

# TEMPUS - The Evening vs Morning Polypill Utilization Study;A randomised controlled cross-over trial to evaluate evening versus morning administration of a cardiovascular polypill

Published: 25-01-2012

Last updated: 28-04-2024

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<b>Ethical review</b>	Not approved
<b>Status</b>	Will not start
<b>Health condition type</b>	Coronary artery disorders
<b>Study type</b>	Interventional

## Summary

### ID

NL-OMON35965

### Source

ToetsingOnline

### Brief title

TEMPUS

### Condition

- Coronary artery disorders
- Central nervous system vascular disorders
- Arteriosclerosis, stenosis, vascular insufficiency and necrosis

### Synonym

cardovascular disease, dyslipidemia, hypertension

### Research involving

Human

## Sponsors and support

**Primary sponsor:** Universitair Medisch Centrum Utrecht

**Source(s) of monetary or material Support:** Financiering door de afdeling vasculaire geneeskunde UMC Utrecht. Geen externe geldstromen.

## Intervention

**Keyword:** cardiovascular, chronotherapy, combination pill, polypill

## Outcome measures

### Primary outcome

- \* Difference in LDL cholesterol between treatment regimen  
(evening administration RHP vs. morning administration RHP)
- \* Difference in mean 24 hour ambulatory systolic BP  
(evening administration RHP vs. morning administration RHP)

### Secondary outcome

- \* Difference in cholesterol spectrum  
(evening administration RHP vs. morning administration RHP)
- \* Difference 24 hour ambulatory BP parameters  
(evening administration RHP vs. morning administration RHP)
- \* Difference in cholesterol spectrum  
(administration RHP vs. administration individual agents)
- \* Difference 24 hour ambulatory BP parameters  
(administration RHP vs. administration individual agents)
- \* Diffence in cardiovascular risk score  
(evening administration RHP vs. morning administration RHP vs. administration

individual agents)

\* Difference in adherence

(evening administration RHP vs. morning administration RHP vs. administration

individual agents)

\* Difference in adverse events

(evening administration RHP vs. morning administration RHP vs. administration

individual agents)

\* Difference in participant acceptability

(evening administration RHP vs. morning administration RHP vs. administration

individual agents)

## Study description

### Background summary

In clinical practice, antihypertensives are generally prescribed for use in the morning, whereas some statins are recommended for use in the evening. There is evidence that the reduction in LDL achieved with some statins is superior when taken in the night, but it is unclear whether the additional reduction in LDL (and the reported improvement in BP control when aspirin is taken in the evening) is offset by a reduction in adherence when taking medication in the evening. Current product labelling recommends night use for simvastatin and does not state a timing preference for aspirin or blood pressure lowering medicines. There is therefore uncertainty concerning the best timing of administration of the polypill. This uncertainty will be addressed by this trial.

### Study objective

The aim of the study is to measure whether there is a difference in LDL cholesterol levels or the 24 hour ambulatory blood pressure in individuals at high risk of cardiovascular disease when the polypill is taken in the morning compared with the evening.

### Study design

Randomized cross-over study with 75 participants.

## **Intervention**

Eligible individuals willing to participate in the trial will receive the polypill and the components of the polypill for a total of 18 weeks; a random sequence of 6 weeks morning, 6 weeks evening administration and 6 weeks administration of the individual agents. After every treatment sequence laboratory blood examination and ambulatory blood measurements will be performed.

## **Study burden and risks**

Measurements:

None of the study measurements are dangerous. Routine blood samples taken may be associated with some bruising, discomfort and local irritation. There is also a small risk of infection whenever the skin barrier is broken by a needle. The ABPM may be uncomfortable due to 24 hours measurement every 30 minutes, including at night. This last measurement may be inconvenient.

Medication:

The polypill combination cardiovascular medication will be an unapproved medication. However all the ingredients in both of the polypill combinations used in this trial are well known medicines with well established efficacy and safety profiles. Although all the drugs in the polypill have been used for many years there are possible risks that both polypill may cause side effects. These are generally mild and infrequent and are usually resolved immediately by stopping the medication. Side effects of the components of the polypills can include low blood pressure, dizziness, headache, nausea, mild stomach pain, heartburn, ulceration, abdominal pain, constipation, flatulence, bleeding, gout, cough, fatigue, liver problems, and muscle pain, tenderness or weakness. As with any medication an allergic reaction is possible such as skin rash, itching, difficulty breathing or swelling of the face, but this is quite rare.

## **Contacts**

### **Public**

Universitair Medisch Centrum Utrecht

Heidelberglaan 100  
3508 GA Utrecht  
Nederland

### **Scientific**

Universitair Medisch Centrum Utrecht

Heidelberglaan 100  
3508 GA Utrecht  
Nederland

## Trial sites

### Listed location countries

Netherlands

## Eligibility criteria

### Age

Adults (18-64 years)

Elderly (65 years and older)

### Inclusion criteria

Adults with

(A) established atherothrombotic cardiovascular disease (CVD)- history of ischaemic heart disease, ischaemic stroke or transient ischaemic attack, or peripheral vascular disease  
OR

(B) a 5 year cardiocvascular risk of at least 5% (SCORE)

### Exclusion criteria

Individuals will NOT be eligible if one or more of the following criteria are satisfied:;\*  
Contraindication to any of the components of the polypill (e.g. known intolerance to aspirin, statins, or ACE inhibitors; pregnancy or likely to become pregnant or breastfeeding women during the treatment period). Such contrindications are fully listed in the Investigator Brochure.

\* The treating doctor considers that changing a participant\*s cardiovascular medications would put the participant at risk (e.g. symptomatic heart failure, high dose \*-blocker required to manage angina or for rate control in atrial fibrillation, accelerated hypertension, severe renal insufficiency, a history of severe resistant hypertension).;\* Other potential reasons for exclusion include:

\* Known situation where medication regimen might be altered for a significant length of time, e.g. current acute cardiovascular event, planned coronary bypass graft operation.

\* Unlikely to complete the trial (e.g. life-threatening condition other than cardiovascular disease) or adhere to the trial procedures or attend study visits (e.g. major psychiatric condition, dementia).

\* Women of child bearing potential should be on a medically accepted form of contraception (oral or implanted contraception, IUD or tubal sterilisation). If there is any possibility of pregnancy, prior to randomisation a blood or urine pregnancy test will be performed. Final decisions about eligibility will be made at the discretion of the trial Investigator and potential trial participant, in light of any additional requirements or guidance from local ethics committees and other regulatory bodies.

\* Night shift workers.

## Study design

### Design

Study type:	Interventional
Intervention model:	Crossover
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

### Recruitment

NL	
Recruitment status:	Will not start
Enrollment:	75
Type:	Anticipated

### Medical products/devices used

Product type:	Medicine
Brand name:	-
Generic name:	acetylsalicylic acid 75mg
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	-
Generic name:	hydrochlorothiazide 12,5mg
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	-

Generic name:	lisinopril 10mg
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	-
Generic name:	simvastatin 40mg
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Red Heart Pill 2C
Generic name:	acetylsalicylic acid 75mg, simvastatin 40mg, lisinopril 10mg, hydrochlorothiazide 12,5mg

## Ethics review

Not approved	
Date:	20-01-2012
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

## Study registrations

### Followed up by the following (possibly more current) registration

No registrations found.

### Other (possibly less up-to-date) registrations in this register

No registrations found.

### In other registers

Register	ID
EudraCT	EUCTR2011-001120-38-NL
CCMO	NL36047.041.11