

# PROPS - Preventative Role of a fixed dose combination Pill in Stroke: a multi-centre open label randomised controlled trial of a fixed dose combination pill versus standard care for secondary prevention of stroke in a primary care setting

<b>Submission date</b> 22/05/2014	<b>Recruitment status</b> Stopped	<input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 25/07/2014	<b>Overall study status</b> Stopped	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
<b>Last Edited</b> 12/12/2016	<b>Condition category</b> Circulatory System	<input type="checkbox"/> Individual participant data <input type="checkbox"/> Record updated in last year

## Plain English summary of protocol

### Background and study aims

Optimal therapy for people who have had a stroke or a Transient Ischaemic Attack (TIA) consists of blood pressure (BP) lowering, cholesterol lowering and anti-platelet agents to reduce risk of further cerebrovascular events. Survey data continue to show that guidelines for secondary prevention of cardiovascular events are not well implemented in clinical practice. This is a worldwide phenomenon, more common in elderly patients. An alternative to traditional 'treat to target' approaches is to adopt simpler regimes such as using a fixed dose combination (FDC) pill. The aim of this study is to test whether such a regime will be non-inferior to standard care. The rationale for such a regime is that it will: reduce pill burden; ensure that all the key pharmacological therapies to lower cardiovascular risk after stroke are used; separate the decision to treat from the underlying level of the risk factor; and reduce monitoring burden (and costs). Evidence from trials in other populations, including people at high risk of cardiovascular disease and people with a history of myocardial infarction, suggests that such a regime is at least as effective as standard care. The purpose of this study is to determine whether an FDC pill has a role for secondary prevention of vascular events in older people who have had a stroke/TIA, in a primary care setting.

### Who can participate?

Patients aged 55 years or over who have had a stroke or mini-stroke.

### What does the study involve?

Following informed consent and initial health check, participants are randomly allocated into one of two groups. One group are given the polypill. The other group continue to receive standard care (separate antihypertensives and cholesterol lowering pills). Participants then have

a follow-up health check at 6 months. After that, the study ends and participants on the polypill go back to standard care.

What are the possible benefits and risks of participating?

The risks of participating in this study are low. For participants treated with Trinomia, the risk of side effects are likely to be similar to those of the medicines they are taking already. Potential benefits for participants may include better management of risk factors for having another stroke. The results of the study may improve the future care of participants and other patients who have had a stroke.

Where is the study run from?

University of Cambridge (UK).

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

September 2015 to March 2018.

Who is funding the study?

British Heart Foundation (UK) and the Stroke Association (UK).

Who is the main contact?

Dr Merel Pannebakker

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## Contact information

### Type(s)

Scientific

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## **Additional identifiers**

### **Clinical Trials Information System (CTIS)**

2013-004722-29

### **Protocol serial number**

PROPS14

## **Study information**

### **Scientific Title**

PROPS - Preventative Role of a fixed dose combination Pill in Stroke: a multi-centre open label randomised controlled trial of a fixed dose combination pill versus standard care for secondary prevention of stroke in a primary care setting

### **Acronym**

PROPS

### **Study objectives**

Current hypothesis as of 28/07/2015:

A fixed dose combination pill, Trinomia, will be non-inferior in terms of systolic blood pressure when compared with standard care in people with a history of stroke/TIA in a primary care setting over a period of 25 weeks.

Previous hypothesis:

A 'polypill' will be non-inferior in terms of systolic blood pressure when compared with standard care in people with a history of stroke/TIA in a primary care setting over a period of six months.

### **Ethics approval required**

Old ethics approval format

### **Ethics approval(s)**

East Midlands – Nottingham 2 REC, 21/07/2015, ref: 15/EM/0277

### **Primary study design**

Interventional

### **Study design**

Randomised controlled trial

### **Study type(s)**

Prevention

## **Health condition(s) or problem(s) studied**

Stroke prevention

## **Interventions**

Current interventions as of 28/07/2015:

Participants in the intervention arm will receive Trinomia, a fixed dose combination pill, and participants in the control arm will receive standard ('normal') care, for a period of 6 months. Participants will be seen 2 weeks after starting the intervention, and again at 6 months for follow-up.

Previous interventions:

Participants in the intervention arm will receive a 'polypill' and participants in the control arm will receive standard ('normal') care for a period of 6 months. Participants will be seen 6 weeks after randomisation and again at 6 months for follow-up.

## **Intervention Type**

Drug

## **Phase**

Phase III

## **Drug/device/biological/vaccine name(s)**

Trinomia (5mg Ramipril, 20mg atorvastatin, 100mg acetylsalicylic acid)

## **Primary outcome(s)**

Current primary outcome measures as of 28/07/2015:

Systolic blood pressure at baseline and follow-up at 25 weeks

Previous primary outcome measures:

To determine whether a 'polypill' will be non-inferior in terms of systolic blood pressure when compared with standard care in people with a history of stroke/TIA in a Primary Care setting over a period of six months

## **Key secondary outcome(s)**

Current secondary outcome measures as of 28/07/2015:

1. Non-HDL, HDL & total cholesterol (baseline and follow-up at 25 weeks)
2. Diastolic BP (baseline and follow-up at 25 weeks)
3. Quality of life (EQ5D-5L; baseline and follow-up at 25 weeks)
4. Side effects (baseline and follow-up at 25 weeks)
5. Participant preference for a single pill (baseline, 2 weeks and follow-up at 25 weeks)
6. Subjective and objective measures of adherence (MARS, NINA, attitudes towards medication, BMQ; baseline, 2 weeks and follow-up at 25 weeks)
7. Lifestyle measures (diet, physical activity [GPPAQ], smoking and alcohol; baseline and follow-up at 25 weeks)
8. Stroke, TIA, myocardial infarction, cardiovascular events, cardiovascular deaths, all-cause mortality and any hospital admissions possibly associated with AEs of Trinomia (follow-up at 25 weeks)
9. Costs (follow-up at 25 weeks)

Previous secondary outcome measures:

To determine:

1. Whether taking the 'polypill' is associated with higher adherence and/or false reassurance in people with a history of stroke/TIA (pill count, single item adherence measure, MARS, NINA, BMQ).
2. The cost effectiveness of a 'polypill' strategy for secondary prevention of stroke as compared to standard practice (participant characteristics [age, gender, existing condition], type and dose of medication, adherence, resource use, EuroQol EQ-5D).
3. Non-inferiority of the 'polypill' for the following measurements: LDL cholesterol; HDL cholesterol; total cholesterol; triglycerides; change in diastolic blood pressure; quality of life (EuroQol EQ-5D); side effects; participant and carer preference for treatment; major cardiovascular events, strokes, myocardial infarction and all-cause mortality.

### **Completion date**

31/03/2018

### **Reason abandoned (if study stopped)**

Lack of funding/sponsorship

## **Eligibility**

### **Key inclusion criteria**

Current inclusion criteria as of 28/07/2015:

1. Men and post-menopausal\* women, aged 55 years or over at the point of the database search
2. On the stroke/TIA register of the general practice.

\*Post-menopausal defined as: no menstrual period for 12 consecutive months or more.

Previous inclusion criteria:

Participants eligible for the trial must comply with all of the following at randomisation:

1. Age 55 or over
2. On the stroke/TIA register of the general practice

### **Participant type(s)**

Patient

### **Healthy volunteers allowed**

No

### **Age group**

Senior

### **Sex**

All

### **Key exclusion criteria**

Current exclusion criteria as of 28/07/2015:

1. Confirmed diagnosis of haemorrhagic stroke
2. Currently receiving treatment with more than the equivalent of 20 mg of atorvastatin
3. Currently receiving treatment with clopidogrel anti-platelet monotherapy
4. Currently receiving treatment with anti-coagulant therapy

5. SBP <120mmHg
  6. Orthostatic hypotension( $\geq$ 20mmHg postural drop in SBP after 1 minute of standing)
  7. Terminal illness
  8. Known left ventricular systolic dysfunction (ejection fraction < 30%)
  9. Absolute contra-indication to atorvastatin, aspirin or ramipril as specified in the SmPC or British National Formulary (BNF) or hypersensitivity to these components
  10. Inability to give informed consent
  11. Deemed unsuitable by General Practitioner (GP) for other reasons
  12. Women of child bearing potential
  13. Unable to swallow tablets or capsules
- Involvement in any other trial is not an exclusion criterion.

Previous exclusion criteria:

1. On 3 or more antihypertensive agents
2. On more than the equivalent of 40mg simvastatin
3. Systolic blood pressure < 120mmHg
4. Orthostatic hypotension ( $\geq$ 20mmHg drop in systolic blood pressure on standing measured after 1 minute of standing)
5. Terminal illness
6. Heart failure
7. Absolute contra-indication to any of the components of the 'polypill'
8. Inability to give informed consent and without a designated representative who is able to provide consent under the terms of the Mental Capacity Act 2008
9. Deemed unsuitable by General Practitioner (GP) for other reasons

**Date of first enrolment**

01/09/2015

**Date of final enrolment**

31/03/2017

## Locations

**Countries of recruitment**

United Kingdom

**Study participating centre**

100 GP practices in the UK

United Kingdom

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## Sponsor information

**Organisation**

Cambridge University Hospitals NHS Foundation Trust (UK)

ROR

<https://ror.org/04v54gj93>

## Funder(s)

### Funder type

Charity

### Funder Name

British Heart Foundation (UK)

### Alternative Name(s)

The British Heart Foundation, the\_bhf, BHF

### Funding Body Type

Private sector organisation

### Funding Body Subtype

Trusts, charities, foundations (both public and private)

### Location

United Kingdom

### Funder Name

Stroke Association (UK)

### Alternative Name(s)

TheStrokeAssociation, TheStrokeAssoc

### Funding Body Type

Private sector organisation

### Funding Body Subtype

Associations and societies (private and public)

### Location

United Kingdom

## Results and Publications

Individual participant data (IPD) sharing plan

## IPD sharing plan summary

Available on request

### Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">HRA research summary</a>			28/06/2023	No	No