

# A randomised controlled trial of the angiotensin converting enzyme (ACE) inhibitor ramipril in asymptomatic aortic stenosis

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| <b>Submission date</b><br>30/09/2004   | <b>Recruitment status</b><br>No longer recruiting | <input checked="" type="checkbox"/> Prospectively registered<br><input type="checkbox"/> Protocol |
| <b>Registration date</b><br>30/09/2004 | <b>Overall study status</b><br>Completed          | <input type="checkbox"/> Statistical analysis plan<br><input checked="" type="checkbox"/> Results |
| <b>Last Edited</b><br>24/03/2015       | <b>Condition category</b><br>Circulatory System   | <input type="checkbox"/> Individual participant data  |

## Plain English summary of protocol

### Background and study aims

For patients with aortic stenosis (a narrowing of the main valve out of the heart), the only effective treatment currently is valve replacement surgery. A group of drugs called ACE inhibitors are of proven benefit in treating heart failure from other causes and reducing increased heart muscle thickness, both of which occur in aortic stenosis. They are however considered to be contraindicated in aortic stenosis, despite a lack of evidence for harm. The aim of our study is to determine whether an ACE inhibitor has any beneficial effects in patients with aortic stenosis.

### Who can participate?

Men and women aged over 18 years with aortic stenosis.

### What does the study involve?

Participants will be randomly allocated to receive either the ACE inhibitor ramipril or a placebo (dummy) drug.

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

Not provided at time of registration.

### Where is the study run from?

John Radcliffe Hospital (UK).

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

The study ran from October 2008 to December 2011.

### Who is funding the study?

1. Heart Research UK (UK)
2. Oxford Comprehensive NIHR Biomedical Research Centre (UK)
3. Department of Health Technology Platform Grant for Advanced Imaging (UK)

Who is the main contact?  
Dr Saul Myerson  
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## Contact information

**Type(s)**  
Scientific

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## Additional identifiers

**Clinical Trials Information System (CTIS)**  
2007-005224-32

**Protocol serial number**  
N0176135469 / OCMR 06.01

## Study information

**Scientific Title**  
A randomised controlled trial of the angiotensin converting enzyme (ACE) inhibitor ramipril in asymptomatic aortic stenosis

**Acronym**  
RIAS

**Study objectives**  
Patients with narrowed aortic valves (the main valve affecting blood flow out of the heart) sometimes develop symptoms of breathlessness or reduced heart function, and this is often accompanied by a thickened heart muscle. This muscle thickening may actually be detrimental to cardiac function, through increased stiffness, and a reduction of this may be beneficial to the patients. A group of drugs called ACE inhibitors are of proven benefit in reducing heart muscle thickness from other causes, and also improve cardiac function and prolong life in patients with

heart failure. We propose a randomised placebo-controlled trial of one ACE inhibitor, ramipril, in patients with narrowed aortic valves to determine if this can reduce muscle thickness, delay the onset symptoms and the need for valve replacement surgery.

On 21/05/2010 the trial record was updated to add the sources of funding.

### **Ethics approval required**

Old ethics approval format

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

Oxfordshire REC C, 06/11/2007, ref: 07/H0606/139

### **Study design**

Randomised controlled trial

### **Primary study design**

Interventional

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

Treatment

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

Cardiovascular: asymptomatic aortic stenosis

### **Interventions**

Factory-prepared randomised packs of identical placebo/ramipril tablets. Initial supply for 2 weeks, then further supply at the second clinic visit, to allow for up-titration of ramipril dose. Randomisation data sealed and unopened until after data analysis at end.

Added 19/05/2010: trial started in 2008 instead of 2002.

### **Intervention Type**

Drug

### **Phase**

Not Applicable

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

Ramipril

### **Primary outcome(s)**

1. Safety of administration in this group of patients
2. Changes in left ventricular mass and function

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

Added 21/05/2010:

1. Change in left ventricular ejection fraction
2. Change in other LV functional parameters assessed by MRI
3. Change in biochemical markers of LV function (BNP)

4. Change in myocardial energetics measured with magnetic resonance spectroscopy
5. Time to symptoms of aortic stenosis or aortic valve replacement
6. Change in distance walked and maximal effort tolerance on exercise treadmill testing

**Completion date**

31/12/2011

## Eligibility

**Key inclusion criteria**

Added 21/05/2010:

1. Male or female, aged 18 years or above
2. Diagnosed with asymptomatic aortic stenosis of at least moderate degree (peak velocity  $\geq 3.0$  m/sec; gradient  $\geq 36$  mmHg or valve area  $< 1.5$  cm<sup>2</sup> by echocardiography) for whom aortic valve replacement surgery is currently not contemplated
3. Left ventricular ejection fraction on echocardiography  $\geq 40\%$  without regional wall motion abnormality suggestive of significant previous myocardial infarction
4. Patient is willing and able to give informed consent for participation in the study
5. Able (in the investigators' opinion) and willing to comply with all study requirements

**Participant type(s)**

Patient

**Healthy volunteers allowed**

No

**Age group**

Adult

**Lower age limit**

18 years

**Sex**

All

**Key exclusion criteria**

Added 21/05/2010:

1. Other significant valve disease
2. Female who is pregnant, lactating or planning pregnancy during the course of the study
3. Significant renal impairment (estimated GFR  $< 30$  ml/min). If moderate renal impairment (GFR 30-59 ml/min) is present, patients may be included in the study, but will not receive gadolinium contrast during the CMR scan
4. Known hepatic impairment (AST/ALT  $> 2$  times the upper limit of normal)
5. Prescription of ACE inhibitors or angiotensin II receptor blockers (ARBs) within the 3 months prior to the start of the study
6. Past history of an allergic reaction or intolerance to ACE inhibitors
7. Sustained systolic blood pressure  $< 100$  mmHg or  $> 200$  mmHg or diastolic blood pressure  $< 40$  mmHg or  $> 110$  mmHg at baseline measurement
8. Contraindication to magnetic resonance scanning (pacemaker, cranial aneurysm clips, metallic ocular foreign bodies, severe claustrophobia)

9. Patient is terminally ill

10. Any other significant disease or disorder which, in the opinion of the investigator, may either put the patient at risk because of participation in the study, or may influence the result of the study, or the patient ability to participate in the study

11. Patients who have participated in another research study involving an investigational product in the past 3 months

**Date of first enrolment**

01/10/2008

**Date of final enrolment**

31/12/2011

## **Locations**

**Countries of recruitment**

United Kingdom

England

**Study participating centre**

**Department of Cardiovascular Medicine**

Oxford

United Kingdom

OX3 9DU

## **Sponsor information**

**Organisation**

University of Oxford (UK)

**ROR**

<https://ror.org/052gg0110>

## **Funder(s)**

**Funder type**

Research organisation

**Funder Name**

Heart Research UK (UK)

**Alternative Name(s)**

HRUK

**Funding Body Type**

Private sector organisation

**Funding Body Subtype**

Trusts, charities, foundations (both public and private)

**Location**

United Kingdom

**Funder Name**

Oxford Comprehensive NIHR Biomedical Research Centre (UK)

**Funder Name**

Department of Health Technology Platform Grant for Advanced Imaging (UK)

## Results and Publications

**Individual participant data (IPD) sharing plan****IPD sharing plan summary****Study outputs**

| Output type                                   | Details                       | Date created | Date added | Peer reviewed? | Patient-facing? |
|---|-------------------------------|--------------|------------|----------------|-----------------|
| <a href="#">Results article</a>               | results                       | 01/08/2015   |            | Yes            | No              |
| <a href="#">Participant information sheet</a> | Participant information sheet | 11/11/2025   | 11/11/2025 | No             | Yes             |