Purpose

People with established cardiovascular disease need secondary prevention that addresses multiple risk factors. Complexity & cost confer particularly difficult barriers to uptake of treatment; recovery from a stroke or heart attack typically necessitates multiple drugs for cholesterol, blood pressure and platelet function. A low-cost, fixed-dose, once-daily combination polypill, the Red Heart Pill, has been formulated by Dr Reddy’s Laboratories. UMPIRE will evaluate whether provision of this polypill compared with usual medications improves adherence and clinical outcomes among high-risk patients in Europe and India. The results will be used to develop recommendations for equitable access.

<table>
<thead>
<tr>
<th>Condition</th>
<th>Intervention</th>
<th>Phase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular Diseases</td>
<td>Drug: polypill</td>
<td>Phase III</td>
</tr>
<tr>
<td></td>
<td>Drug: Usual cardiovascular medications</td>
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</tbody>
</table>

Study Type: Interventional  
Study Design:  
Allocation: Randomized  
Control: Active Control  
Endpoint Classification: Safety/Efficacy Study  
Intervention Model: Parallel Assignment  
Masking: Open Label  
Primary Purpose: Treatment  

Official Title: A Randomised Controlled Trial of a Fixed-dose Combination Polypill Medication (the Red Heart Pill) and Usual Care in Those at High Risk of Cardiovascular Disease.

Resource links provided by NLM:
- MedlinePlus related topics: Cholesterol, Statins
- U.S. FDA Resources

Further study details as provided by Imperial College London:

Primary Outcome Measures:
- Adherence to medication; self-reported current use of antiplatelet, statin and combination (≥ 2) blood pressure lowering therapy [ Time Frame: End of trial follow-up ] [ Designated as safety issue: Yes ]
- Change in blood pressure [ Time Frame: End of trial follow-up ] [ Designated as safety issue: Yes ]
- Change in LDL cholesterol [ Time Frame: End of trial follow-up ] [ Designated as safety issue: Yes ]

Secondary Outcome Measures:
- Self reported current use of antiplatelet, statin and combination (>2) blood pressure lowering therapy [ Time Frame: 12 months ] [ Designated as safety issue: Yes ]
- Reasons for stopping cardiovascular medications [ Time Frame: Throughout trial ] [ Designated as safety issue: Yes ]
Eligibility Criteria:

- Serious adverse events [Time Frame: Throughout trial] [Designated as safety issue: Yes]
- New onset cardiovascular events [Time Frame: Throughout trial] [Designated as safety issue: Yes]
- Participant ‘Quality of Life’ assessment [Time Frame: At 12 months and end of trial] [Designated as safety issue: No]
- Changes in total cholesterol and other lipid fractions (HDL-cholesterol, triglycerides) [Time Frame: 12 months and end of trial] [Designated as safety issue: Yes]

Estimated Enrollment: 2000
Study Start Date: June 2010
Estimated Study Completion Date: January 2013
Estimated Primary Completion Date: June 2012 (Final data collection date for primary outcome measure)

<table>
<thead>
<tr>
<th>Arms</th>
<th>Assigned Interventions</th>
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</thead>
<tbody>
<tr>
<td>polypill: Experimental</td>
<td>Drug: polypill</td>
</tr>
<tr>
<td>Red Heart Pill Version 1 and Red Heart Pill Version 2.</td>
<td>The polypill will be taken once/day in the form of a hard capsule, to be taken orally. There are two versions of the polypill (Red Heart Pill): Version 1 contains aspirin 75mg, simvastatin 40mg, Lisinopril 10mg and Atenolol 50mg; Version 2 contains aspirin 75mg, simvastatin 40mg, Lisinopril 10mg and Hydrochlorothiazide 12.5mg.</td>
</tr>
<tr>
<td>Usual Care: Active Comparator</td>
<td>Drug: Usual cardiovascular medications</td>
</tr>
<tr>
<td>Participants in the usual care arm will take their usual cardiovascular medications. The participants will be seen as needed by their usual doctor between study visits.</td>
<td>Participants in the ‘Usual Care’ arm will continue to take the separate, individual medications prescribed by their usual doctor, e.g. aspirin, blood pressure lowering drugs, statins.</td>
</tr>
</tbody>
</table>

Detailed Description:

The UMPIRE trial has been modelled on similar trials running concurrently in Australia and New Zealand. The design is straight forward in making comparisons between cardiovascular preventative therapy delivered as a polypill (the Red Heart Pill) on the one hand, and as separate component multiple tablets (usual care) on the other hand. In both groups (the polypill group and the usual care group,) the GP or managing physician will be able to adjust or add additional medications as appropriate to meet the targets for control of blood pressure, cholesterol and other risk factors as directed by local or national guidelines. The Primary end-point - adherence to prescribed cardiovascular preventative medication at the end of the trial follow-up - will be evaluated by self reported use of anti-platelet, statin and blood pressure lowering therapy. This evaluation will be supported by the recording of blood pressure and cholesterol levels, and measuring the differences between the two groups at the end of the trial. Treatment allocation is open label - both investigator and subject will know which arm of the study they are on. Patients will be identified and recruited from GP surgeries or hospital clinics, and also via local advertisement. Recruitment into the study is planned to start in Summer 2010 with a 12 month recruitment phase. Recruited subjects will spend between 12 - 30 months (average 18 months) being followed up. The target study population is 1000 patients in European sites in London, Dublin and Utrecht; and 1000 subjects in India at approximately 30 sites. Subjects will be randomly allocated to receive either the “polypill” or “usual care”. If allocated to the polypill group, the study investigator will decide on the version of polypill to be prescribed, and adjust any current medications as necessary. If the subject is in the “usual care” group, they will be seen as needed by their usual doctor between study visits, and continue on their current medicines. Participants will have at least 5 study visits, but no more than 8 study visits, and these visits include registration, randomisation and follow-up visits at 1 month, 6 months, and 12 months, and depending on when the subject is recruited to the study, study visits at 18 and 24 months/end of trial visit.

Eligibility:

Ages Eligible for Study: 18 Years and older
Genders Eligible for Study: Both
Accepts Healthy Volunteers: No

Criteria:

Inclusion Criteria:

- Adults (≥ 18 years)
- The participant is able to give informed consent.
- Established athereothrombotic cardiovascular disease (CVD) or high cardiovascular risk, of for individuals without established cardiovascular disease, a calculated 5 year CVD risk of 15% or greater (calculated using the 1991 Anderson Framingham risk equation with adjustments as defined by the New Zealand Guidelines Group recommendations)
- The trial Investigator considers that each of the polypill components are indicated

Exclusion Criteria:

- 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 during the treatment period).
- 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)
- 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).
Contacts and Locations

Please refer to this study by its ClinicalTrials.gov identifier: NCT01057537

Contacts

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The George Institute for International Health India
Public Health Foundation of India
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No publications provided

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Last Updated: July 26, 2010
Health Authority: United Kingdom: Medicines and Healthcare products Regulatory Agency (MHRA); Ireland: Irish Medicines Board (IMB); The Netherlands: Dutch Healthcare Inspectorate (CCMO); India: Drugs Controller General, India (DCGI)

Keywords provided by Imperial College London:
- Polypill
- Red Heart Pill
- Cardiovascular disease
- Adherence
- Secondary prevention

Additional relevant MeSH terms:
- Cardiovascular Diseases

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