# Treatment in morning versus evening study

Submission date	Recruitment status No longer recruiting	<ul><li>Prospectively registered</li></ul>		
21/08/2014		[X] Protocol		
Registration date	Overall study status	[X] Statistical analysis plan		
20/10/2014	Completed	[X] Results		
Last Edited	Condition category	[] Individual participant data		
13/10/2022	Circulatory System			

## Plain English summary of protocol

Background and study aims

Treatment in Morning versus Evening (TIME) is a study to compare the treatment for high blood pressure using hypertensive drugs given in the evening with the usual morning medication. This is done using an online system to record any side effects or changes due to the change in their medication. This automated system has worked well in our initial phase of this study with good patient response. Record-linkage to hospitalisations and deaths will be carried out and events monitored. Heart attack, stroke or death will be recorded and analysed to see if the timing of the medication has any impact.

#### Who can participate?

People who are already taking antihypertensive medication in usual care

#### What does the study involve?

Participants take part by registering on a secure, study-specific website. Those who are eligible are randomly allocated to continue taking medication at their usual time (usually morning) or to switch to taking medication in the evening. Participants receive regular emails with simple links to record responses to track progress. Participants, people on their behalf, or GPs can record any side effects at any time online. Participants are followed up for 4 years.

## What are the possible benefits and risks of participating?

Taking hypertensive medication in the evening may reduce the number of heart attack or stroke compared with usual morning dosing, and so is potentially of benefit to all hypertensive patients in the future. There are no known risks for patients taking part in the study.

## Where is the study run from?

The study is sponsored by the University of Dundee, UK and run from the Medicines Monitoring Unit (MEMO) within this. The study is internet based and participants can be recruited from across the UK. They will be recruited from general practices, hospitals or by social media.

When is the study starting and how long is it expected to run for? August 2011 to July 2022

Who is funding the study? British Heart Foundation (UK)

Who is the main contact? Ms Wendy Saywood wendys@memo.dundee.ac.uk

## Contact information

## Type(s)

Scientific

#### Contact name

Dr Rebecca Barr

#### Contact details

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## Additional identifiers

## Clinical Trials Information System (CTIS)

Nil known

## ClinicalTrials.gov (NCT)

Nil known

#### Protocol serial number

17071

# Study information

#### Scientific Title

Treatment In Morning versus Evening: an observational study

#### Acronym

TIME

## Study objectives

A trial comparing evening dosing of usual antihypertensive therapy with conventional morning dose is proposed.

## Ethics approval required

Old ethics approval format

## Ethics approval(s)

East of Scotland Research Ethics Service (EoSRES) REC 1; 28/05/2011 (approval for the pilot study), 26/05/2014 (approval to move on to full study); ref. 11/AL/0309

#### Study design

Randomised controlled trial

#### Primary study design

Interventional

## Study type(s)

Treatment

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

Topic: Primary Care, Cardiovascular disease; Subtopic: Other Primary Care, Cardiovascular (all Subtopics); Disease: All Diseases, Other

#### **Interventions**

Timing of medication switch: Subjects already taking hypertensive medication in usual care will be identified from collaborating practices and within secondary care clinics. Subjects will be invited to participate in the study by registering on a study website. Registered subjects who meet the inclusion criteria will be randomised to continue taking medicine at their usual time (most often in the morning) or to switch to taking medication in the evening (or morning if evening is their usual time).

#### Intervention Type

Other

#### Phase

Not Applicable

#### Primary outcome(s)

The Anti Platelet Trialists' Collaboration: composite endpoint of non-fatal myocardial infarction, non-fatal stroke or vascular death.

## Key secondary outcome(s))

- 1. Each component of the primary endpoint
- 2. Hospitalisation for non-fatal stroke
- 3. Hospitalisation for non-fatal MI
- 4. Vascular death
- 5. All-cause mortality
- 6. Hospitalisation or death from congestive heart failure.
- 1. Adherence to the evening dosing regimen vs morning (patient reported) with particular reference to patients taking diuretic therapy.
- 2. Patient reported and hospitalised adverse events in the morning versus evening groups will be compared. In particular falls and fractures will be recorded.
- 3. Home BP readings taken by a subset of patients will be compared between morning & evening dosing.
- 4. An additional proposed substudy is a telephone administered cognitive function assessment to compare patients on morning and evening dosing.

#### Completion date

27/07/2022

# **Eligibility**

## Key inclusion criteria

- 1. Both diagnosed and treated for hypertension (all forms) with at least one antihypertensive drug
- 2. Aged above 18 years
- 3. Have a valid email address

## Participant type(s)

Patient

### Healthy volunteers allowed

No

### Age group

Adult

#### Lower age limit

18 years

#### Sex

Αll

#### Total final enrolment

21104

#### Key exclusion criteria

- 1. Subjects who take twice daily antihypertensive therapy.
- 2. Subjects who work shift patterns that include a night shift.
- 3. Subjects who unwilling to consent to:
- 3.1. Follow up
- 3.2. Provide a surrogate to be contacted and/or
- 3.3. Give consent for their family practice to release follow up clinical data
- 3.4. To have their physical case records abstracted if required
- 3.5. To have their electronic case records searched and abstracted if required
- 3.6. To allow their consent from to be copied to authorities from whom the study team is requesting medical data
- 4. Those participating in another clinical trial or who have done in the last 3 months

#### Date of first enrolment

07/12/2011

#### Date of final enrolment

05/06/2018

## Locations

#### Countries of recruitment

**United Kingdom** 

Scotland

Study participating centre
Ninewells Hospital and Medical School
Dundee
United Kingdom
DD1 9SY

# Sponsor information

### Organisation

NHS Tayside (UK)

#### **ROR**

https://ror.org/000ywep40

# Funder(s)

## Funder type

Charity

#### **Funder Name**

British Heart Foundation (BHF) (UK); Grant Codes: CS/14/1/30659

### Alternative Name(s)

the\_bhf, The British Heart Foundation, BHF

#### Funding Body Type

Private sector organisation

#### **Funding Body Subtype**

Trusts, charities, foundations (both public and private)

#### Location

**United Kingdom** 

## **Results and Publications**

## Individual participant data (IPD) sharing plan

Access to a de-identified participant dataset and data dictionary is available upon reasonable request to researchers who provide a methodologically sound proposal, with no prespecified restrictions on data use. Any such requests should be sent to the corresponding author for consideration by the trial steering committee. There might be restrictions on sharing data derived from record-linkage to NHS datasets. A period of 18 months after publication of the main study results should elapse before requests are made, to allow the authors to publish substudies and further analyses.

## IPD sharing plan summary

Available on request

#### **Study outputs**

Output type	Details	Date created	Date added	Peer reviewed?	Patient- facing?
Results article		11/10 /2022	13/10 /2022	Yes	No
Protocol article	protocol	09/02 /2016		Yes	No
Protocol article	substudy protocol	07/06 /2018		Yes	No
Other publications	analysis of recruitment, retention and follow- up rates	01/12 /2017	18/03 /2020	Yes	No
Participant information sheet	Participant information sheet	11/11 /2025	11/11 /2025	No	Yes
Plain English results	version 1.0	11/10 /2022	13/10 /2022	No	Yes
Statistical Analysis Plan	version 1	29/06 /2022	29/07 /2022	No	No
Study website	Study website	11/11 /2025	11/11 /2025	No	Yes