

Pharmacological Treatment For Reducing The Risk Of Cognitive Decline And Dementia After Stroke/TIA: A Systematic Review

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Background

Stroke is a leading cause of death and disability worldwide. Advances in stroke care have improved survival and recovery, but it remains unclear whether pharmacological treatments can prevent long-term consequences such as cognitive decline and dementia.

Objective

As part of the 2026 update of the WHO guidelines on risk reduction of cognitive decline and dementia, this systematic review examined whether pharmacological interventions reduce the risk of cognitive decline, mild cognitive impairment (MCI), or dementia in adults with a history of stroke or symptomatic transient ischemic attack (TIA).

Methods

Design

Umbrella review of systematic reviews and meta-analyses of randomized controlled trials (RCTs) of adults with prior stroke/TIA

- Medline, EMBASE, PsycINFO, Cochrane Central
- Up to January 2025

Intervention

Pharmacological interventions using three drug classes

- Blood-pressure lowering drugs
- Antithrombotic drugs
- Lipid-lowering drugs

vs. placebo, no treatment, or usual care

Two types of interventions

- Specific drug/dose within drug class
- Stricter blood pressure or cholesterol level management

Primary outcomes

- Incident dementia
 - MCI
 - Cognitive decline
- in post-acute phase (≥3 months post-stroke)

Quality rating

AMSTAR-2

Certainty of evidence

GRADE profiles

Protocol registration

PROSPERO: CRD420251000825

Results

- 1343 records screened, 49 full texts assessed, 8 systematic reviews met criteria
- One systematic review, covering all relevant studies, was selected (Quinn et al., 2021)
- Including 5 relevant RCTs; from which data were individually extracted (**Table 1**)
- Mean follow-up of 2 to 5 years
- Certainty of evidence ranged from low to high (**Table 2**)

Table 1. RCT study characteristics.

Study	N	Intervention	Comparator	Outcome
Blood-pressure lowering drugs				
PROFESS	20,332	Telmisartan	Placebo	Dementia + Cognitive decline (MMSE)
PROGRESS	6,105	Perindopril + indapamide	Placebo	Dementia + Cognitive decline (MMSE)
Tzourio et al., 2003				
SPS3	2,916	BP management	BP management	MCI
Pearce et al., 2014		SBP < 130 mmHg	SBP < 150 mmHg	
PODCAST	83	BP management	BP management	Cognitive decline (MMSE)
Bath et al., 2017		SBP < 125 mmHg	SBP < 140 mmHg	
Antithrombotic drugs				
PROFESS	20,332	Acetylsalicylic acid + dipyridamole	Clopidogrel	Dementia + Cognitive decline (MMSE)
SPS3	2,916	Aspirin + clopidogrel	Aspirin + placebo	MCI
Pearce et al., 2014				
Lipid-lowering drugs				
J-STARS	1,578	Pravastatin	No statins	Dementia
Hosomi et al., 2015				
PODCAST	77	LDL-C management	LDL-C management	Cognitive decline
Bath et al., 2017		LDL-C < 2.0 mmol/L	LDL-C < 3.0 mmol/L	

BP = blood pressure, SBP = systolic blood pressure, LDL-C = low density lipoprotein cholesterol, MMSE = Mini-Mental State Examination, MCI = mild cognitive impairment.

Table 2. Visual summary of GRADED evidence.

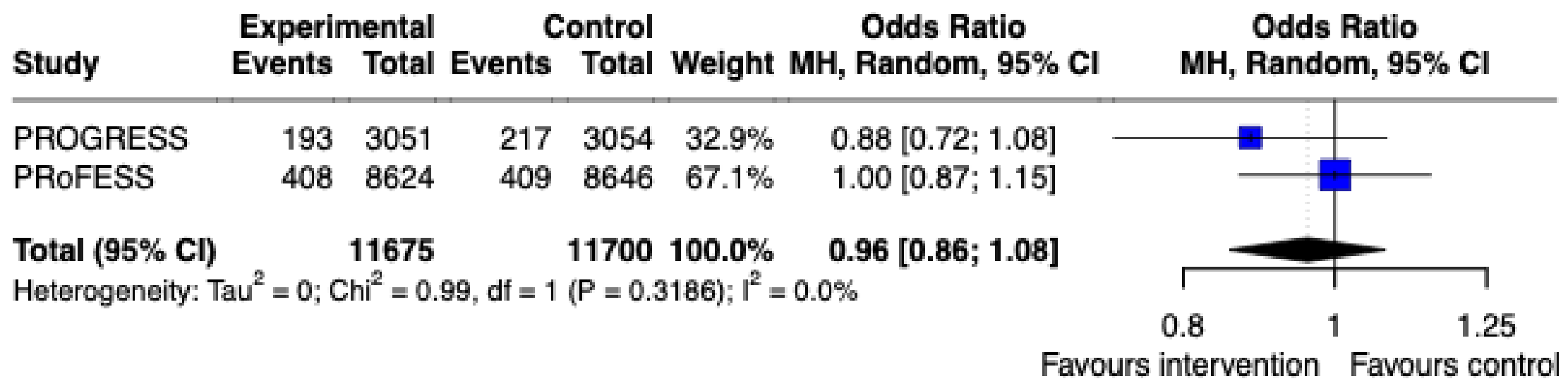
Intervention	Dementia	MCI	Cognitive decline
BP lowering drugs	No meaningful effect 2 fewer per 1,000	No studies	Benefit 11 fewer per 1,000
Strict BP management	No studies	No meaningful effect 6 more per 1,000	No meaningful effect MMSE 1.2 pts lower
Antithrombotic drugs	No meaningful effect 4 more per 1,000	No meaningful effect 8 fewer per 1,000	No meaningful effect 10 fewer per 1,000
Lipid-lowering drugs	No meaningful effect 1 fewer per 1,000	No studies	No studies
Strict LDL-C management	No studies	No studies	No meaningful effect MMSE 1.9 pts higher

Certainty of the evidence based on GRADE: **very low certainty**; **low certainty**; **moderate certainty**; **high certainty**.
To define minimally important difference, we used an absolute thresholds for benefit/harm of >10 per 1000 cases. For cognitive decline measured continuously, we used >10% of raw score range in MMSE (= 3 pts).
BP = blood pressure, LDL-C = low density lipoprotein cholesterol, MMSE = Mini-Mental State Examination.

- Meta-analysis could only be performed for blood pressure lowering drugs in association with dementia and cognitive decline (**Figure 1**), all other intervention-outcome pairs involved no or only 1 study.

Across drug classes and outcomes, effect estimates for dementia, MCI, and cognitive decline generally showed no meaningful benefit.

A. Dementia incidence



B. Cognitive decline

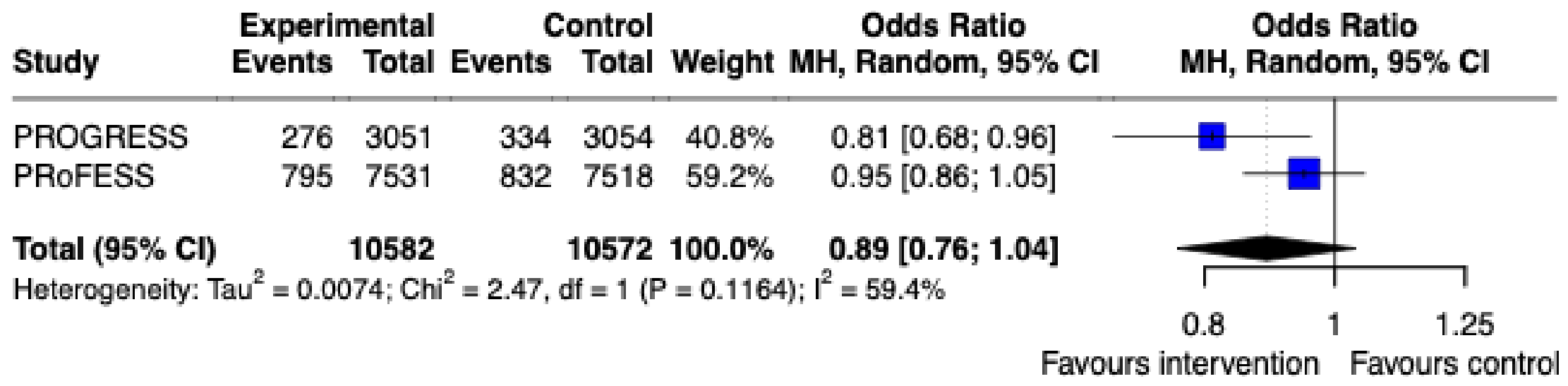


Figure 1. Forest plots of meta-analyses for blood pressure lowering drugs and (a) dementia, and (b) cognitive decline.

Conclusions

Current evidence does not provide support for pharmacological interventions after ischemic stroke or TIA in reducing the risk of subsequent dementia, MCI, or cognitive decline.

Given the limited number of studies, further high-quality studies with longer follow-ups are needed.

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