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Shantou Amsterdam study on blood pressure reduction and dementia prevention

Submission date 17/07/2026	**Recruitment status** Not yet recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 17/07/2026	**Overall study status** Ongoing	
Last Edited 17/07/2026	**Condition category** Nervous System Diseases	

Plain English summary of protocol

Background and study aims

Hypertension in midlife is a well-established risk factor for dementia in later life, and blood pressure lowering using antihypertensive treatment may reduce dementia risk. Observational studies suggest that specific classes of antihypertensive medication (AHM), particularly angiotensin receptor blockers (ARBs), may confer additional neuroprotective effects beyond blood pressure lowering. Current (inter)national guidelines consider all AHM classes to be equally effective for blood pressure management and cardiovascular disease prevention, except in individuals with specific comorbidities. The aim of this study is to determine whether long-term use of an AHM strategy based on ARBs, compared to the ones based on ACE inhibitors (ACEi) reduces the incidence of cognitive decline and dementia.

Who can participate?

Individuals aged 65–80 with untreated hypertension and without dementia.

What does the study involve?

Participants are randomly assigned to one of the two treatment groups (ARBs or ACEi) and undergo follow-up assessments of their cognitive functioning at one, three, and five years. Additionally, incident cardiovascular disease (including myocardial infarction and stroke), cardiovascular and all-cause death, and daily functioning are measured.

What are the possible benefits and risks of participating?

Treatment in both groups follow existing clinical guidelines for treating hypertension. The risks associated with participation are comparable to those of standard care and primarily involve the known side effects of high blood pressure medication.

Where is the study run from?

Amsterdam University Medical Center, Netherlands. The study is conducted across 34 primary care community health centres in the Shantou region, China

When is the study starting and how long is it expected to run for?

August 2026 to August 2033. Intervention and follow-up last five years.

Who is funding the study?
1. First Affiliated Hospital of Shantou University Medical College
2. Shantou University Medical College
3. Pro Senectute
4. Alzheimer Nederland

Who is the main contact?
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Study information

Scientific Title
Shantou-Amsterdam study on blood pressure Reduction and dementia Prevention (SHARP)

Acronym
SHARP

Study objectives
To determine whether long-term use of an antihypertensive treatment strategy based on angiotensin receptor blockers (ARBs), compared to one based on ACE inhibitors (ACEi), reduces the incidence of cognitive decline and dementia.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 08/05/2026, The Ethics Committee of First Affiliated Hospital of Shantou University Medical College (No. 57 Changping Road Jinping District, Shantou, 515041, China; +86 754-88905647; sdfyllwyh@163.com), ref: B-2026-094

Primary study design
Interventional

Allocation
Randomized controlled trial

Masking
Open (masking not used)

Control
Active

Assignment
Parallel

Purpose
Prevention

Study type(s)

Health condition(s) or problem(s) studied
Dementia, cognitive decline, hypertension

Interventions

The study is a two-arm, randomized controlled clinical trial using a prospective, open-label, blinded endpoint (PROBE) design. The study is conducted in China.

Participants with newly diagnosed hypertension receive oral antihypertensive medication (AHM) in accordance with the national Chinese guidelines, which align with international recommendations for the management of primary hypertension.

Randomization is performed centrally via the electronic CRF. Participants are randomized to four treatment groups (1:1:1:1), which differ in the sequence of second- and third-line therapy. For the primary analysis, these groups are combined into two treatment arms (ARB-based vs. ACEi-based).

- Groups 1–2 (Intervention): Protocolized, stepped antihypertensive treatment initiated with an ARB, with dihydropyridine calcium channel blocker (diCCB) and thiazide allocated as second- and third-line therapy in alternate sequences.
- Groups 3–4 (Comparator): Protocolized, stepped antihypertensive treatment initiated with an ACEi, with diCCB and thiazide allocated as second- and third-line therapy in alternate sequences.

Since hyperuricemia (serum uric acid level >420 µmol/L or >7 mg/dL) is a contraindication for thiazides, individuals with these conditions follow an adapted treatment scheme. The same scheme is also provided to those with hypokalemia.

For all groups, a beta-blocker may be added as fourth-line therapy if needed.

Dosage modifications follow a predefined stepwise protocol to achieve blood pressure control (Systolic Blood Pressure (SBP) ≤ 140 mmHg and diastolic blood pressure (DBP) ≤ 90 mmHg).

At treatment initiation and after each medication adjustment (dose change or addition), a 4-week follow-up is scheduled to assess blood pressure. Laboratory tests are performed as needed. If the blood pressure is adequately controlled and no safety concerns are identified, treatment is continued and reassessed after 6 months. If blood pressure remains controlled at that point, the same treatment is continued and reviewed at the 1-year assessment, after which monitoring continues at regular intervals for the remainder of the five-year intervention period.

Intervention and follow-up last five years.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Angiotensin receptor blockers, ACE inhibitors, Dihydropyridine calcium channel blocker, Thiazide, Beta-blockers

Primary outcome(s)
1. Clinical diagnosis of all-cause dementia at any time during the study and/or clinically meaningful cognitive decline measured using >3-point decrease on the Mini Mental State Examination (MMSE) versus baseline at baseline, 1, 3 and 5 and five years

Key secondary outcome(s)
1. All-cause dementia measured using data collection on the clinical diagnosis made at any time during the study

2. Cognitive decline measured using >3-point decrease on the MMSE versus baseline at baseline, 1, 3 and 5 and five years

3. Incident cardiovascular events (myocardial infarction and stroke) measured using self-report at study assessments via electronic CRF, and using primary care records, hospital records, and/or death registry at any time during the study

4. Cardiovascular and all-cause death measured using primary care records, hospital records, and /or death registry at any time during the study

5. Changes in daily functioning from baseline measured using the Lawton Instrumental activity of daily living scale at baseline and daily at any time during the study

Completion date
01/08/2033

Eligibility

Key inclusion criteria
1. Individuals aged 65–80 years
2. Not currently on AHM
3. Willing to receive regular (ATC-listed) antihypertensive treatment
4. Current mean SBP ≥140 and/or DBP ≥90 mmHg
5. Who are either:
5.1. Newly diagnosed with primary hypertension
5.2. Previously diagnosed but never treated;
or
5.3. Previously treated but stopped AHM >3 years before baseline

Healthy volunteers allowed
No

Age group
Senior

Lower age limit
65 Years

Upper age limit
80 Years

Sex
All

Total final enrolment
0

Key exclusion criteria
1. Current use of AHM
2. Dementia or relevant cognitive decline (defined as MMSE < 24 points; or < 21 points for ISCED level 1)
3. Contra-indications to use of an ARB or an ACEi

Date of first enrolment
01/08/2026

Date of final enrolment
01/08/2028

Locations

Countries of recruitment
China

Study participating centre
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Sponsor information

Organisation
First Affiliated Hospital of Shantou University Medical College

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https://ror.org/02bnz8785

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Shantou University Medical College

ROR
https://ror.org/02gxych78

Funder(s)

Funder type

Funder Name
Pro Senectute

Funder Name
Alzheimer Nederland

Alternative Name(s)
Alzheimer Netherlands, Stichting Alzheimer Nederland, Alzheimer Nederland Foundation, Alzheimer's Netherlands

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
Netherlands

Funder Name
Shantou University Medical College

Alternative Name(s)
SUMC

Funding Body Type
Government organisation

Funding Body Subtype
Local government

Location
China

Funder Name
First Affiliated Hospital of Shantou University Medical College

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Data sharing statement to be made available at a later date