

# Treatment in morning versus evening study

<b>Submission date</b> 21/08/2014	<b>Recruitment status</b> No longer recruiting	<input type="checkbox"/> Prospectively registered <input checked="" type="checkbox"/> Protocol
<b>Registration date</b> 20/10/2014	<b>Overall study status</b> Completed	<input checked="" type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 13/10/2022	<b>Condition category</b> Circulatory System	<input type="checkbox"/> Individual participant data

## 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

**Study website**

<https://www.timestudy.co.uk/>

## Contact information

**Type(s)**

Scientific

**Contact name**

Dr Rebecca Barr

**Contact details**

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## Additional identifiers

**EudraCT/CTIS number**

Nil known

**IRAS number**

**ClinicalTrials.gov number**

Nil known

**Secondary identifying numbers**

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

**Secondary study design**

Randomised controlled trial

**Study setting(s)**

Hospital

**Study type(s)**

Treatment

**Participant information sheet**

[https://www.timestudy.co.uk/info\\_sheets/TIME%20STUDY%20-%20Patient%20Information%20Sheet.pdf](https://www.timestudy.co.uk/info_sheets/TIME%20STUDY%20-%20Patient%20Information%20Sheet.pdf)

**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 measure**

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

**Secondary outcome measures**

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.

**Overall study start date**

03/08/2011

**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

**Age group**

Adult

**Lower age limit**

18 Years

**Sex**

Both

**Target number of participants**

Proposed following AM09: >20,000; Actual number recruited to date: 20,860 (AM09 (REC ref AM11): Approved 22/12/2015)

**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 form 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**

Scotland

United Kingdom

**Study participating centre**

**Ninewells Hospital and Medical School**

Dundee

United Kingdom

DD1 9SY

## Sponsor information

**Organisation**

NHS Tayside (UK)

**Sponsor details**

R&D Office

Level 9

Ninewells Hospital and Medical School

Ninewells Avenue

Dundee

Scotland

United Kingdom

DD1 9SY

**Sponsor type**

Hospital/treatment centre

**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**

**Publication and dissemination plan**

Presentation of results at European Society of Cardiology (ESC) Congress (Barcelona 26-29 August 2022) and ISH (Kyoto, 12-16 October 2022)

Substudies will be published separately.

Results have been shared by email with all participants and participating research networks (see attached lay summary).

**Intention to publish date**

12/10/2022

**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?
<a href="#">Protocol article</a>	protocol	09/02/2016		Yes	No
<a href="#">Protocol article</a>	substudy protocol	07/06/2018		Yes	No
<a href="#">Other publications</a>	analysis of recruitment, retention and follow-up rates	01/12/2017	18/03/2020	Yes	No
<a href="#">Statistical Analysis Plan</a>	version 1	29/06/2022	29/07/2022	No	No
<a href="#">Plain English results</a>	version 1.0	11/10/2022	13/10/2022	No	Yes
<a href="#">Results article</a>		11/10/2022	13/10/2022	Yes	No