (EUCTR).

Main outcome(s) Trials were assessed on whether they used specific categories of inclusion criteria, exclusion criteria, primary and secondary outcomes, and interventions. These categories were developed through an initial assessment of methodologies of included trials. Final categories for each data extraction sheet are as follows:
1. Inclusion/Exclusion Criteria: Comorbidities, Cognition, Functional status, Neu-roimaging, Neurological impairments, Neuropsychiatric and Mood Disorders, Physio-logical measurements, Stroke occurrence (Clinical evidence or previous history of any stroke type before enrolment into trial), Tissue Biomarkers, Vascular risk factors, Ha-chinski Ischaemic Scale (VCI only), and Other Selection Criteria.
2. Interventions: Antihypertensives, Antithrombotics, Cognitive enhancers / An-ti-dementia drugs, Vasoactive drugs, Cognitive rehabilitation, Physiological interventions, Exercise and Lifestyle interventions, Traditional Chinese Medicine, Other pharmacologi-cal interventions, and Other non-pharmacological interventions.
3. Outcomes: Clinician assessment, Cognition, Economic outcomes, Functional outcomes, Neuroimaging (Other), Neuroimaging (Structural), Neurological impairments, Neuropsychiatric & Mood Disorders, Physiological measurements, Safety and Adherence Outcomes, Stroke occurrence (Occurrence of a clinical stroke event from the start of the tri-al), Tissue Biomarkers, and Other outcomes.
Definitions of categories will be provided in the data dictionary in the supplementary material.

Data management Data from included trials were extracted onto Microsoft Excel 2020 files for cSVD and VCI trials. For each file, five data extraction sheets were created. One sheet contained basic trial information, including registry identifiers, (expected) date of completion, num-ber of participants, interventions, comparators, trial status and phase.

Quality assessment / Risk of bias analysis Not applicable. This review involves a descriptive synthesis of methodological practices in clinical trials of cSVD and VCI. We did not conduct an evaluation of the efficacy of interventions trialled, therefore we did not assess the quality of the studies.

Strategy of data synthesis All basic characteristics of trials, and categories used as selection criteria, interven-tions, and outcomes were summarised descriptively using counts and percentages.

Subgroup analysis Not applicable.

Sensitivity analysis Not applicable.

Country(ies) involved United Kingdom.

Keywords Cerebral small vessel disease; Vascular cognitive impairment; Vascular dementia; Clinical trials; Trial design.

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