NIHR | Oxford Biomedical Research Centre

NIHR Oxford BRC Cardiovascular theme

Vision: Improved stratification of patients with acute and chronic cardiovascular disease (CVD) is crucial to target complex and costly interventional and pharmacological therapies to specific patient groups, whilst avoiding treatment risks and accelerating hospital discharge in others. We will take advantage of our unique bioresources, world-leading expertise in patient/population-based research, and state-of-the-art technologies to refine patient stratification for prognosis and for developing and targeting new therapies in the following 6 areas:

1) **Acute Coronary Syndromes**: *PI Banning, Channon, Choudhury, Ferreira, Kharbanda,*
Building on the excellence of the clinical services, we have established an acute MI cohort (OxAMI, target: 1000 patients) which provides the context for programmes of investigation in 4 areas:

- Identification/validation of novel markers for patient stratification (miRNA; monocyte transcriptomics, proteomics)
- Development and validation of imaging techniques, especially with MRI
- Clinical validation of point of care invasive physiological measures
- Optimising reperfusion therapies

2) **Acute Stroke**: *PI Kennedy, Harston*
Two major programmes of research result from this integrated clinical academic service:

- Define ischaemia-reperfusion injury post-thrombectomy using combined markers of perfusion and metabolism, to see how applicable the invasive measures of microcirculatory resistance developed for post-STEMI patients are in patients with acute ischaemic stroke
- Implement a measurement of post-stroke secondary injury due to oedema and/or haemorrhage in large clinical and trial cohorts following agreement with industry partners (negotiations under way) and academic colleagues (agreed) to transform patient care

3) **Aneurysmal subarachnoid haemorrhage (SAH)**: *PI Pattinson*
The aim of this programme is to develop and validate neuromarkers that better predict outcome and may eventually be used to guide therapy. The two main areas of research supported by the BRC are:

- Development of a bedside prognostic test based upon dynamically probing EEG responses with a brief infusion of intravenous sodium nitrite
- Establish role of the NO signalling pathway in the pathogenesis of early brain injury, through pharmacological manipulation of NO levels

4) **Atrial Fibrillation (AF) and Heart Failure (HF)**: *PI Betts, Bowman, Casadei, Collins, Hopewell, Jebb, Neubauer, Parish, Wijesurendra*
The overarching aim of this novel sub-theme is to improve risk stratification and deliver more efficacious, safer and cost-effective therapies in individuals with chronic acquired cardiovascular conditions (such as AF, stable ischaemic heart disease (IHD), and HF).

- Identify and test new causal risk factors and therapeutic targets for AF
- Refine stroke prediction in patients with AF by using brain, heart, body MRI and carotid U/S imaging and genetic scores in the UK Biobank imaging cohort
- Assess cost-effectiveness of mail-based screening for AF in individuals with high stroke risk identified in general practice (AMALFI RCT)
- Investigate the left atrial phenotype in patients with stroke using advanced MRI
- Test the impact of weight loss on AF burden/symptoms and physical performance in elderly patients with AF and obesity (LOSE-AF RCT)

5) **Valvular heart disease (VHD)**: *PI Myerson, Hobbs*
VHD is common but poorly researched. The OxBRC VHD sub-theme sets out to address neglected areas of clinical practice by identifying:

- The prevalence of valve disease
- Patients at risk
- Factors that may limit disease progression/reduce risk

6) **Hypertrophic Cardiomyopathy**: *PI Neubauer, Watkins*
The aim of this subtheme is to identify biomarkers underpinning heterogeneity in disease progression/complications and to test novel agents. These investigations will improve our understanding of disease pathogenesis and more accurately assess treatment response in individual patients. Based upon these insights, we are proposing to undertake Early-Phase Clinical Trials of re-purposed and novel, potentially disease-modifying, agents.