



# King's Health Partners

King's Health Partners brings together:

- three of the UK's leading NHS Foundation Trusts
- a world-leading university for health research and education
- nearly 4.8 million patient contacts each year
- 40,000 staff
- nearly 30,000 students
- a combined annual turnover of more than £3.7 billion
- services provided across central and south London and beyond, including nine mental health and physical healthcare hospitals and many community sites
- a comprehensive portfolio of high-quality clinical services with international recognition in cancer, diabetes, mental health, regenerative medicine, transplantation, cardiac and clinical neurosciences
- a major trauma centre and two hyper-acute stroke units

# About King's Health Partners

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King's Health Partners Academic Health Sciences Centre brings together one of the world's top research-led universities, King's College London, and three NHS Foundation Trusts – Guy's and St Thomas', King's College Hospital and South London and Maudsley.

Our partnership provides a powerful combination of complex clinical specialties that cover a wide range of physical and mental health conditions and a breadth of research expertise that spans disciplines from medicine and biomedical sciences to the social sciences and humanities.

There are three parts to our mission: excellence in research, education and clinical care. To support our mission, we are delivering programmes of work to:

- Join up mental and physical healthcare so that we treat the whole person, mind and body;
- Increase the value of the care we provide and the outcomes we achieve for our patients and service users;
- Integrate care across local primary, secondary and social care services to make it easier for people to get the care and support they need;
- Improve the public health of our local community by tackling inequalities and supporting people to live healthy lives;
- Bring together our collective strength and expertise in a range of specialist areas to deliver world-leading care, research and education;
- We are uniquely structured to deliver our mission for excellence. Our 22 Clinical Academic Groups bring together all the clinical services and staff from the three trusts with the relevant academic departments of King's College London.

# Foreword

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Since coming together in 2009, our partnership has sought to combine our collective strength to achieve excellence, and to improve health and well-being, locally and globally.

We are always looking for ways in which we can challenge ourselves to do more for our patients and service users, and to attract the best talent to work with us. We have also always said that our collective ambition is to be one of the top 10 academic healthcare organisations in the world. The significant public health challenges we face locally mean it is more important than ever before that we work in partnership to deliver high impact innovation, supported by the latest research and education, resulting in better outcomes for our patients in a more sustainable model of care.

Cardiovascular and respiratory diseases are some of the most profound and pressing health challenges we face. With much of the premature morbidity and mortality caused by these conditions being preventable or amenable to treatment.

To address this challenge, in 2017 we began working with Royal Brompton & Harefield NHS Foundation Trust on plans to revolutionise heart and lung research and care across London, the south of England, the rest of the UK and beyond.

We have an unrivalled opportunity to bring together our capabilities in a pioneering, globally significant new partnership to deliver the best outcomes and improve the health and wellbeing of up to 15 million children and adults.

King's Health Partners and Royal Brompton & Harefield NHS Foundation Trust are both leaders in respiratory and cardiovascular research and care. Each year our teams support thousands of patients of all ages with both rare and common heart and lung conditions. The breadth of our collaboration, coupled with our strength in mental and physical health and the rich diversity of the population we serve, mean we are uniquely placed to create a new model of care that delivers the right care, at the right time, in the right place.

This would be a UK first in terms of the scale of the partnership and the clinical, education and research benefits it could provide, rivalling the world's largest centres, and becoming the most advanced cardiovascular and respiratory health system in Europe.

We know that working in partnership and sharing our clinical academic expertise across organisational boundaries allows us to deliver better patient care and outcomes. We believe

that this partnership provides a real opportunity for us to rethink and transform how we deliver services and care that will impact on patients, carers, families and our population throughout their lifetimes.

A handwritten signature in black ink, appearing to read 'R Lechler', written in a cursive style.

**Professor Sir Robert Lechler**

Executive Director

# Foreword

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At King's Health Partners we are committed to improving outcomes for our patients and service users and achieving maximum value for money in everything we do. We believe that being open and transparent about the care and outcomes we deliver results in a culture of improvement across our partnership.

This is why we are publishing a series of outcomes books that will help patients, service users, carers, referring clinicians and commissioners to make better informed decisions, and our staff to drive up the quality of the care we provide. The books report key outcomes for treatments provided by our 22 Clinical Academic Groups. Clinical Academic Groups form the building blocks of our Academic Health Sciences Centre. By bringing together our clinical and academic staff across teaching, training and research, we can use their combined expertise to achieve better outcomes for our patients and service users.

Our books are designed for a clinical and lay audience and contain a summary of patient volumes and measures (e.g. length of stay, re-admissions, patient experience), clinical outcomes, educational activities, technological and research innovations and publications.

They also focus on other important measures, such as staff satisfaction and wellbeing. The primary purpose of King's Health Partners is to improve health and wellbeing locally and globally. We must deliver this goal in a challenging economic environment with rising demand for, and costs of, healthcare. We will only achieve sustainable health improvement if we strive always to increase value. We define value in terms of outcomes that matter to patients, over the full cycle of care, divided by the cost of producing those outcomes. By publishing outcomes books, we have more information to support us measuring the value of the healthcare we provide.

We hope you find these data valuable. Please send comments and suggestions to us at [kingshealthpartners@kcl.ac.uk](mailto:kingshealthpartners@kcl.ac.uk).

For more information please visit our website at [www.kingshealthpartners.org](http://www.kingshealthpartners.org).

A handwritten signature in black ink that reads "John Moxham". The signature is fluid and cursive.

**Professor John Moxham**

Director of Value Based Healthcare, May 2019

# Cardiovascular foreword

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The King's Health Partners Cardiovascular Clinical Academic Group integrates the adult cardiology, cardiac surgery and vascular surgery teams at Guy's and St Thomas' and King's College Hospital NHS Foundation Trusts with the academic groupings of the School of Cardiovascular Medicine & Sciences of King's College London.

We provide specialist cardiovascular services to an extensive population network spanning south east London and Kent, and in some specialities even further afield, in partnership with other local and regional providers. Our services encompass a comprehensive range of sub-specialities including leading-edge programmes in percutaneous and minimally invasive heart valve replacement, emergency services for heart attack, complex electrophysiology, heart failure, inherited heart disease, endovascular interventions and complex imaging. We are pioneering novel integrated patient care pathways both locally (e.g. in heart failure) and regionally (e.g. in vascular surgery), with the aim to enhance overall quality of care, outcomes, value and sustainability of services. There is also a focus on addressing mental and physical well-being in a holistic fashion.

The Cardiovascular Clinical Academic Group has substantial academic strengths that are anchored in our British Heart Foundation Centre of Research Excellence – now in its eleventh year as the highest-funded UK British Heart Foundation Centre – and in the research pursued in the cardiovascular theme of the National Institute for Health Research Biomedical Research Centre at Guy's and St Thomas' NHS Foundation Trust and King's College London. Research highlights include world-leading work in heart failure, biomarkers and imaging from bench to bedside, which is underpinned by outstanding infrastructure and by collaborations with other foci of excellence at King's Health Partners, such as Biomedical Engineering and Imaging Sciences. In education, there are an extensive and distinctive range of postgraduate research training programmes for clinicians and non-clinical scientists; clinical training programmes in cardiology, cardiac surgery, vascular surgery and clinical pharmacology; and a significant contribution to undergraduate programmes in medicine, bioscience, nursing and other allied health professions.

Based on the above strengths and the compelling need to address the high burden of cardiovascular disease and the heterogeneity of service provision in our population network, the Cardiovascular

Clinical Academic Group is developing **King's Health Partners Cardiovascular** to transform service delivery and generate research advances to revolutionise cardiovascular prevention and care. Very recently, the scope of this development has expanded significantly through a partnership between King's Health Partners and Royal Brompton & Harefield NHS Foundation Trust, which will potentially involve the integration of Royal Brompton Hospital services with King's Health Partners.

Our aims are to:

- Deliver the best **patient experience** and **clinical outcomes** across a comprehensive range of high quality specialised cardiovascular services, addressing both **'mind and body'**;
- Create an **innovative population network** of care, **setting standards** for what defines **'best practice'** in cardiovascular prevention and care;
- Be **global leaders in research and innovation** to advance the prevention, early diagnosis and treatment of cardiovascular disease, through **ground-breaking studies** and a **Medtech hub**;
- Be a beacon centre delivering **outstanding education and training programmes**;
- Maximise commercial opportunities for King's Health Partners and the local economy and **ensure financial sustainability** of the services;
- Be the **centre of choice in Europe** for cardiovascular patients, staff, trainees and students.



**Professor Ajay Shah**

King's Health Partners Cardiovascular Lead, May 2019

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# The value of partnership at King's Health Partners

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King's Health Partners aims to create a centre where world-class research, education and clinical practice (the 'tripartite mission') are brought together for the benefit of patients.

We want to make sure that the lessons from research and innovation are used swiftly, effectively and systematically to achieve better patient outcomes, improve public health and join up health and care services for people with physical and mental health problems.

By working together in this way, integrating care across different organisations and sectors, we can not only improve the health of the people we care for, but we can also achieve better value for money.

## Integrating mental and physical health

The mind and body are inseparable, and mental and physical health conditions are often connected. Mental health illness can have a significant negative impact on physical health. Likewise, many people with long-term physical health conditions and progressive illnesses suffer from depression or other mental health conditions. Despite this, many health services separate care into physical and mental and often fail to share patient information. At King's Health Partners we are working to overcome these barriers by treating the whole person, through our Mind & Body Programme and across all of our CAGs. We are committed to caring for vulnerable patients with both physical and mental ill health in an integrated manner with better, faster diagnosis and treatment because we know that addressing mental distress improves physical health outcomes and vice versa.



**Nearly  
half**

of people with mental illness also have at least one long-term physical condition



**30%**

of people with long-term physical health conditions also have a mental illness



**15-20  
years**

shorter life expectancy for someone with a severe mental illness or learning disability than for those without



**£8bn**

a year is spent by the NHS treating the effect of poor mental health on physical illnesses

Across all King's Health Partners, we will treat the whole person by:

- Screening all patients with chronic physical diseases for mental health conditions, and using the learning from this to improve the care we provide;
- Improving our understanding of the physical health needs of people with severe mental ill health;
- Addressing the traditional distinctions between the mind and body in research and education allowing us to train students and staff to deliver more integrated care;
- Better organising and expanding current training provision for physical and psychiatric comorbidity;
- Working with our local commissioners to find new ways of paying for integrated services;
- Linking IT systems across our partner trusts so that clinicians have access to a person's physical and mental care records;
- Investing in innovative programmes such as IMPARTS (Integrated Mental and Physical Healthcare: Research, Training and Services) and 3DLC (3 Dimensions of care for Long Term Conditions);
- Recognising the importance of employee mental and physical health and wellbeing.

## Public health

Public health is one of our biggest challenges. At the root of much of the ill health in south London is a high incidence of smoking, alcohol abuse and obesity. With our health and social care partners, we are developing strategies to tackle these public health priorities. We are also developing plans for a new Institute for Population Health, a collaboration with local partners to bring about transformational change to health in local communities. We want to achieve a measurable improvement and impact on health gain and local management of physical and mental health problems through new evidence-based interventions, particularly supported by our strategies relating to alcohol and tobacco.

## Alcohol strategy – key aims

- Developing appropriate resources for clinical staff and patients;
- Developing and implementing training for all staff on harmful drinking supporting early identification and intervention;
- Establishing ourselves as a centre of excellence for integrated research, training and practice in the management and prevention of alcohol misuse;
- Attracting funding for future alcohol clinical, training and research initiatives;
- Monitoring the impact of the strategy on indicators of alcohol related harm;

- Embed in-reach alcohol teams in our hospitals to identify and support patients who misuse alcohol.

### Tobacco strategy – key aims

- Supporting all clinical sites to be smoke-free;
- Developing an informatics structure for routinely and systematically recording smoking status;
- Support, referrals and treatment uptake for smoking cessation across the partnership;
- Co-producing clinical care pathway for nicotine dependence treatment;
- Developing and implementing training packages for smoking cessation interventions for all our healthcare professionals;
- Monitoring the impact of our smoking cessation strategy in relation to knowledge and uptake of skills by staff, uptake of smoking interventions, outcomes of interventions, user satisfaction, prevalence of smoking, cost-effectiveness of interventions;
- Implement the Ottawa model of smoking cessation across our Trusts.

### The Vital 5

*Addressing the front end of the complete pathway of care*

**Overall aim:** Improve the population's health and reduce health inequalities by focusing on the Vital 5 to support prevention, detection, health promotion, management and treatment wherever there is an opportunity to do so.

Vital 5	Aim
Blood pressure	To reduce stroke and heart attack, and improve wellbeing.
Obesity	To reduce diabetes, renal dialysis, liver transplants, amputations and other comorbidities, and improve wellbeing.
Mental health score	To reduce the burden of mental illness, improve physical health, recovery and wellbeing.
Alcohol intake	To reduce liver transplants and malignant disease, and to improve wellbeing.
Smoking habits	To reduce respiratory and malignant disease, and improve wellbeing.

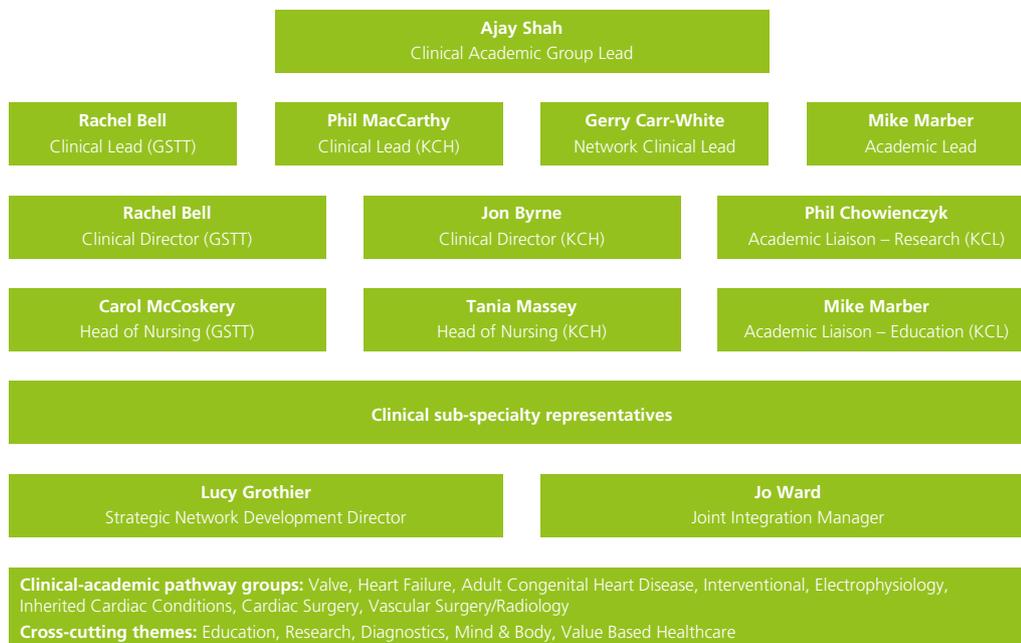
Standardised routine recording, sharing and clinical management of these five measures for all our patients would greatly improve care and outcomes.

## Informatics

Informatics is at the heart of our plans to join up care, research and education. Data is one of our most important assets at King's Health Partners. We are proud of our ability to control information systems for the purpose of data creation, curation and analysis with strong and transparent information governance processes throughout. This control enables our exploration of the relationship between clinical and biological data, extending at one end to clinical decision support embedded in electronic medical records (EMRs), sharing of clinical data to enhance care and outcomes, through to research recruitment and participation, with strong patient engagement throughout. We have developed a clear strategy and action plan to maintain and develop leadership in the field of informatics.

Systems have been developed to enable electronic healthcare records to be shared across our partner organisations and with other healthcare organisations. Our work includes the award-winning 'HealthLocker' programme, the Clinical Record Interactive Search (CRIS) and King's Health Partners Online. We are working with patients to make electronic patient information available in an anonymised format between partner trusts, primary care and social care. Together we have a powerful information resource for both practitioners and researchers.

# King's Health Partners Cardiovascular leadership structure



# Introduction to our clinical service pathways

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King's Health Partner's Cardiovascular provides a comprehensive range of services through multi-disciplinary pathways for the following presentations:

- Chest pain and heart attack;
- Breathlessness;
- Palpitations and heart rhythm disturbance;
- Murmurs and heart valve disorders;
- Hypertension and cardiovascular risk;
- Inherited cardiovascular conditions;
- Vascular conditions such as aneurysm, limb ischaemia, claudication, venous ulcers, TIA.

The services that are provided encompass the following:

- Imaging and diagnostics;
- Interventional cardiology including a heart attack service;
- Cardiac surgery;
- Vascular surgery;
- Electrophysiology;
- Structural heart disease;
- Heart failure and inherited disease;
- Adult congenital heart disease;
- Hypertension and vascular risk.

Most of the complex in-patient services are provided at both of our two main specialist sites, i.e. King's College Hospital and St Thomas' Hospital. In the subsequent sections of this report, we make comparisons with other large UK units and with the Cleveland Clinic, which has been the leading unit in the USA for over 15 years.



Imaging and diagnostics

# Imaging and diagnostics

## Description of service

Cardiovascular imaging and diagnostics are essential in the management of patients with suspected or established cardiovascular disease.

We have among the largest units in Europe, with the cutting-edge clinical service continually benefiting from in-house research advances. Clinical services include:

- **Echocardiography:** 3D transthoracic echo, stress imaging, transoesophageal echo, peri-operative echo;
- **Cardiac magnetic resonance imaging (CMR):** including complex perfusion imaging and tissue characterisation;
- **Computed tomography (CT):** including CT calcium score and angiography;
- **Electrocardiogram (ECG):** including exercise and ambulatory ECG;
- **Cardiopulmonary exercise testing.**

Many of the simpler investigations are open access from primary care.

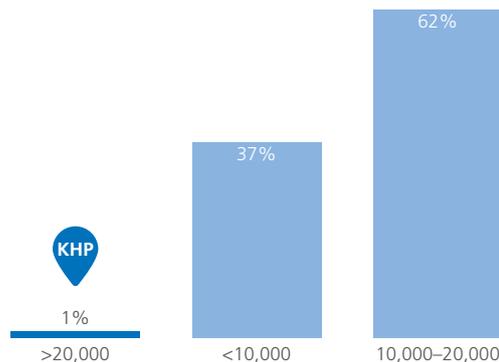
We provide accredited training in Echo, CMR and CT for physicians.

## Volumes and outcomes

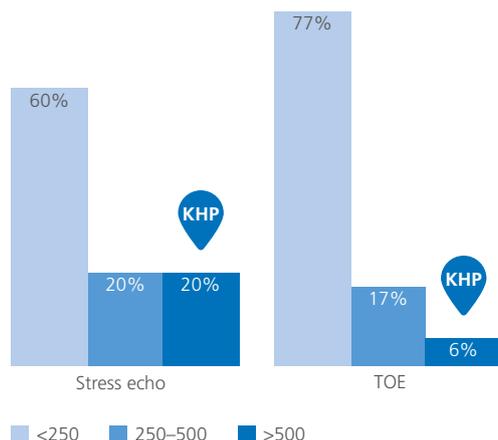
### Echocardiography

The service is accredited for advanced level transthoracic echo, transoesophageal echo, stress echo and training both by the British Society of Echocardiography (BSE) and the European Association of Cardiovascular Imaging.

**Figure 1 |** Echocardiograms performed in UK cardiology departments, by percentage (King's Health Partners is in the top 1% of UK centres performing the most transthoracic echocardiograms)



**Figure 2 |** Stress echo and transoesophageal echo (TOE) procedures performed in UK cardiology departments, by percentage (King's Health Partners is one of the few departments in the UK performing >500 stress echo and >500 TOE per year)



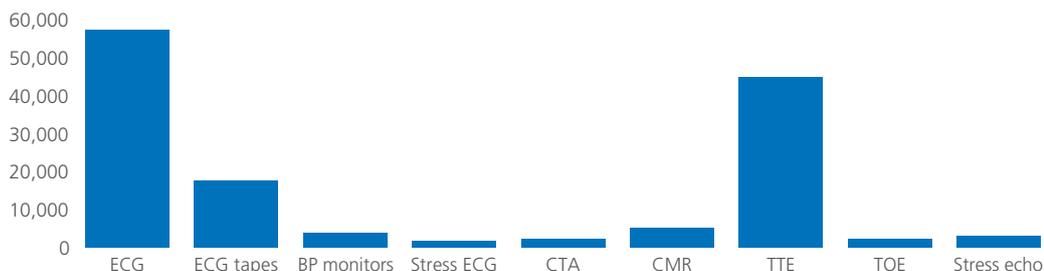
## CMR

The CMR service has grown substantially over the last 5 years and in 2017 provided >7,000 scans across Guy's and St Thomas' NHS Foundation Trust and King's College Hospital NHS Foundation Trust, of which >30% included a stress protocol. There are four state-of-the-art cardiac scanners, including two wide bore magnets for claustrophobic and overweight patients and a smaller bore high-field (3T) magnet.

## Cardiac CT

The cardiac CT service is jointly provided between cardiology and radiology and is currently equipped with four cardiac capable CT scanners. These include two top of the range Siemens Somatom Force dual source scanners. In 2017, the total number of scans was >2,000.

**Figure 3 |** Number of diagnostic procedure types and numbers performed throughout King's Health Partners in 2016



ECG: electrocardiogram; BP: Blood pressure; CTA: Computer tomography angiogram; CMR: Cardiac magnetic resonance imaging; TTE: Transthoracic echocardiography; TOE: Transoesophageal echo.

## Research and innovation

### Echo

There are a wide range of research interests which include:

- **Structural heart disease:** development of new methodologies such as 3D printing and modelling to accurately size the aortic annulus for Transcatheter aortic valve implantation valves, trans-nasal transoesophageal echocardiography to guide structural interventions performed under conscious sedation, imaging for Transcatheter aortic valve implantation under conscious sedation versus general anaesthetic.
- **3D echo:** new methodology for 3D rendering with a moveable light source to reveal anatomical details not seen with conventional 3D imaging, quantification of right ventricular dimensions and function.
- **Collaborations with major industry partners.**

### Cardiovascular magnetic resonance

Clinical Cardiovascular Magnetic Resonance research benefits from extensive interaction with the School of Biomedical Engineering and Imaging Sciences at King's College London, which has one of the largest imaging sciences groups in the world – including physicists, engineers and other technical experts ([www.kcl.ac.uk/lsm/research/divisions/imaging/index.aspx](http://www.kcl.ac.uk/lsm/research/divisions/imaging/index.aspx)). Examples of significant advances that are benefiting patient care include combined MRI and cardiac catheterisation (XMR), which is being used in electrophysiological procedures; advanced myocardial perfusion imaging; and new diagnostic modalities.

### Cardiac computed tomography

There are numerous active collaborations with industry and involvement in major clinical trials. A particular area of research focus is the application of computed tomography for planning advanced pacing, electrophysiology and structural intervention which won the Society of Cardiovascular CT "Innovations in CT Award" in 2017.

## Echo in Africa

### *Screening for childhood heart disease in South Africa*

Childhood rheumatic fever has virtually disappeared in the industrialised world but remains prevalent in under-developed countries. Recurrent episodes cause progressive damage to heart valves, with 500,000 new cases and 250,000 deaths from rheumatic heart disease each year across the world. The early detection of heart disease in childhood allows long term treatment with antibiotics to prevent recurrent infection – a simple intervention that is limited by the lack of screening programmes.

The King's Health Partners echo team led by Professor Mark Monaghan has led the "Echo in Africa" project in partnership with the British Society of Echocardiography and South African Cardiologists at Tygerberg Hospital in Cape Town, screening children in the Townships by echocardiography for early signs of the disease. Last year, nearly 1,300 children were screened and almost 100 of these have required follow-up. The success of the project has attracted volunteers from many other UK units as well as the US and Australia. In addition to the humanitarian aspect, the team are undertaking an academic analysis of the programme to inform a broader screening strategy.





Interventional cardiology

RUN	
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#004	LAO 54 CAU 24 F DA
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#006	LAO 1 CRA 32 F DA
#007	LAO 20 CRA 32 F DA

# Interventional cardiology

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## Description of the service

Interventional cardiology involves the diagnosis of cardiac disorders by cardiac catheterisation and coronary angiography and the treatment of coronary artery disease by percutaneous coronary intervention (PCI). PCI involves balloon angioplasty followed by implantation of intracoronary stents. This is performed either in the elective setting for the relief of angina or in urgent and emergency situations for the treatment of heart attacks and cardiogenic shock.

The King's Health Partners interventional cardiology service includes:

- A high rate of radial compared to femoral access (>80%) which means earlier mobilisation of patients after the procedure, a high rate of day-case procedures, and a lower risk of bleeding complications;
- The use of state-of-the-art adjunctive diagnostic devices beyond simple angiography that provide valuable information to guide management – such as intracoronary pressure and flow, intravascular ultrasound (IVUS) and optical coherence tomography (OCT);
- An exemplar 24/7 acute heart attack service that was the first such service to be established in the UK, working in close liaison with the London Ambulance Service;
- An urgent service for acute coronary syndromes (non-ST segment elevation heart attacks) involving patient transfer from numerous district hospitals;
- A 24/7 service for the management of cardiogenic shock and cardiac arrest survivors;
- The use of adjunctive treatment modalities such as rotational atherectomy, embolic protection devices, intracoronary lithotripsy, intra-aortic balloon pumps, percutaneous LV support devices and extracorporeal membrane oxygenation (ECMO).

## Volumes and outcomes

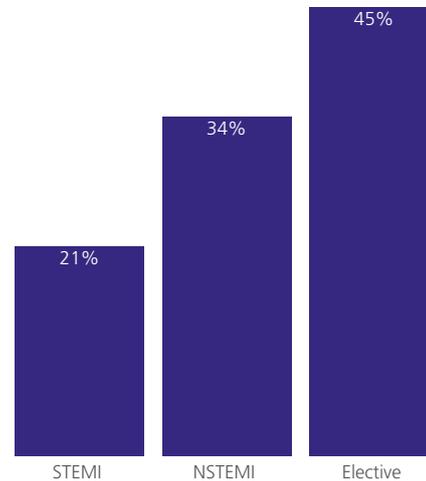
In 2016, the King's Health Partners intervention team performed 2,435 percutaneous coronary intervention (PCI) cases across two sites, placing King's Health Partners as one of the busiest UK interventional units.

**Risk adjusted rates for Major Adverse Cardiac and Cerebral complications (MACCE) show excellent outcomes for PCI at King's Health Partners sites.**

**Figure 4** | Numbers of PCI procedures in the highest-volume UK centres (data from the Cleveland Clinic, USA are also shown)



**Figure 5** | Proportion of PCI cases that are ST-segment elevation (STEMI) heart attacks, non-ST elevation heart attacks (NSTEMI), or elective



## Research and innovation

There is a wide range of research underpinning the clinical service, with particular emphasis on translating new advances into clinical practice.

### Coronary physiology

Coronary angiography provides merely images of the lumen of coronary arteries and is an imperfect method to guide patient management. King's Health Partners undertakes internationally-leading research in the quantitative evaluation of the functional significance of coronary narrowing or patient symptoms. Areas of focus include:

- Using intracoronary pressure and flow measurements (and MRI) to evaluate the large proportion of patients with angina who do not have obvious coronary disease on angiography. Many of these patients may have dysfunction of coronary microvessels that cannot be visualised on angiography;
- Analysing how circulatory support (e.g. with LV assist devices) affects coronary perfusion and the interplay with heart contractility.<sup>1</sup>

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1 Coronary and microvascular physiology during intra-aortic balloon counterpulsation. De Silva K, Lumley M, Kailey B, Alastruey J, Guilcher A, Assress KN, Plein S, Marber M, Redwood S, Perera D. *Journal of the American College of Cardiology Cardiovascular Interventions* 2014;7(6):631–640.

## Clinical trials

Changing clinical practice beyond a single institution requires well-conducted clinical trials. Examples of major studies led by King's Health Partners include:

- **MR-INFORM.** A large multi-centre randomised study that evaluated an MRI-guided versus an invasive approach for the management of patients with stable coronary disease (accepted for publication in the *New England Journal of Medicine*);
- **REVIVED (REVascularisation for Ischaemic Ventricular Dysfunction).** A National Institute for Health Research funded multi-centre randomised trial of Percutaneous Coronary Intervention versus medical treatment for patients with heart failure due to coronary disease;<sup>2</sup>

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2 Percutaneous Revascularization for Ischemic Ventricular Dysfunction: Rationale and Design of the REVIVED-BCIS2 Trial: Percutaneous Coronary Intervention for Ischemic Cardiomyopathy. Perera D, Clayton T, Petrie MC, Greenwood JP, O'Kane PD, Evans R, Sculpher M, Mcdonagh T, Gershlick A, de Belder M, Redwood S, Carr-White G & Marber M. *Journal of the American College of Cardiology Heart Failure* 2018;6(6):517–526.

- **ARREST (A Randomised tRIal of Expedited transfer to a cardiac arrest centre for non-ST elevation out of hospital cardiac arrest).** A pan-London study evaluating two treatment approaches for patients who have been resuscitated out-of-hospital after a cardiac arrest and brought to a regional Heart Attack Centre.<sup>3</sup>

In addition, King's Health Partners is currently recruiting to FAME 3 – a multicentre trial comparing physiology-guided angioplasty/stenting vs angiographically-guided coronary bypass surgery.<sup>4</sup> This trial builds on the practice-changing FAME and FAME 2 trials, both of which King's Health Partners recruited to significantly and both of which were published in the New England Journal of Medicine.

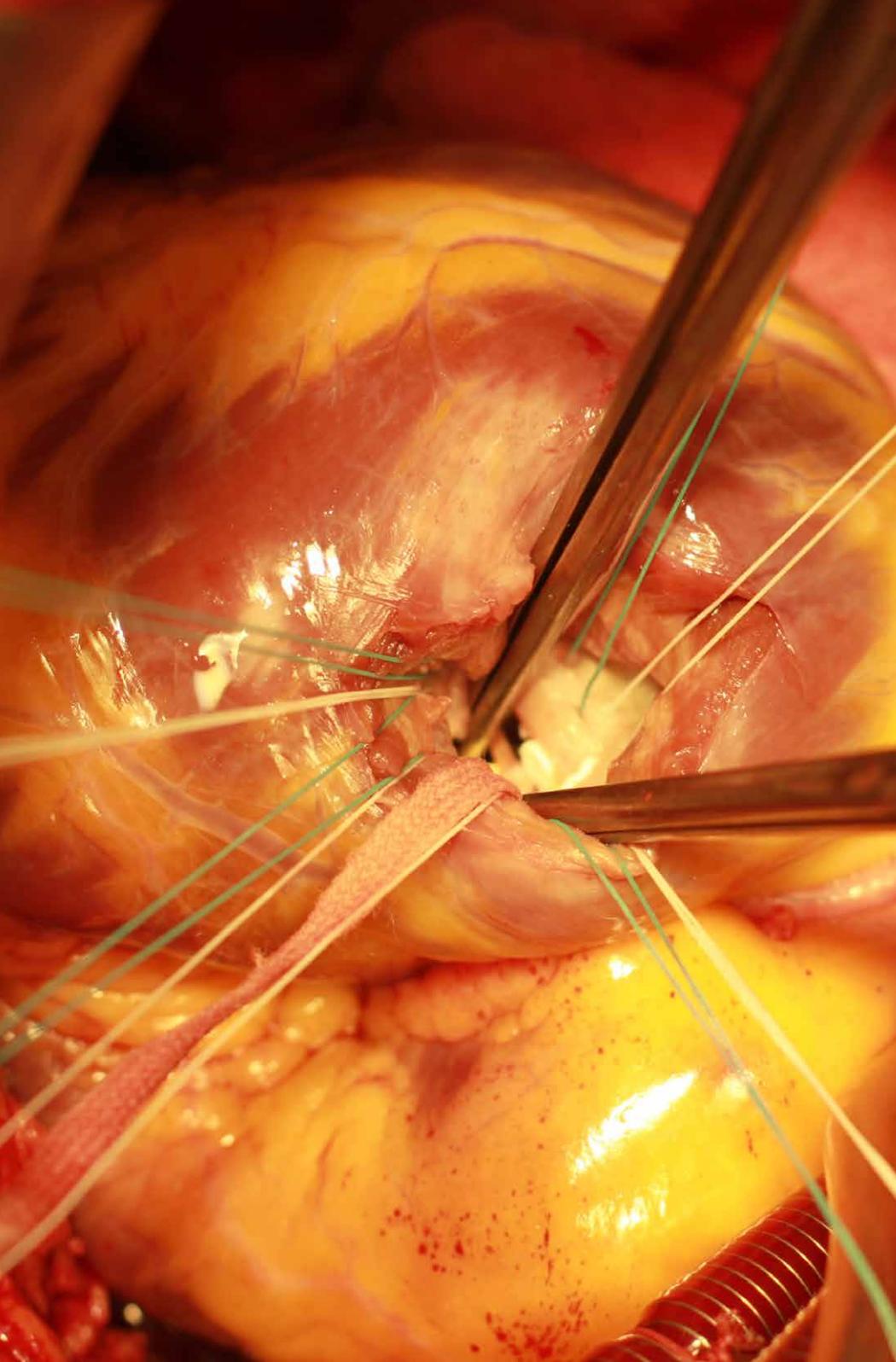
3 Rationale and design of: A Randomized tRIal of Expedited transfer to a cardiac arrest centre for non-ST elevation out-of-hospital cardiac arrest: The ARREST randomized controlled trial. Patterson T, Perkins A, Perkins GD, Clayton T, Evans R, Nguyen H, Wilson K, Whitbread M, Hughes J, Fothergill RT, Nevett J, Mosweu I, McCrone P, Dalby M, Rakhit R, MacCarthy P, Perera D, Nolan JP, Redwood SR. *American Heart Journal* 2018; 204:92–101.

4 Rationale and design of the Fractional Flow Reserve versus Angiography for Multivessel Evaluation (FAME) 3 Trial: a comparison of fractional flow reserve-guided percutaneous coronary intervention and coronary artery bypass graft surgery in patients with multivessel coronary artery disease. Zimmerman EM, De Bruyne B, Pijls NH, Desai M, Oldroyd KG, Park SJ, Reardon MJ, Wendler O, Woo J, Yeung AC, Fearon WF. *American Heart Journal* 2015;170(4):619–626.



Heart failure has a 1-year mortality of up to 25% and affects more than half a million people

in the UK. The commonest cause is coronary artery disease, which either results in heart attacks and subsequent irreversible scarring of the heart or causes parts of the heart muscle to enter a low-functioning adaptive state called hibernation, which is potentially reversible. We do not know the best way to deal with hibernation. Some evidence suggests that coronary artery bypass surgery (CABG) to restore full blood flow may improve survival in the long-term but the operation itself carries significant risk of death and major complications in patients with heart failure. The alternatives would be to treat patients with medication or to restore coronary blood flow by angioplasty/stenting. Angioplasty is a very effective treatment for angina but we do not know its value in heart failure patients with hibernation. The REVIVED trial (REVascularisation for Ischaemic VENTricular Dysfunction) led from King's Health Partners is the first randomised clinical trial to evaluate the benefit of angioplasty compared to current best medical therapy alone in patients with severe heart failure and hibernation. It is funded by a National Institute for Health Research grant and is being conducted across 35 UK cardiac centres, aiming to enrol 700 patients in total by April 2020. We are currently over halfway through the trial which is expected to have a major impact on how clinicians manage patients with heart failure around the world.



Cardiothoracic surgery

# Cardiothoracic surgery

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## Description of the service

King's Health Partners delivers a comprehensive range of open-heart and minimally invasive cardiac surgery services for a large catchment population across south east London and Kent. Close links with Evelina London Children's Hospital means that cardiac surgery is provided for all ages, from neonates to the extremely elderly. Multi-disciplinary team meetings (MDT) that include cardiologists and other specialities are part of the management of all complex patients. Procedures that are provided include:

- Coronary artery bypass grafting (CABG), conventional and complete arterial, either with cardiopulmonary bypass, on the beating heart or through endoscopic access;
- Heart valve repair or replacement by open-chest surgery or minimally invasive approaches, including port access mitral valve surgery;
- Transcatheter valve replacement (see page 54);

- Specialist thoracic aortic surgery including emergency treatment for acute aortic syndromes;
- Adult congenital cardiac surgery;
- Complex cardiac surgery including repeat cardiac operations, concomitant cardiac and non-cardiac surgeries;
- Surgery for rare conditions such as carcinoid heart valve disease and septal muscular hypertrophy.

## Volumes and outcomes

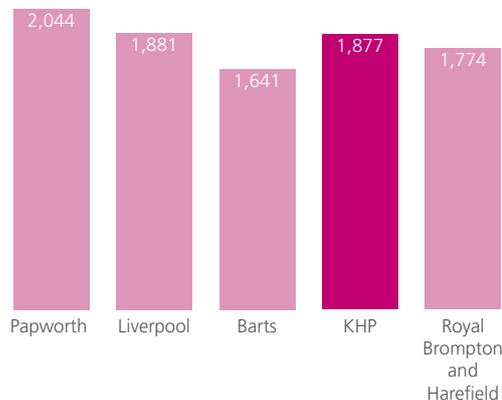
The Society for Cardiothoracic Surgery in Great Britain & Ireland (SCTS) collects outcome data on all patients over the age of 18 who undergo major cardiac surgery, which is analysed by the National Institute for Cardiovascular Outcomes (NICOR). Survival rates are risk adjusted. However, some types of patients and operations are excluded from this analysis as their

risk profile does not fit into the NICOR risk model (see [scts.org/patients/understanding-the-graphs](http://scts.org/patients/understanding-the-graphs)), so that the actual number of operations performed is higher than the published NICOR figures. The most recent figures cover the period 1st April 2014 to 31st March 2016. The total published King's Health Partners caseload for this period is 5,390 and is in the top 5 in the UK in terms of volume. The total caseload including those procedures that are not nationally analysed was 5,813.

The survival rates for the five largest units are very tightly grouped, with no significant differences among units. Overall mortality at King's Health Partners has steadily fallen over the last five years from 3.47% to 1.94% in 2016–2017.

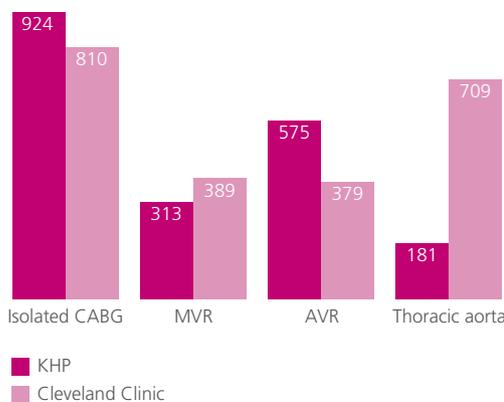
The main surgical procedures that were performed at King's Health Partners are shown in Figure 7. Aortic valve surgery accounts for about 30% of our surgeries, separate from aorto-vascular work such as aortic root replacement. Mitral valve surgery accounts for around 16% of surgeries.

**Figure 6 |** Cardiothoracic procedures performed by UK centres in 2015



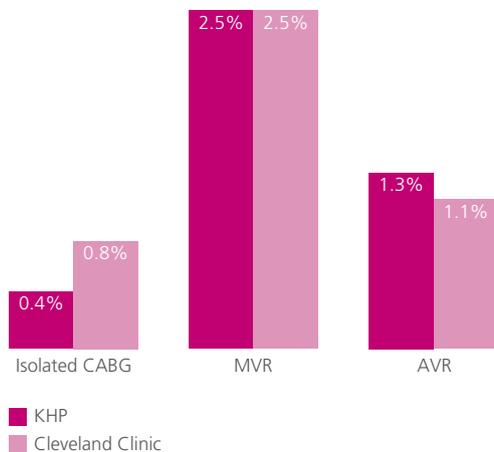
Source: SCTS blue book.

**Figure 7 |** Distribution of Cardiothoracic Cases, King's Health Partners 2016/2017 with figures from Cleveland Clinic, USA (2016) for comparison



Source: Local Audit data.

**Figure 8 |** King's Health Partners mortality rates for surgical procedures, with Cleveland clinic data (2017) used as comparison



Source: Local audit data. These data do not take into account risk-adjusted predicted mortality. Also note that the King's Health Partners data is for 30-day mortality and Cleveland data is in-hospital (these data are representative data only and not designed for direct comparison).

average of approximately 10%. Newer heart valve substitutes such as the sutureless tissue aortic valve are commonly used. The latest tissue valve to be introduced potentially offers a major increase in durability and King's Health Partners was the first centre worldwide to implant this valve.

In elective patients with bicuspid aortic valves who undergo aortic valve surgery, the aortic root is replaced according to guidelines and in these patients very low mortality has been observed.

### Mitral valve

Repair of the mitral valve results in a better long-term outcome for patients than valve replacement. King's Health Partners mitral surgery is performed by dedicated mitral valve teams which function within an MDT context.

An endoscopic "mini-mitral" valve programme has been recently established at King's Health Partners, with excellent outcomes.

## Research and innovation

Constant innovation is a feature of all aspects of the King's Health Partners cardiac surgical service.

### Aortic valve surgery

Nearly 50% of isolated aortic valves (i.e. without CABG) are replaced via a minimally invasive keyhole approach, compared with the UK

**Since its inception in 2012, a total of 168 endomitral procedures have been performed. In degenerate mitral valve disease, the repair rate is 94%. Overall, mortality is 1.3% and the rate of conversion to open surgery is 1.2%.**

## Aortic vascular surgery

The combination of a high volume cardiothoracic aortic vascular practice and a very large vascular surgical unit has allowed the development of a highly expert team able to deliver all aspects of aortic surgery – from personalised external aortic root support to replacement of the entire thoracic and abdominal aorta. The team also includes adult congenital aortic vascular and genetics expertise. King's Health Partners was the first centre in the UK to offer a dedicated 24/7 specialist rota for acute thoracic aortic vascular emergencies (see page 30).

## Specialised carcinoid heart valve disease service

**King's Health Partners attracts larger numbers of patients with carcinoid disease. We have established a novel multidisciplinary approach to the treatment of these patients and published the lowest in-hospital mortality ever reported (0%).<sup>5</sup>**

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<sup>5</sup> Optimized Outcomes Using a Standardized Approach for the Treatment of Patients with Carcinoid Heart Disease. Silaschi M, Barr J, Chaubey S, Nicou N, Srirajaskanthan R, Byrne J, Ramage J, MacCarthy P, Wendler O. *Neuroendocrinology* 2017;104(3):257–263.

## King's Health Partners acute thoracic aortic dissection service

Following recommendations from the London Cardiac Surgery Review Group, King's Health Partners implemented a 24/7 emergency service for patients with Acute Thoracic Aortic Dissection, which is staffed exclusively by cardiac surgeons specialising in aortic surgery.

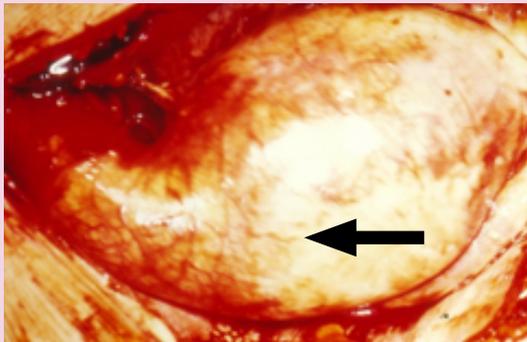
**This has led to an improvement in mortality for this catastrophic and life-threatening cardiac surgical emergency, to 11.5% (compared to a UK average of 23.1% in the last national level audit).**

In comparison, the Cleveland Clinic performed 183 emergency repairs of ascending aorta/aortic arch (including aortic dissections and ruptures) in 2016, with an in-hospital mortality of 6.5%.

Based on the King's Health Partners work, there are now plans to roll out such a service nationally. The Getting It Right First Time Programme National Specialty Report for Cardiothoracic surgery states that "there should be networks of surgeons crossing traditional geographical boundaries so that patients presenting with difficult or unusual problems could be discussed and, if need be, moved to a unit or surgeon with a particular expertise".

**The *Getting It Right First Time* report highlights King's Health Partners as a 'good practice case study' in aortovascular surgery.**

**Figure 9 |** Operative photograph from a patient undergoing surgery for an aortic dissection



The arrow points to the aneurysmal aorta within which the dissection is contained.



Vascular surgery

# Vascular surgery

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## Description of the service

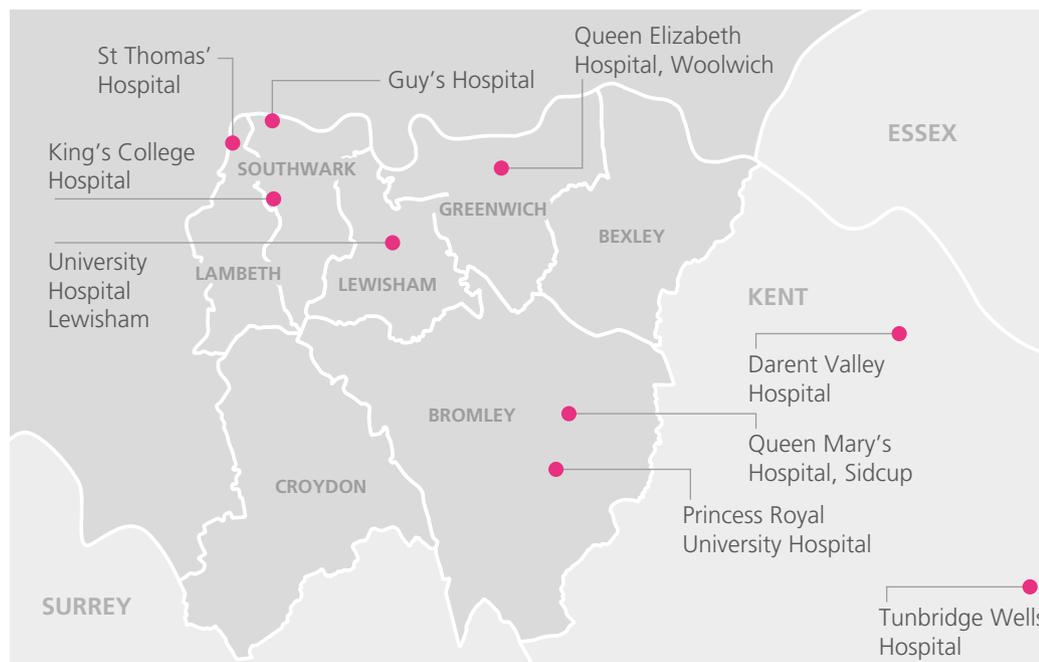
The King's Health Partners vascular service is a national tertiary referral service providing emergency and elective services to patients living in south east London and west Kent. Our 'network' hospitals are:

- Guy's and St Thomas' Hospitals;
- King's College Hospital and Princess Royal University Hospital;
- Lewisham Hospital and Queen Elizabeth Hospital, Woolwich;
- Darent Valley Hospital and Queen Mary's Hospital, Sidcup;
- Tunbridge Wells Hospital.

The vascular surgical service aims to evaluate, diagnose and treat conditions of the blood vessels (arteries, veins and lymphatics). It comprises a large multi-disciplinary team of specialist surgeons, radiologists, physicians, podiatrists, clinical scientists and nurses and covers the following conditions:

- Complex aortic disease, including endovascular and open surgery for aneurysms and aortic dissection;
- Diabetic patients with vascular disease. Diabetes services in our network hospitals are supported through the diabetic foot network;
- Management of deep venous disease;
- Complex vascular access for haemodialysis.

**Figure 10** | Geographical location of hospitals in the Vascular Network

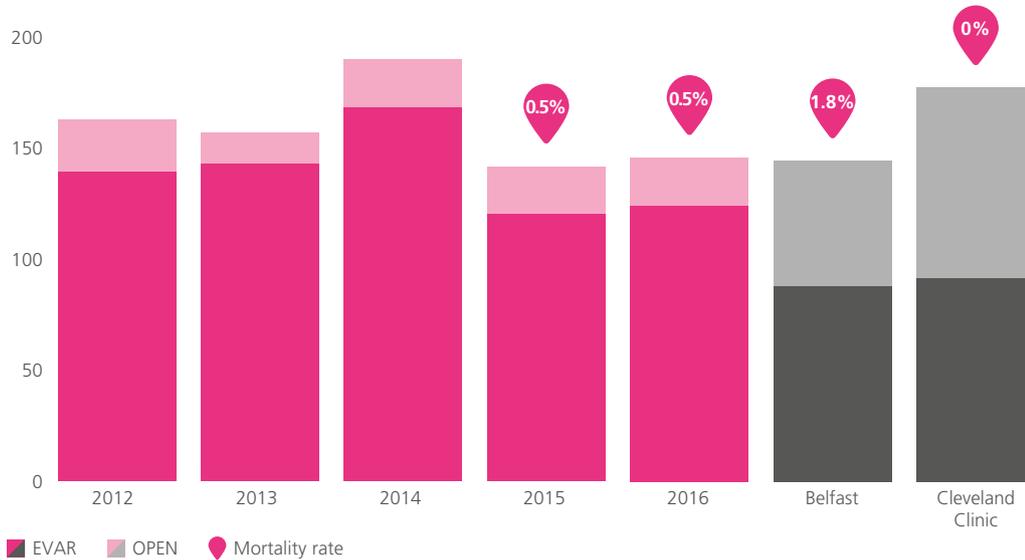


## Volumes and outcomes

### Elective Infrarenal Abdominal Aortic Aneurysm (AAA) repair

King's Health Partners is a high-volume centre for aortic surgery. Elective AAA repair is performed predominantly by a minimally invasive endovascular route (EVAR) rather than open surgery, with very low mortality.

**Figure 11** | Number of cases of infrarenal AAA repair from 2012 to 2016 at King's Health Partners, compared to the largest UK centre (Belfast) and the Cleveland Clinic, USA

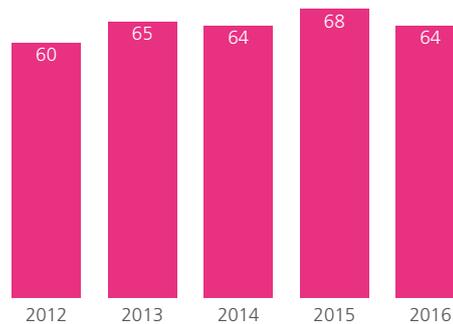


### Emergency AAA repair

**King's Health Partners performs the highest number of emergency aneurysm repairs per annum in the UK and has low mortality (26%) compared with other centres (>35%).**

We also provide emergency services for aortic dissection, thoracic aneurysms and thoraco-abdominal aortic pathology.

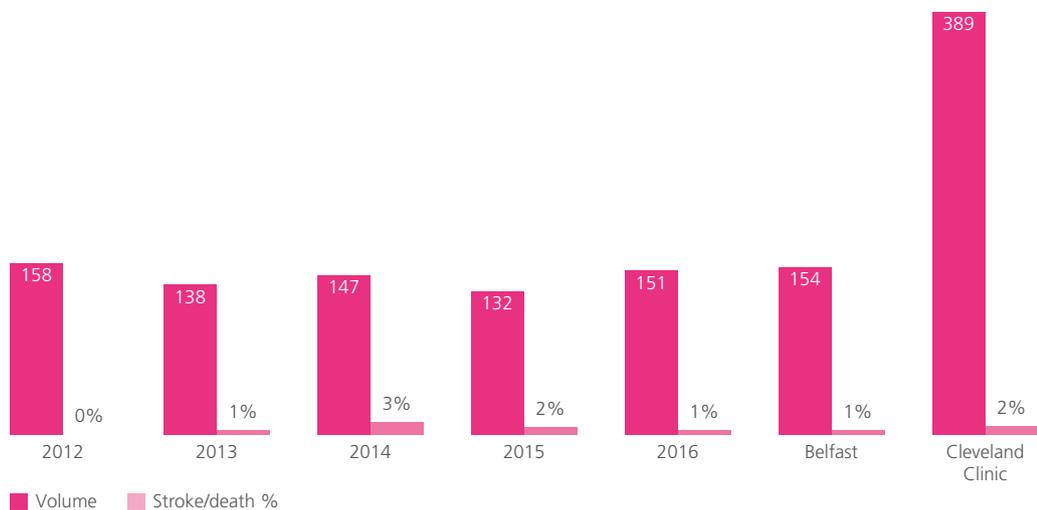
**Figure 12** | Cases of emergency AAA repair from 2012 to 2016 at King's Health Partners



## Carotid endarterectomy

King's Health Partners is one of the largest UK centres for this procedure, with the lowest mortality of any UK centre.

**Figure 13** | Number of cases of carotid surgery from 2012 to 2016 at King's Health Partners and rates of serious complications compared to the largest UK centre (Belfast) and the Cleveland Clinic, USA

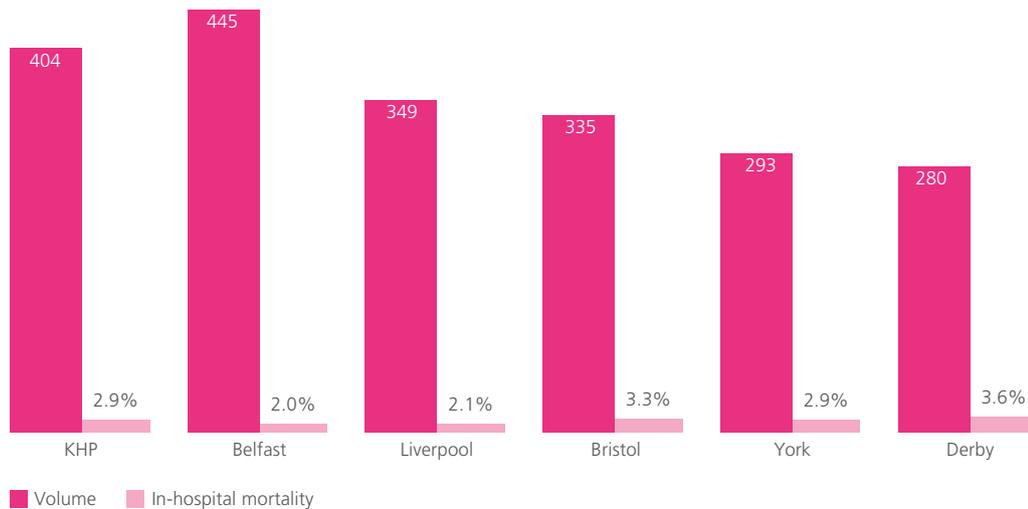


## Lower limb revascularisation

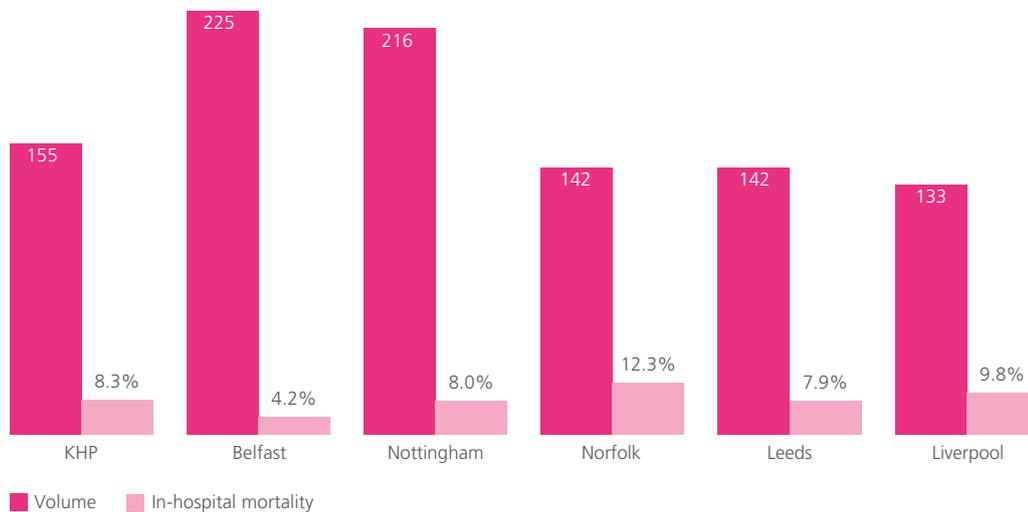
King's Health Partners has a long track record in innovative surgical and percutaneous options for the treatment of patients with critical limb ischaemia, especially in our large diabetic practice. Endovascular, open bypass and hybrid procedures are used to revascularise patients at risk of limb loss.

**The major amputation rates for this group of patients are very low.**

**Figure 14** | Numbers of lower limb revascularisations in leading UK centres



**Figure 15** | King's Health Partners major lower limb amputations in 2016 compared to other major UK centres



## Research and innovation

### King's Health Partners deep venous service

This pioneering programme is developing new treatments and better pathways for individuals with acute or chronic deep venous occlusive disease, which often leads to chronic leg ulcers. The service is engaged in multiple clinical registries and trials and industry partnerships, including the use of venous stents. We are the global lead site for the Virtus study (a prospective study to evaluate the safety and efficacy of a venous stent in the setting of chronic iliofemoral venous obstruction) and the UK lead site for several other studies. We are also a European training site for venous stents and recently hosted the European Venous Forum, which brings together international experts in the field.

The service is supported by a strong pre-clinical and translational research programme to develop innovative therapies. For example, we are studying the mechanisms of thrombus formation and resolution, and venous stent thrombosis, using cutting edge methods.

### Venous valve failure

Venous reflux affects up to 40% of the adult population and is often hereditary. We have identified the first two gene mutations that cause widespread valve failure and have developed specific imaging of venous valves.<sup>6</sup>

### Total endovascular aortic repair

Building upon the long experience of endovascular procedures at King's Health Partners, we are now developing a total endovascular aortic repair service in conjunction with cardiac surgery and cardiology, the aim being to provide endovascular solutions for the whole of the aorta from the aortic valve to the aortic bifurcation.

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<sup>6</sup> Human venous valve disease caused by mutations in FOXC2 and GJC2. Lyons O, Saha P, Seet C, Kuchta A, Arnold A, Grover S, Rashbrook V, Sabine A, Vizcay-Barrena G, Patel A, Ludwinski F, Padayachee S, Kume T, Kwak BR, Brice G, Mansour S, Ostergaard P, Mortimer P, Jeffery S, Brown N, Makinen T, Petrova TV, Modarai B, Smith A. *Journal of Experimental Medicine* 2017; 214(8):2437–2452.

**Figure 16** | CT reconstruction of a total endovascular aortic repair using custom-made stent grafts



## Clinical trials

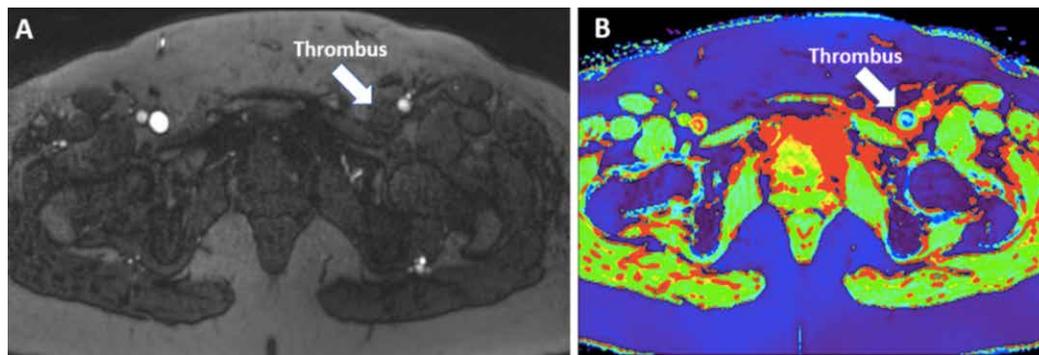
We are involved in a variety of clinical trials, including:

- Bypass versus Angioplasty in Severe Ischaemia of the Leg;
- Effective Treatments for Thoracic Aortic Aneurysms (ETTAA);
- The UK COMpLEx Aneurysm Study (UK-COMPASS).

## Imaging in deep vein thrombosis and carotid atherosclerosis

We are developing new MRI-based imaging techniques to identify patients in whom thrombus is likely to be dissolved by thrombolysis, thus enabling a personalised approach to therapy. In carotid disease, data using novel MR sequences can be correlated with histology of operative specimens.

**Figure 17** | MRI left common femoral vein thrombus



A: Time of flight sequence demonstrating the absence of blood flow in a thrombosed vessel.  
B: T1 mapping sequence demonstrating thrombus structure.

## Aortic graft infection service

We work with the Infectious Diseases team and nuclear medicine to provide treatment regimens for this complex group of patients. We led the development of consensus criteria for diagnosis of this condition (which occurs in 1–4% of aortic grafts) and have also established a National Service Evaluation database.<sup>7</sup>

## Complex Neurological Tumour and Brachial Plexus Injury Service

Since 2015 we have established a monthly collaboration with the Peripheral Nerve Injury Unit at the Royal National Orthopaedic Hospital

<sup>7</sup> Management of Aortic Graft Infection Collaboration (MAGIC): [www.gsttbrc.com/MAGIC](http://www.gsttbrc.com/MAGIC).

in Stanmore for the treatment of complex neurological tumours and traumatic brachial plexus injuries with arterial and venous involvement.

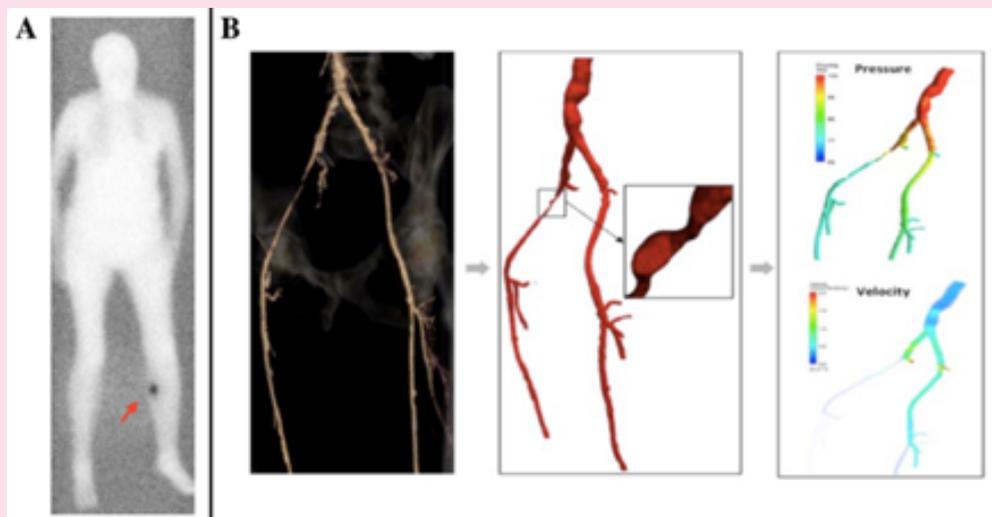
## Effects of Radiation Exposure during X-ray guided vascular interventions

We have been at the forefront of research into the deleterious effects of radiation exposure to patients and operators during X-ray guided vascular interventions.<sup>8</sup>

<sup>8</sup> Radiation-Induced DNA Damage in Operators Performing Endovascular Aortic Repair. El-Sayed T, Patel AS, Cho JS, Kelly JA, Ludwinski FE, Saha P, Lyons OT, Smith A & Modarai B. *Circulation* 2017; 136(25):2406–2416.

## Cell therapy to stimulate new blood vessel growth

Blockage of leg blood vessels causes severe pain or gangrene (critical limb ischaemia, CLI), leading to amputation in up to 30% of patients despite modern surgical and angioplasty/stenting techniques. We have developed potential cell therapy approaches that promote the growth of new blood vessels to restore blood flow to the leg, as an alternative to amputation for CLI. We have recently completed a first-in-human study to demonstrate the feasibility of delivering a novel cell therapy product in the ischaemic leg of patients (Figure A) in readiness for a larger clinical trial.<sup>9</sup>



Aligned to this, we have developed sensitive invasive and non-invasive methods, including MRI and computational fluid dynamics, for accurate assessment of blood flow in the leg (Figure B). These methods will help determine the efficacy of our cell therapy in the clinical trials that are planned.

<sup>9</sup> CD16+ monocytes stimulate arteriogenesis to salvage the ischaemic limb – a bench to bedside study: ISCT 2018 Annual Meeting. Patel AS, Ludwinski F, Kapoor P, Kerr A, Cho J, Fisher C, Hope A, Livieratos L, Saha P, Lyons O, Smith A, Modarai B. *Cytotherapy* 2018; 20(5): S112–S113.



Electrophysiology

# Electrophysiology

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## Description of the service

King's Health Partners is one of the UK's leading centres for managing arrhythmia (abnormal heart rhythms). In addition to offering a full range of clinical electrophysiology services King's Health Partners also has particular expertise in complex ablation therapy and device extraction.

### Services offered at King's Health Partners

Implantation of cardiac implantable electronic devices:

- Pacemakers;
- Defibrillators, including subcutaneous;
- Cardiac resynchronisation pacemakers and defibrillators;
- Implantable cardiac monitors;
- Remote follow-up (via the internet) of cardiac pacemakers, defibrillators and monitors – one of the first and most active centres in the UK.

Cardiac ablation (where abnormal heart rhythms can be prevented and/or treated by creating small scars inside the heart to disrupt abnormal electrical pathways):

- Atrial flutter;
- Atrial fibrillation and complex atrial arrhythmias;
- Supraventricular tachycardias (caused by extra electrical connections in the heart);
- Ventricular arrhythmias.

Specialist services:

- Pacemaker and defibrillator lead extraction;
- Arrhythmias in children and adults with congenital heart disease;
- Leadless cardiac pacing;
- High risk ventricular tachycardia ablation, requiring epicardial approach and/or the use of cardiac support devices;

- Arrhythmias in pregnancy and rare conditions such as sarcoid and inherited cardiac conditions e.g. cardiomyopathies.

Neurocardiology service:

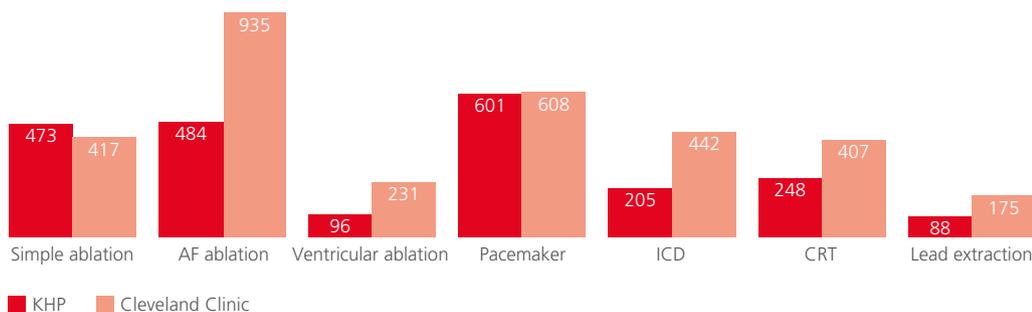
- This is a unique specialist service for patients with conditions overlapping neurology and cardiology, including postural orthostatic tachycardia syndrome (PoTS), inappropriate sinus tachycardia (IST) and vasovagal syncope and other complex cases of loss of consciousness. The service involves a close working relationship between neurocardiology, autonomic neurology and other specialties. Approximately 400 new patients from all over the UK per year are seen in the clinic.

## Volumes, outcomes and metrics

A high volume of invasive procedures per year (>2,500) are performed across the King's College Hospital and St Thomas' sites. King's Health Partners volumes for ablation (n=1,110) and device implantation (n=1,054) are well above the recommended minimum centre volume for invasive EP procedures (100 ablations/year, 80 devices/year). Procedural success rates are high and complications rates low.

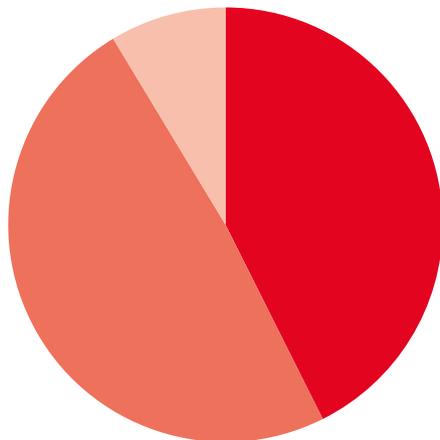
UK benchmarking is difficult as there is no single body collecting data on procedural volumes and complication rates (in the way NICOR does for coronary interventions). King's Health Partners data are therefore presented on procedural complications compared to data from the Cleveland Clinic, a major US EP Centre.

**Figure 18** | King's Health Partners volume (2017), with the most recent available Cleveland Clinic data (2016) for comparison



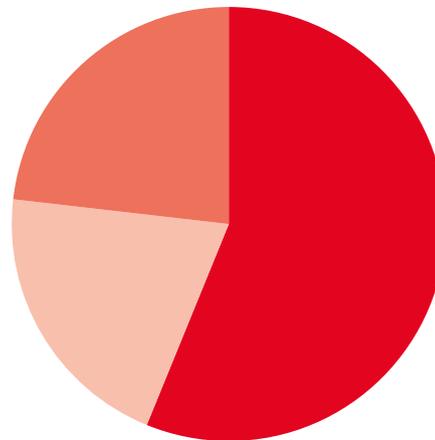
For lead extraction, the King's Health Partners figure indicates 'major' lead extractions, i.e. recent lead implants which were removed with simple traction are not included. Cleveland data does not specify whether it includes such 'simple' lead extractions.

**Figure 19** | Proportions of ablation procedures performed at King's Health Partners



■ Simple ablation    ■ Ventricular ablation  
 ■ Atrial ablation

**Figure 20** | Proportions of device implants at King's Health Partners



■ Pacemaker    ■ CRT    ■ ICD

## Research and innovation

The King's Health Partners' arrhythmia research team comprises a multi-disciplinary group of over 30 researchers from diverse disciplines including Cardiology, Biomedical Engineering, MR Physics, Computational modelling, cellular cardiac electrophysiology and cardiac radiology. The core group has 8 Postgraduate Doctoral Degree students, jointly supervised by clinical cardiologists and King's College London academics. In the last year, they have published over 40 peer reviewed papers and have an active grant income of over £5 million from UK research

councils, medical charities, National Institute for Health Research and many industry collaborators. Strong collaborations exist with leading European (Bordeaux, Berlin) and US centres (Boston). The group participates in and coordinates several multicentre trials including RADI-CRT (invasive measures to improve Cardiac Resynchronisation Therapy response), STRIVE-HF (multisite vs standard CRT), MPP VARR (multipoint pacing vs standard CRT on ventricular arrhythmia burden), VISTAX (ablation-index guided AF ablation) and SHINE (linear catheter ablation in persistent AF).

Key research themes include:

1. Advanced image-guided cardiac intervention
2. Non-invasive and invasive arrhythmia assessment: Predicting arrhythmias and response to treatment
3. Development of innovative techniques and therapies to manage and avoid transvenous leads.

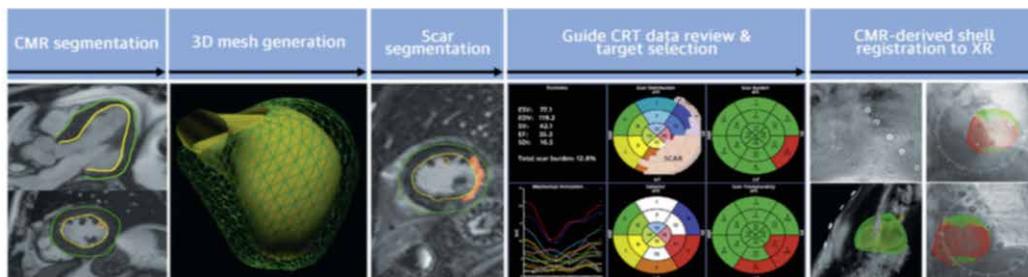
## 1. Advanced image-guided cardiac intervention

### Cardiac CT and MRI-guided LV lead implantation

Cardiac Resynchronisation Therapy (CRT) is an effective cardiac device-based treatment for selected patients with heart failure but approximately a third of patients do not achieve

a significant benefit. We have successfully developed in conjunction with Siemens Healthcare the world's first real time image guidance system for CRT using both MRI and CT guidance. The same CT-guided image technology has recently been used to guide delivery of endocardial leadless left ventricular pacemaker implantations (WiSE CRT).

**Figure 21** | MRI guided left ventricular lead implantation



The first step is to create a 3-dimensional copy of the left ventricle called a 3D mesh from the cardiac MRI scan. This is performed automatically using computer software. Next, we identify and draw around the scar in the left ventricle shown in red in the scar segmentation panel. The 3D mesh is then used to track the contraction and relaxation of the heart during one single beat to identify which areas of the heart are not contracting properly. This information is then combined to identify the latest contracting area of the heart that is free of scar which is our target for implanting the left ventricular lead. We then overlay the MRI-generated 3D mesh with the chosen target area for the left ventricular lead onto the X-Ray images during the CRT implantation procedure.

We have recently published on successful MRI-guided CRT implants<sup>10</sup> and are now launching TACTIC-CRT which is an MRI-guided international multicentre randomised control trial in heart failure patients undergoing CRT implantation. The aim is to increase the number of patients responding to CRT by choosing the best place in the heart to deploy the pacing leads. An example of the MRI guided workflow is shown in Figure 21.

## MR-guided ablation system for ventricular tachycardia (MR-GAST-VT)

Ventricular tachycardia (VT) is a very rapid heart rhythm that is the leading cause of sudden cardiac death. It can be treated by 'ablation' to destroy the abnormal scarred region of heart muscle using minimally invasive catheter-delivered energy. In collaboration with industry, we are using MRI to improve VT ablation accuracy by allowing direct scar assessment at the time of a procedure. Our work has established imaging sequences and complex mapping to locate areas of scar that cause VT after heart attacks.

MR technology can also be used to provide real-time evaluation of ablation lesions by MR-based non-invasive temperature measurement and potentially reduce energy delivery during ablation, thereby reducing the risks of the procedure.<sup>11</sup>

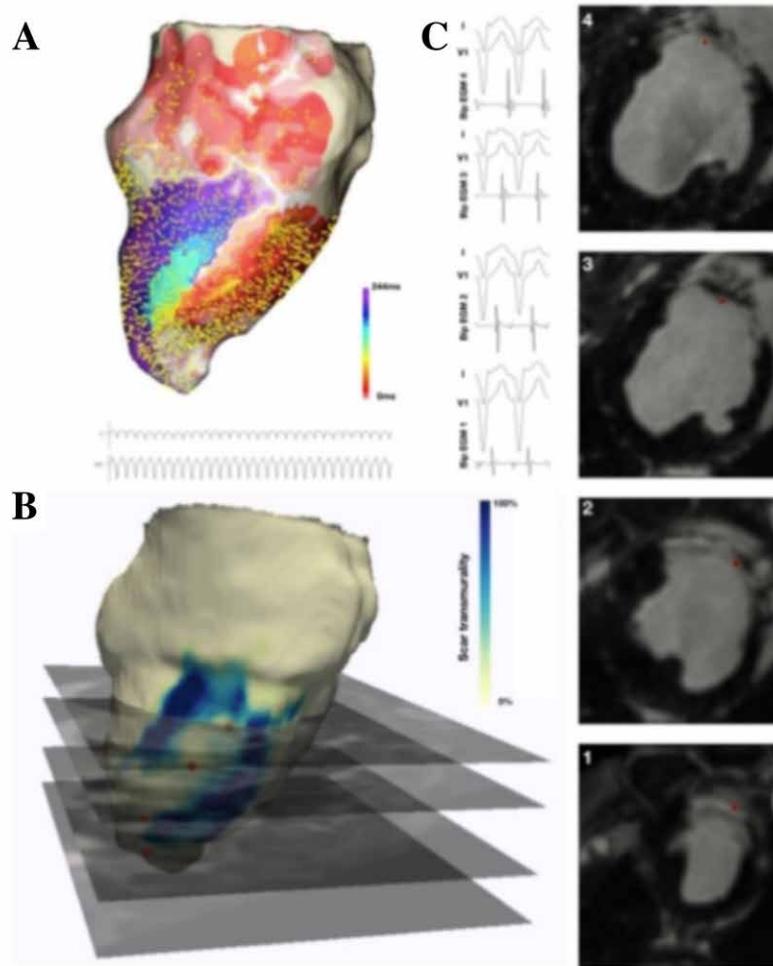
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10 Real-Time X-MRI-Guided Left Ventricular Lead Implantation for Targeted Delivery of Cardiac Resynchronization Therapy. Behar JM, Mountney P, Toth D, Reiml S, Panayiotou M, Brost A, Fahn B, Karim R, Claridge S, Jackson T, Sieniewicz B, Patel N, O'Neill M, Razavi R, Rhode K, Rinaldi CA. *Journal of the American College of Cardiology: Clinical Electrophysiology* 2017; 3(8):803–814.

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11 Epicardial electroanatomical mapping, radiofrequency ablation, and lesion imaging in the porcine left ventricle under real-time magnetic resonance imaging guidance – an *in vivo* feasibility study. Mukherjee RK, Roujol S, Chubb H, Harrison J, Williams S, Whitaker J, O'Neill L, Silberbauer J, Neji R, Schneider R, Pohl T, Lloyd T, O'Neill M, Razavi R. *Europace* 2018; 20(F12): f254–f262.

**Figure 22** | Scar assessment in ventricular tachycardia

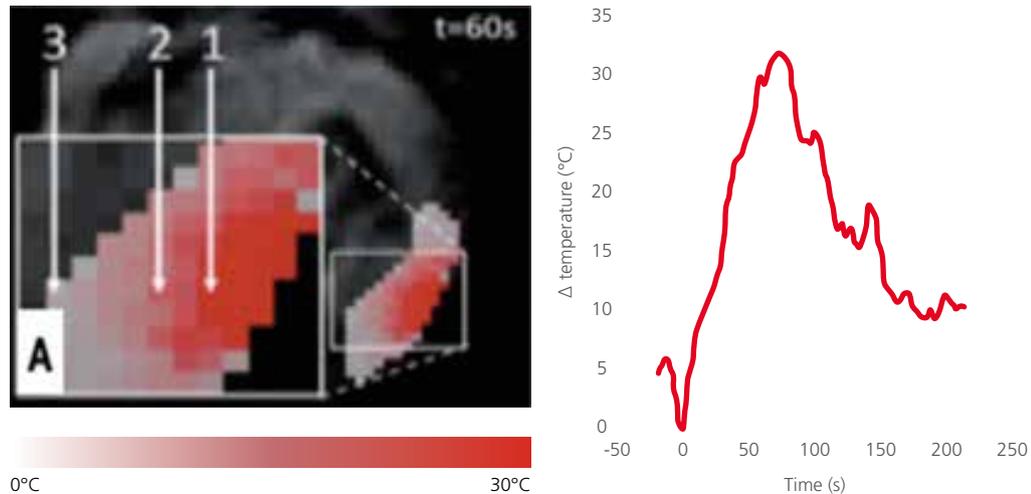


A: Image of heart showing pattern of electrical activity during rapid and dangerous heart rhythm according to a colour scale.

B: Same heart as panel A with colour scale showing depth of scar across wall of heart.

C: Electrical recordings from heart during rapid and dangerous heart rhythm and MRI images of heart.

**Figure 23** | An example of the use of MRI imaging to accurately deliver treatment



A: Heart tissue as it is seen inside an MRI scanner (black and white) with a colour overlay in red demonstrating the change in temperature during treatment: more red means higher temperature. The graph on the right shows the change in temperature of tissue at position one during ablation treatment delivery. This technique is known as 'MR thermometry'. Reproduced from Mukherjee *et al.* 2018; *Europace*.

## 2. Non-invasive and invasive arrhythmia assessment: Predicting arrhythmias and response to treatment

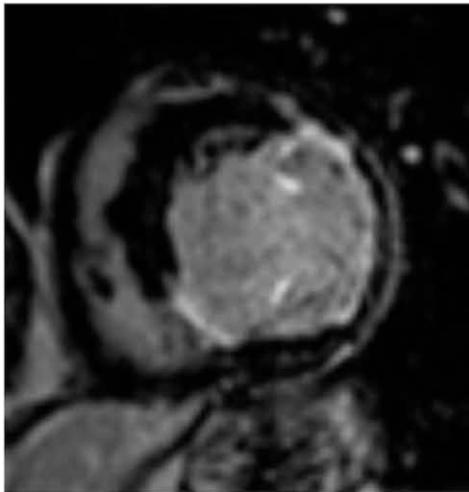
### Ventricular arrhythmia prediction

Deciding which patients are the most suitable to receive an ICD is complex. We have used dedicated tissue texture analysis software to analyse scarred regions of heart muscle using cardiac MR images to help predict which

patients are likely to require ICD shock therapy in the future (see Figure 24). This can help decide which patients should receive ICD therapy and to guide VT ablation.

**Figure 24** | Raw MRI image showing scar and tissue texture

**Raw MRI image showing scar**



**Tissue texture filtered scar image**

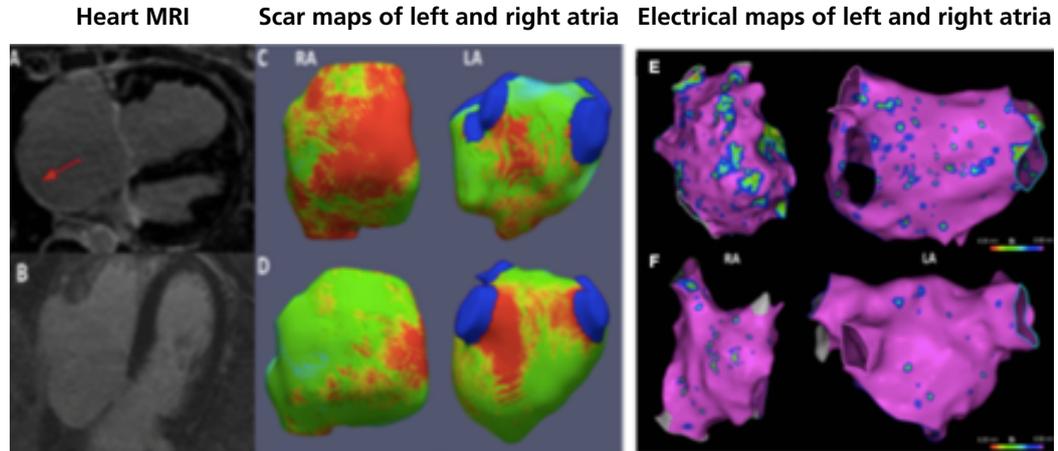


### Prediction of arrhythmia in patients with an Atrial Septal Defect (ASD)

This project aims to determine the risk of heart rhythm disorders in patients born with structural abnormalities, specifically a 'hole' in the heart, known as an 'atrial septal defect', or ASD, by combining cardiac MR imaging and assessment

of the electrical activity in the heart using a technique known as electro-anatomic mapping. Patients with ASDs are assessed before the defect is treated and then again a year later to assess for reversal of abnormalities after defect closure.

**Figure 25** | Arrhythmia prediction in patients with atrial septal defect



A and B: MR images of the heart from a patient born with a 'hole in the heart' (Atrial Septal Defect or ASD) (panel A) compared with a healthy patient (panel B).

C and D: 3D models of the hearts from the same patients showing scar (red) and healthy tissue (green). More red scar is seen in the patient born with an ASD.

E and F: 3D electrical recordings of the left and right atrium from the same patients showing healthy electrical signals in purple and evidence of electrical abnormalities in blue and green. There are more electrical abnormalities in the patient born with an ASD.

## Assessment of the atrial fibrillation substrate and response to ablation

Atrial fibrillation is the most common heart rhythm problem in the UK, but current treatment is unsuccessful for up to half of patients. More precise patient selection is needed. We are using bespoke cardiac imaging, high resolution invasive assessment and mathematical modelling to predict who is likely to respond best to ablation for AF. Together with teams in King's College London Bioengineering and industrial partners, we are developing improved methods for scar

detection by cardiac MRI and measurement of electrical activity to allow patient-specific (individual) assessment of arrhythmia and planning of treatment.

## Optical mapping of the atrium

We have developed experimental models of atrial fibrillation and atrial scarring that will allow us to better understand how measurements (such as voltage) made during ablation relate to scar and important electrical changes in the heart.

## Using intracardiac electrical signals to detect dangerous arrhythmia

We have undertaken research into the potential of incorporating intracardiac electrical signals obtained from implanted cardiac devices into automated algorithms to allow advanced detection and treatment of dangerous heart rhythms. The aim is to improve treatment strategies in patients with defibrillators to improve patient outcomes and quality of life.

## 3. Development of innovative techniques and therapies to manage and avoid transvenous leads

### Optimal site selection during LV Endocardial CRT

Conventional pacemakers require a pacing lead implanted through a vein and positioned on the inside or outside of the heart. We are working on novel, leadless pacing technology that may allow the optimal sites for left ventricular pacing to be used, thereby improving patient outcomes. This work was successful in the Young Investigator Category at both the European Heart Rhythm Association meeting in 2017<sup>12</sup> and the UK Heart Rhythm Congress, Birmingham.

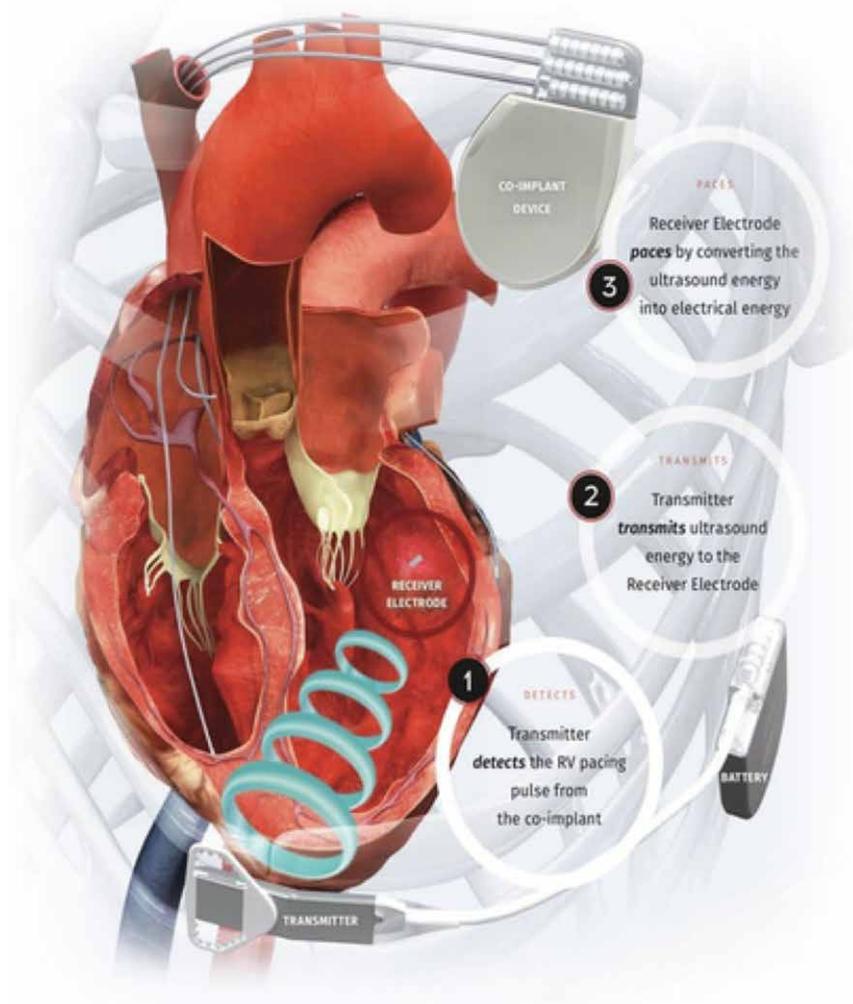
### Extraction of cardiac implanted electronic devices

King's Health Partners is a nationwide referral centre for the extraction of transvenous pacing leads that are no longer required or need replacement. This offers us the experience, expertise and ability to analyse what is becoming an increasingly common procedure. Currently we are focusing on CRT vs. non-CRT extraction and extraction for different types of infection as well as looking at the cost effectiveness and healthcare costs associated with lead extraction.

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12 Identifying the optimal location for LV endocardial pacing: results from a multicentre international registry. Sieniewicz JB, Behar J, Sohal M, Gamble J, Betts TR, Jais P, Derval N, Spragg D, Steendijk PB, Van Gelder B, Bracke F, Rinaldi A. *Europace* 2018; 19(supplement 3):iii144–iii145.

Figure 26 | Left ventricular endocardial pacing





Percutaneous intervention  
for structural heart disease

# Percutaneous intervention for structural heart disease

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## Description of the service

Patients with severe disease of the heart valves and other structural heart problems would typically have required open heart surgery to correct the defects. However, an increasing number of such structural disorders are now tackled by minimally invasive percutaneous (“keyhole”) procedures, often without the need for a general anaesthetic. In some cases, the percutaneous approach is now the first-line therapy whereas in others the percutaneous approach is used for patients whose risk from conventional open heart surgery is excessively high.

The King's Health Partners percutaneous (or transcatheter) structural heart disease service comprises a multi-disciplinary team (MDT) with cardiologists, cardiac surgeons, multi-modality imaging specialists, anaesthetists, specialist

nurse practitioners and care-of-the-elderly physicians. All patients are formally discussed in an MDT meeting where their procedure and care are planned.

## Transcatheter Aortic Valve Intervention (TAVI)

Aortic stenosis (or narrowing of the aortic valve) is one of the most common and serious valve disorders, with a high prevalence in the elderly. In the past, many of these patients were too high risk for surgery due to the presence of multiple other health problems. TAVI involves the percutaneous replacement of the diseased aortic valve without the need for an open chest operation or cardiopulmonary bypass. It represents

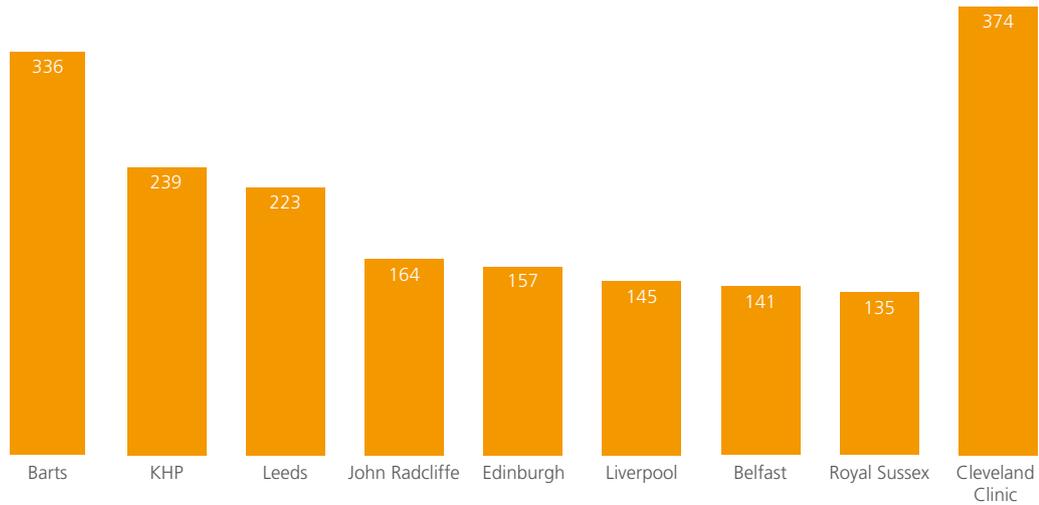
a major technological advance that has become the first-line treatment for high and intermediate risk patients with severe aortic stenosis.

King's Health Partners performed the first TAVI procedure in the UK using the Edwards Sapien device in August 2007 and the first trans-apical TAVI procedures in the UK in the same month. We have participated in numerous groundbreaking and practice-changing TAVI trials

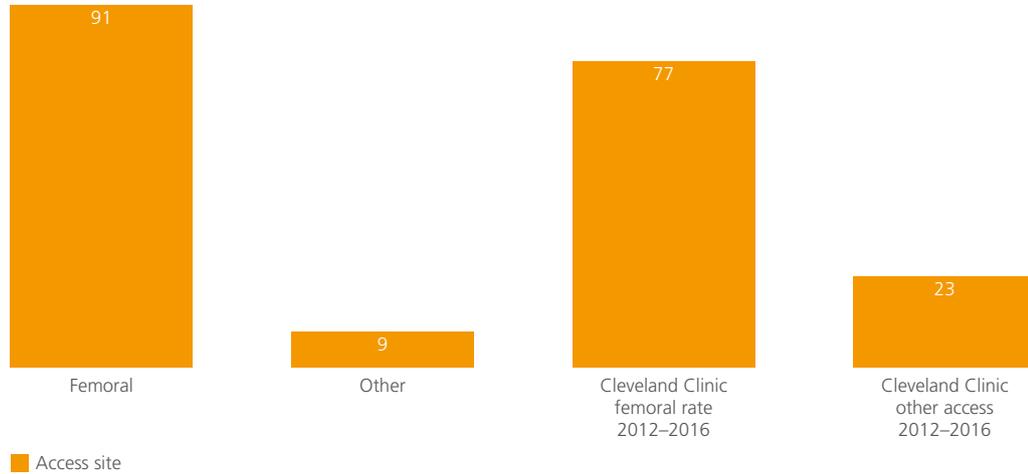
since, including PARTNER-EU, PREVAIL, SOURCE, SOURCE-XT, SOURCE 3 and ULTRA. We now have a mature TAVI service across both sites.

Figure 27 outlines TAVI procedural volumes for 2016, benchmarked against other centres, both UK and international. Reflecting the growth of the TAVI service, in 2018 we performed over 380 cases.

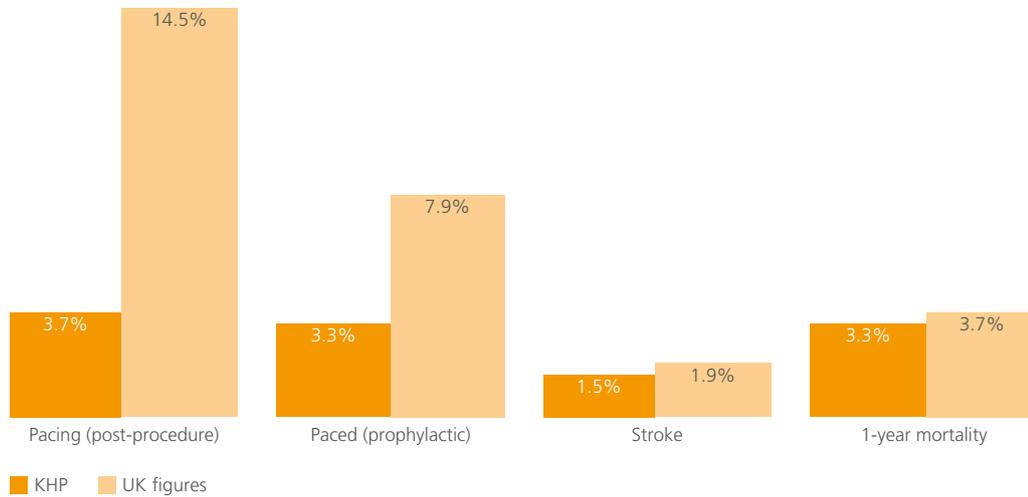
**Figure 27** | TAVI volumes for major UK centres in 2016, with comparative figures for the Cleveland Clinic (USA) over the same period



**Figure 28** | King's Health Partners TAVI procedural details, with relevant data from Cleveland Clinic for comparison



**Figure 29** | Procedural outcomes and mortality for TAVI in 2016 compared to the UK national average



## Transcatheter Mitral Valve (MV) intervention

Mitral regurgitation (leaking) in patients at high-risk for surgery, such as those with severe heart failure, is treated with a variety of transcatheter therapies. This field has been invigorated recently by the publication of the CoApt trial in the NEJM in Sept 2018. The following therapies are being offered by the King's Health Partners team in selected cases or as part of research studies:

- MitraClip. 30 patients have been treated to date;
- Transcatheter mitral valve-in-valve implantation. Degenerated prosthetic mitral valves can be treated using transcatheter systems designed for aortic valves, thereby avoiding the need for a second operation. King's Health Partners was the first centre in the UK to perform these procedures. Approximately 10 patients per year receive this innovative treatment.
- Mitral balloon valvuloplasty is an established treatment for mitral valve stenosis (narrowing). The number of patients needing this treatment is low because rheumatic fever (the major cause) has virtually disappeared in the UK.

- Fully percutaneous mitral valve replacement – St Thomas' Hospital is a recruiting centre for the INTREPID valve and King's College Hospital NHS Foundation Trust is a recruiting centre for the TIARA valve;
- Percutaneous indirect mitral valve annuloplasty – St Thomas' Hospital is a recruiting centre for the MAVERICK registry, evaluating the ARTO annuloplasty device. 8 cases have been recruited to date.

## Closure of Patent Foramen Ovale (PFO)

A PFO is a common abnormality that results in a hole between the right and left atria. Some patients with PFO require closure if it has caused significant problems. Percutaneous closure is the first-line treatment for PFOs. In 2016 King's Health Partners performed 52 percutaneous PFO closures.

## Closure of left atrial appendage

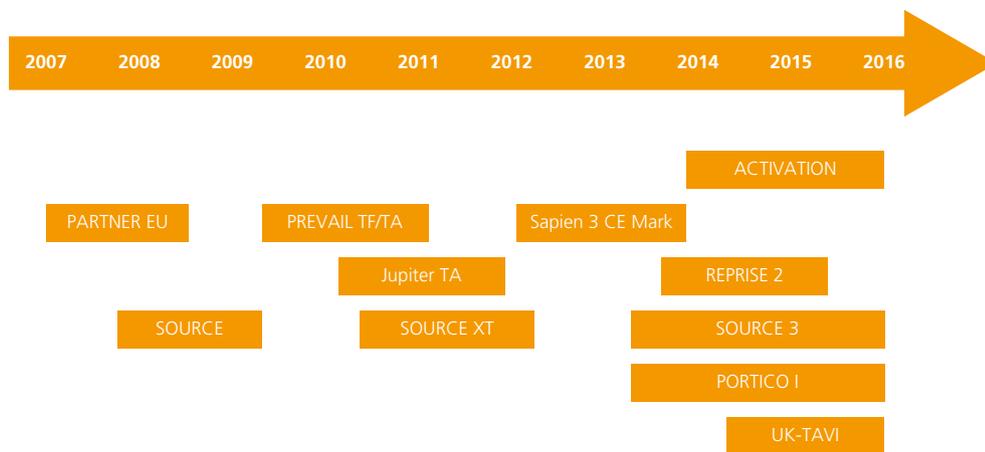
Patients with atrial fibrillation (AF, irregular heart beat) have an increased risk of clot formation in the heart, which can lead to stroke and other problems. The clot usually forms in the left atrial appendage (LAA). The LAA can be percutaneously occluded in a relatively new procedure which is performed in approximately 30 patients per year.

## Research and innovation

The percutaneous structural heart disease programme at King's Health Partners is strongly research-based and many new procedures were performed at King's Health Partners for the first time in the UK or the world. Significant areas of research focus include:

- Clinical trials in TAVI. King's Health Partners participates in and/or has led major international studies in TAVI (see Figure 30);<sup>13</sup>
- Hypothesis-driven research examining the behaviour of the left ventricle before and after aortic device implantation;<sup>14</sup>
- Imaging research including use of the EchoNav system – the only fusion imaging system of its kind in the UK;

**Figure 30 | TAVI Clinical Trials at King's Health Partners**



13 SOURCE 3: 1-year outcomes post-transcatheter aortic valve implantation using the latest generation of the balloon-expandable transcatheter heart valve. Wendler O, Schymik G, Treede H, Baumgartner H, Dumonteil N, Neumann FJ, Tarantini G, Zamorano JL, Vahanian A. *European Heart Journal* 2017;38(36):2717–2726.

14 Successful transcatheter aortic valve implantation (TAVI) is associated with transient left ventricular dysfunction. Dworakowski R, Wendler O, Bhan A, Smith L, Pearson P, Alcock E, Rajagopal K, Brickham B, Dew T, Byrne J, Monaghan MJ, Sherwood R, Shah AM, MacCarthy PA. *Heart* 2012;98(22):1641–1646.

- Innovative imaging to plan percutaneous procedures, including 3D echo and co-registration of echo and radiography;<sup>15</sup>
- Evaluation of the haemodynamic effects of TAVI and the predictors of peri-operative risk.

## TAVI 'firsts' at King's Health Partners

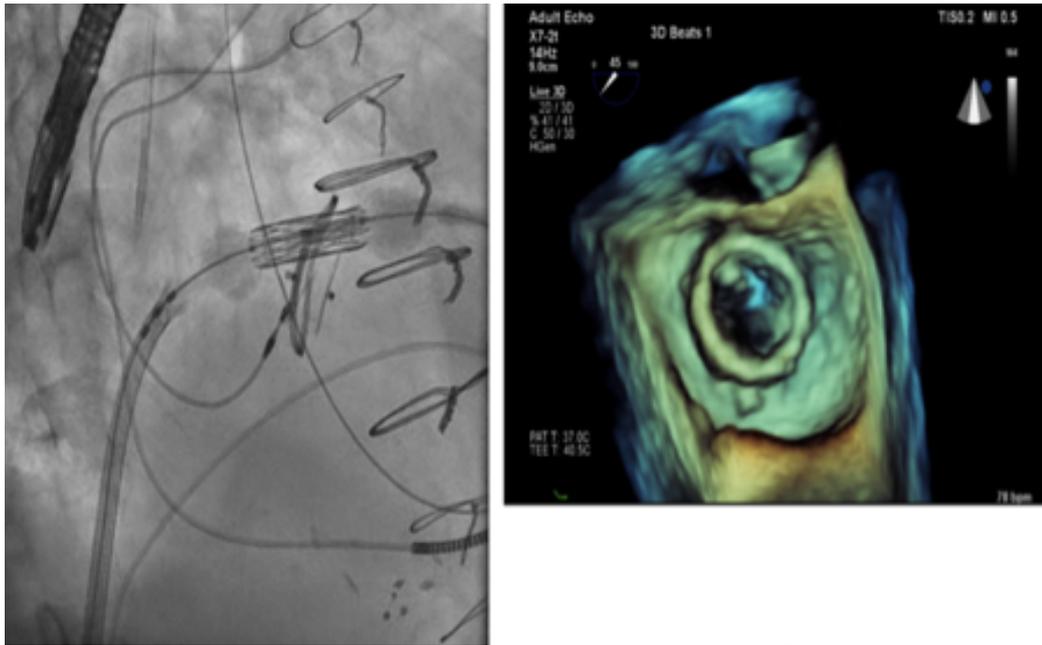
King's Health Partners has a long history of leading the UK in TAVI innovation, relating both to novel TAVI devices and to vascular access. King's Health Partners operators performed the UK's first Transapical and Transcaval TAVIs, providing important alternative vascular access options for patients in whom the standard Transfemoral route cannot be used.

**Figure 31** | The history – TAVI 'firsts'



15 Automated quantification of mitral valve geometry on multi-slice computed tomography in patients with dilated cardiomyopathy - Implications for transcatheter mitral valve replacement. Banks T, Razeghi, O, Ntalis I, Aziz W, Behar JM, Preston R, Campbell B, Redwood S, Prendergast B, Niederer S, Rajani R. *Journal of Cardiovascular Computed Tomography* 2018;12(4):329–337.

**Figure 32 |** Transcatheter mitral valve in valve implantation



The left panel shows x-ray images of the catheter (bottom left) leading up from the leg to the heart, with the new valve in place within the existing valve ready to be deployed. The transoesophageal echo (TOE) probe is seen in the top left-hand corner. The right panel shows the type of image the TOE probe obtains.



Heart failure

# Heart failure

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## Description of the service

### Overview

King's Health Partners provides the UK's largest multi-professional Heart Failure Service with comprehensive care delivered across three acute hospital sites (Guy's and St Thomas', King's College Hospital and Princess Royal University Hospital) and integrated Community Heart Failure Services to ensure seamless care for patients in Lambeth, Southwark and Bromley.

The heart failure team includes Consultant Cardiologists with a specialist interest in heart failure, Clinical Nurse Specialists in the acute sites, community-based Clinical Nurse Specialists, dedicated Pharmacists and specialist trainees. In addition, there is close liaison with specialists in care-of-the-elderly, clinical psychologists and palliative care for those patients who require additional input.

### Inpatient care

Acute Heart Failure pathways operate at the acute sites, ensuring rapid diagnosis and access to consultant-led specialist heart failure care for patients both on cardiology and general wards. There is access to comprehensive diagnostics (see Imaging & Diagnostics). Regular multi-disciplinary team meetings (MDTs) consider the care of individual patients, including referral for:

- Cardiac resynchronisation;
- Implantable defibrillators;
- Coronary revascularisation by percutaneous coronary intervention or surgery;
- Other surgical procedures including cardiac transplantation.

The community-based nurse specialists also have access to in-hospital MDTs.

### Outpatient care

Consultant-led heart failure clinics provide rapid access and are supported by nurse-led education and up-titration of disease modifying drugs. Specialist clinics are run for:

- Cardio-oncology – dealing particularly with potential cardiac side-effects of chemotherapeutic agents;
- Cardiac device assessment and optimisation;
- Rheumatological/connective tissue disorders.

### Volumes and outcomes

King's Health Partners serves a secondary care population of 1 million, with a heart failure prevalence of 1.5% and a tertiary population of up to 8 million. Approximately 3,500 new patients a year are seen with suspected heart failure, with approximately 8,500 outpatient attendances.

### Research and innovation

Redesign of patient pathways and the overall service is a major focus of innovation. The Box on page 65 highlights a recent comprehensive service redesign supported by a grant from the Guy's and St Thomas' Charity. Other areas of service redesign include developing the optimal

**Figure 33 |** King's Health Partners heart failure outcomes from the 2015/16 National Heart Failure Audit, with national and international comparators



model of care for patients admitted with acute heart failure, virtual clinics, improved access to psychological care, and patient lounges to facilitate intravenous therapy (e.g. diuretics) as an outpatient.

There is an extensive range of basic and clinical research that underpins the service. This includes:

- New biomarkers to guide the management of heart failure;
- Computational modelling to develop personalised therapy;
- Research on cardiac resynchronisation strategies;
- Mechanisms and management of HFpEF (heart failure with preserved ejection fraction);<sup>16</sup>
- Heart failure in patients with cancer or rheumatological diseases;
- Clinical trials of new heart failure therapies;
- Cardiac side-effects of anti-psychotic medications;
- Basic science studies investigating heart failure pathophysiology.<sup>17</sup>

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16 The Emerging Role of Cardiac Magnetic Resonance Imaging in the Evaluation of Patients with HFpEF. Webb J, Fovargue L, Tøndel K, Porter B, Sieniewicz B, Gould J, Rinaldi CA, Ismail T, Chiribiri A, Carr-White G. *Current Heart Failure Reports* 2018;15(1):1–9.

17 Effect of Iron Isomaltoside on Skeletal Muscle Energetics in Patients with Chronic Heart Failure and Iron Deficiency: The FERRIC-HF II Randomized Mechanistic Trial. Charles-Edwards G, Amaral N, Sleight A, Ayis S, Catibog N, McDonagh T, Monaghan M, Amin-Youssef G, Kemp GJ, Shah AM, Okonko DO. *Circulation* 2019 (In press. DOI:10.1161/CIRCULATIONAHA.118.038516).

## Community heart failure services

King's Health Partners has been establishing an innovative model for heart failure services in the community which provides a platform for joint working across secondary and primary care and has the patient at the centre of the pathway. A community-based multidisciplinary heart failure team provides holistic specialist care throughout the patients' pathway (inpatient, outpatient or in primary care), aiming to remove inequalities of access (e.g. based on geography and ethnicity).

The heart failure team links to the current long-term conditions infrastructure and by placing the team alongside other community based services, ensures truly integrated care that covers both physical and mental health. The service includes:

- **An integrated education programme.** We provide an education programme to GPs both via virtual clinics and practice-based education. In future this will be led by an education manager and will be expanded further to local care network and borough levels. The emphasis is on early and accurate diagnosis (using BNP testing and one stop diagnostic clinics), mental health issues, and appropriate up-titration of medications;
- **Local heart failure pharmacists** who provide expert advice on medications and run up-titration clinics, as well as linking with other specialist pharmacists and more general pharmacists;
- **A single point of access** for all heart failure referrals with appropriate vetting and feedback by the heart failure consultants working with the local cardiovascular disease leads;
- **Psychological support.** Up to 40% of heart failure patients have anxiety or depression and currently psychological support for them is very poor. A community-based psychologist will work closely with nurse specialists and GPs to improve their skills in recognition and support. They will also run individual clinics and help set up web-based support modules individualised for heart failure patients;
- **End of life care** in collaboration with primary care and the locality based palliative care teams.



Inherited cardiac conditions

# Inherited cardiac conditions

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## Description of the service

Our Inherited Cardiac Conditions (ICC) service covers both adult and paediatric patients across south east London, Kent and south coast (approximately 8 million people). We are currently the only UK service to cover every aspect of ICC. The services provided include:

- Cardiomyopathies or heart muscle diseases – hypertrophic, dilated, restrictive and arrhythmogenic;
- Inherited heart rhythm disorders such as Long QT syndrome and Brugada syndrome;
- Inherited aortic disorders – such as Marfan, Ehler Danlos and connective tissue disorders. We are the only UK service that is approved as a specialist provider for heritable thoracic disorders and medium-sized arterial diseases;
- Inherited cardiac metabolic conditions – such as Fabry's disease and mitochondrial disease;

- Cardiac involvement in neuromuscular disorders such as muscular dystrophy and myotonic dystrophy;
- Familial hypercholesterolaemia (integrated with chemical pathology);
- Family screening for patients at risk of inherited disease or families in which there are unexpected sudden deaths.

Cardiovascular genetics is a core component of the service, involved both in supporting patients and clinicians.

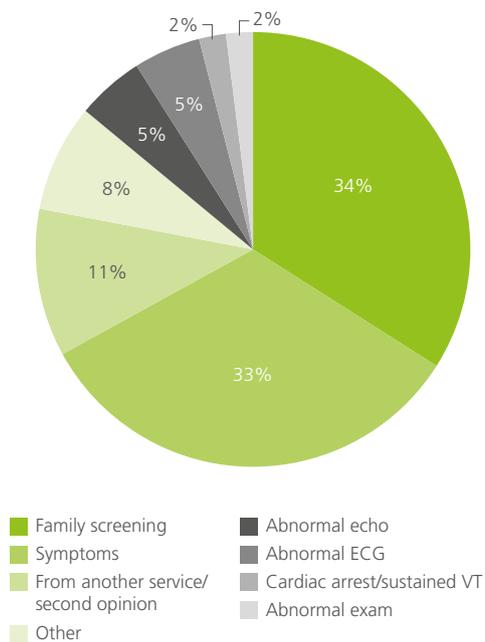
We work closely with multiple patient groups and charities to improve patient and carer experiences, and to inform service development and research.

We also work with European and international committees, for example to establish criteria for diagnosis and management of rare genetic disorders.

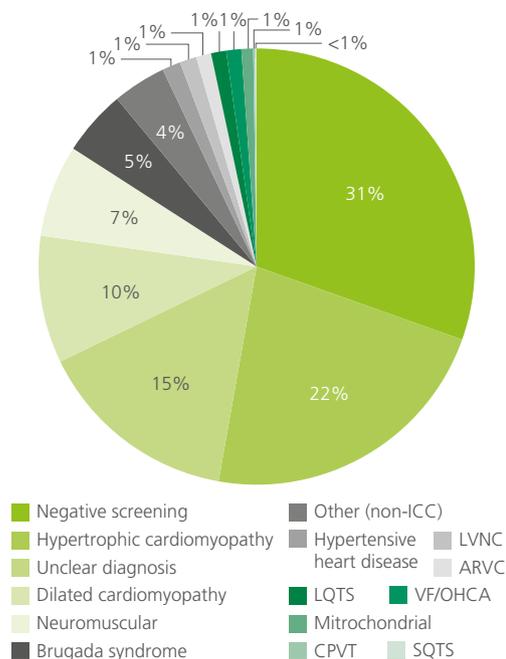
## Volumes and outcomes

Approximately 1,800 patients are seen within the King's Health Partners ICC services per year. Family screening of relatives of patients with a confirmed relevant cardiac condition represents a significant proportion of referrals to the service. Utilising the clinical expertise of the team, the service is able to reassure a large number of patients via negative screening.

**Figure 34** | Chart demonstrating referral reasons for Inherited Cardiac Conditions clinic



**Figure 35** | Chart demonstrating clinical diagnoses of patients seen in the Inherited Cardiac Conditions clinic



LVNC: Left ventricular non-compaction; ARVC: Arrhythmogenic right ventricular cardiomyopathy; LQTS: Long QT syndrome; VF/OHCA: Ventricular Fibrillation/Out-of-hospital Cardiac arrest; CPVT: Catecholaminergic Polymorphic Ventricular Tachycardia; SQTS: Short QT syndrome.

## Research and innovation

We are part of the 100k Genomes Project, a UK-based project to sequence 100,000 genomes from NHS patients. The information gained from studying the genomes may provide breakthroughs in understanding the development of rare diseases and designing new therapies.

We have recently obtained further funding from the British Heart Foundation to grow our network model through the Miles Frost Fund.

Internationally-leading basic research into how genetic mutations in muscle proteins lead to cardiomyopathy is conducted within our British Heart Foundation Centre of Excellence. This includes a new on-line diagnostic tool that is freely available to anyone ([fraternallab.kcl.ac.uk/TITINdb](http://fraternallab.kcl.ac.uk/TITINdb)).

The ICC Nursing team has been nominated for a British Heart Foundation Alliance Team award. We offer a unique training programme for nurses to acquire a combination of ICC and genetic counselling knowledge and skills. Our lead nurse is the incoming President of the British Association for Nursing in Cardiovascular Care and is also spearheading the development of an National Institute for Health Research James Lind Alliance Priority Setting Partnership for cardiovascular nursing and Allied Health Professional research on behalf of King's Health Partners.

## Selected references

TITINdb – a computational tool to assess titin's role as a disease gene. Laddach A, Gautel M, Fraternali F. *Bioinformatics* 2017;33(21):3482–3485.

Recessive mutations in EPG5 cause Vici syndrome, a multisystem disorder with defective autophagy. Cullup T, Kho AL, Dionisi-Vici C, Brandmeier B, Smith F, Urry Z, Simpson MA, Yau S, Bertini E, McClelland V, Al-Owain M, Koelker S, Koerner C, Hoffman GF, Wijburg FA, ten Hoedt AE, Rogers RC, Manchester D, Miyata R, Hayashi M, Said E, Soler D, Kroisel PM, Windpassinger C, Filloux FM, Al-Kaabi S, Hertecant J, Del Campo M, Buk S, Bodi I, Goebel HH, Sewry CA, Abbs S, Mohammed S, Josifova D, Gautel M, Jungbluth H. *Nature Genetics* 2013;45(1):83–87.



# Adult congenital heart disease

# Adult congenital heart disease

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## Description of the service

The King's Health Partners congenital heart disease (CHD) services cover the complete pathway from foetus to adult. Adult CHD services (ACHD) are closely linked to paediatric cardiology and transition CHD services in the Evelina London Children's Hospital, and are provided by a core group of specialist ACHD consultants, congenital cardiothoracic surgeons, clinical nurse specialists and congenital physiologists.

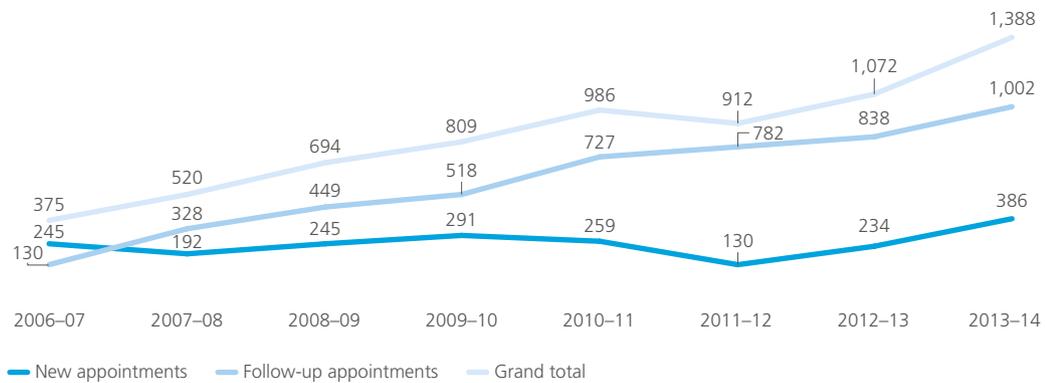
The ACHD service is based on a tiered network model of care in keeping with current NHS England ACHD Standards and Service Specifications, with complex diagnostics, specialist surgery and advanced care delivered at St Thomas' and other services provided closer to patients in partnership with local centres across the South East and East of England.

Services include:

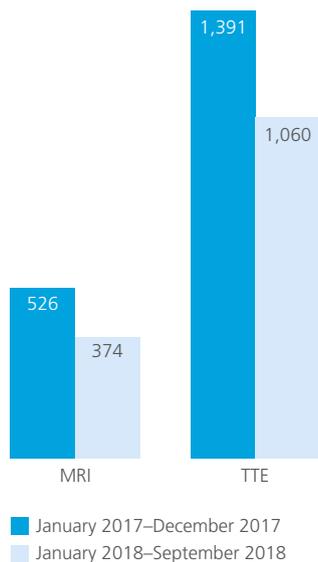
- Specialist congenital and peri-procedural imaging;
- Percutaneous catheter intervention;
- Cardiac surgery;
- Specialist clinics in cardiac obstetric medicine and pulmonary hypertension;
- Nurse-led and physiologist-led clinics;
- Outreach services across the network;
- Training provision to colleagues across the network.

## Volumes and outcomes

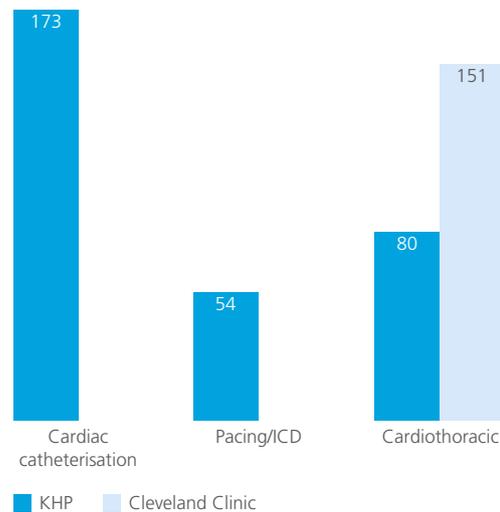
**Figure 36** | Outpatient clinical assessment volume



**Figure 37** | ACHD cardiac imaging volumes



**Figure 38** | ACHD procedural data: June 2016–June 2017 with comparable data from Cleveland Clinic where available



**Figure 39** | Total number of adult congenital interventions submitted to NICOR



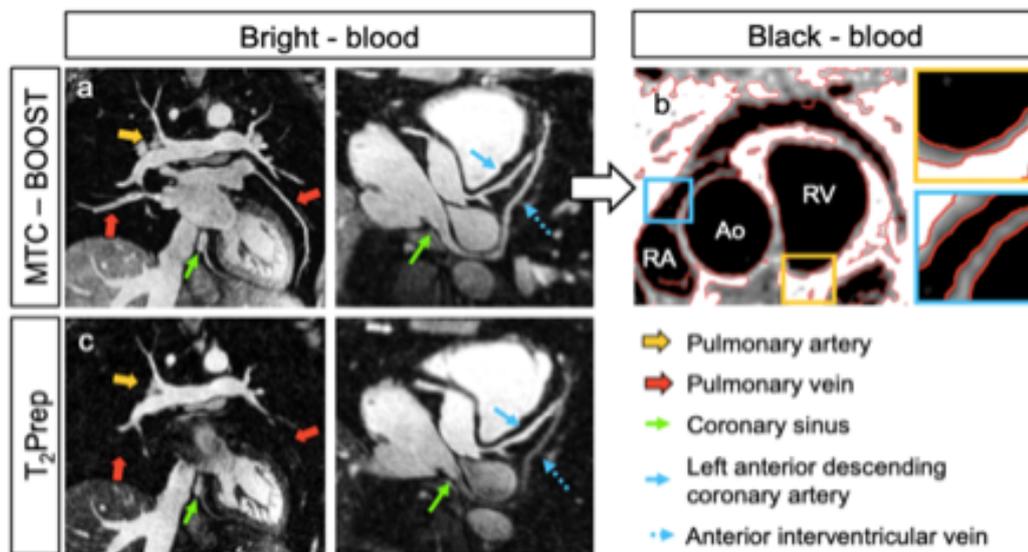
## Research and innovation

The ACHD service is characterised by its highly multi-disciplinary approach which is applied to develop new treatments for the complex abnormalities seen in our patients. Some examples of the King's Health Partners ACHD team's innovative work are listed below:

- **Percutaneous replacement of the pulmonary valve.** The pulmonary valve controls blood flow from the right side of the heart into the lungs. Replacement of this valve has historically required open heart surgery, but our team has been leading the way in implanting a new larger type of valve through a percutaneous (catheter) approach, thereby avoiding open surgery.
- **Transcatheter correction of sinus venosus atrial septal defect.** An innovative treatment to treat this complex condition by a transcatheter (minimally invasive) approach has been developed (see Box 'Transcatheter correction of congenital heart defects').

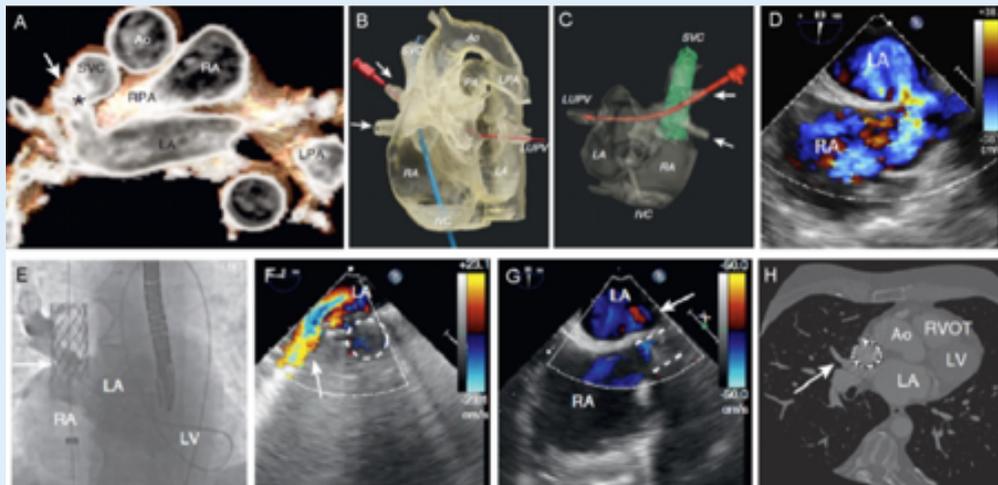
- **Personalised external root support in aortic disease.** Personalised external root support is a technique that places a custom-made external support around a dilated aorta, avoiding the need to replace the aorta and thereby reducing the risk of surgery. It was developed for use in Marfan syndrome but the King's Health Partners team has pioneered its use in other complex aortic conditions and now also trains other centres in the use of this new procedure.
- **Non-contrast enhanced multi-contrast 3D whole-heart (BOOST).** Regular collaboration with physicists and biomedical engineers ensures that state of the art cardiac MR Images can be developed and applied for clinical use. We are currently working on a new sequence able to simultaneously provide 3D Bright- and black-blood MR images under free breathing and without the need of contrast administration. Preliminary results show increased resolution compared to standard technique which is valuable in CHD to plan intervention (see Figure 40).

**Figure 40** | Bright- (a) and black- (b) blood MTC-BOOST for atrial ablation procedures (pulmonary vein visualisation and atrial wall quantification). MTC-BOOST shows homogenous depiction of both arterial (yellow, solid blue arrows) and venous (red, green, dashed blue arrows) systems (a) in comparison to the conventional T<sub>2</sub> prepared sequence (c) (arrows).



## Transcatheter correction of congenital heart defects

Many complex congenital heart defects are conventionally treated by open heart surgery. The King's Health Partners team are developing ways of treating many of these through keyhole techniques. This example is a condition where there is abnormal drainage of veins bringing oxygenated blood from the lungs as well as a hole between the right and left atrial chambers (sinus venosus atrial septal defect). First, cardiac magnetic resonance imaging is used to identify the precise anatomy in the patient (A). Next, 3D printing technology is used to produce an individualised model of the patient's heart in order to allow simulation of stent placement via a catheter procedure, to restore correct blood flow. The stent is implanted on the blue catheter while a dilator in pulmonary vein passes into the left atrium (B). X-rays are then taken of the model to visualise all the structures (C). During the actual procedure, a transoesophageal echocardiogram (TOE) is used to monitor heart function and blood flow (D). A stent is implanted under X-ray guidance (E) and correct positioning and blood flow are confirmed by angiography as well as TOE (F). The stent is highlighted by the dotted lines in F and G. Finally, cardiac CT after the procedure (H) confirms that correct blood drainage has been achieved and there is no residual hole. This complex procedure has been successfully performed in 15 patients since March 2016 without any complications.





# Hypertension and vascular risk

# Hypertension and vascular risk

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## Description of the service

King's Health Partners Cardiovascular provides a specialist service for hypertension and vascular risk, which is fully integrated with an internationally-leading research programme that allows patients to rapidly benefit from new advances or involvement in clinical trials.

The service is run by Cardiovascular Clinical Pharmacology and includes:

- **Specialist hypertension clinics.** Patients are referred locally and nationally by GPs, community cardiovascular clinics, and as tertiary referrals. The clinics lead in evidence-based medicine with expertise in the investigation and management of complex/resistant hypertension in patients with multi-morbidity/polypharmacy, and in African-Caribbean people who often have resistant hypertension.
- **'HOT' clinic facility.** This is a rapid access (usually within one week) service for patients presenting to the emergency department, with the aim of avoiding/shortening admission and providing definitive management.
- **Specialist inpatient services.** These cover a wide range of specialities including vascular surgery (for patients presenting with aortic dissection, aortic aneurysm, carotid disease); stroke; obstetrics; and acute medicine (accelerated or resistant hypertension).
- **Multidisciplinary team approach.** We link with other MDTs such as the Endocrine MDT (hyperaldosteronism, phaeochromocytoma) and interventional radiology/renal (patients with renal artery stenosis).

## Volumes and outcomes

We receive approximately 700 referrals and see approximately 2,800 follow up patients a year.

Whilst specific comparison data is not available, many of our patients are enrolled in local and national blood pressure trials, such as the British Heart Foundation/BHS Pathway Trials, which contribute to changes in practice and practice guidelines. Our robust and efficient study recruitment enables our studies to meet their recruitment goals.

For example:

- In the first year of recruitment, we enrolled 109 patients into the AIM HY study (see box), 50 of which came from King's Health Partners clinics;
- In the last year (June 2017–2018), the *Cardiovascular Function in Hypertension* study has recruited 50 patients;
- The study *Vascular homeostasis and mental stress* recruited 60 patients over the calendar year 2016.

## Research and innovation

Clinical research in this area is an important component of the King's British Heart Foundation Centre of Excellence. Major areas of focus include:

- **Personalisation of treatment for hypertension.** We are leading a large Medical Research Council (MRC) funded stratified medicines programme.
- **British Heart Foundation/BHS Pathway trials.** These include studies in patients with resistant hypertension and comparison of which drug combinations are best in hypertensive patients who need treatment with a diuretic.
- **Curing hypertension.** A substantial proportion of people with hypertension may have it due to over-production of the hormone aldosterone from a nodule in one of the adrenal glands – hyperaldosteronism. Although this condition is treatable by minimally invasive surgery and often cures hypertension, it can be difficult to identify. We are part of a UK-wide trial (the National Institute for Health Research-funded MATCH Trial) to assess a new simple imaging technique for the diagnosis of hyperaldosteronism.
- **New treatments for hypertension.** We are researching the effect of dietary nitrate to lower blood pressure. This is found in green leafy vegetables and beetroot and could be a very simple treatment for blood pressure.

- **Risk stratification.** We have developed a new imaging biomarker that offers much promise for guiding treatment to prevent future heart failure related to hypertension.
- **Mental stress and hypertension.** We have recently identified an important link between the brain and blood pressure which involves an enzyme called nNOS that is found in both the brain and blood vessels. This may account for the well-recognised but poorly understood relationship between stress and hypertension.<sup>18,19</sup>

## Using genetics to match the drug to the patient in hypertension

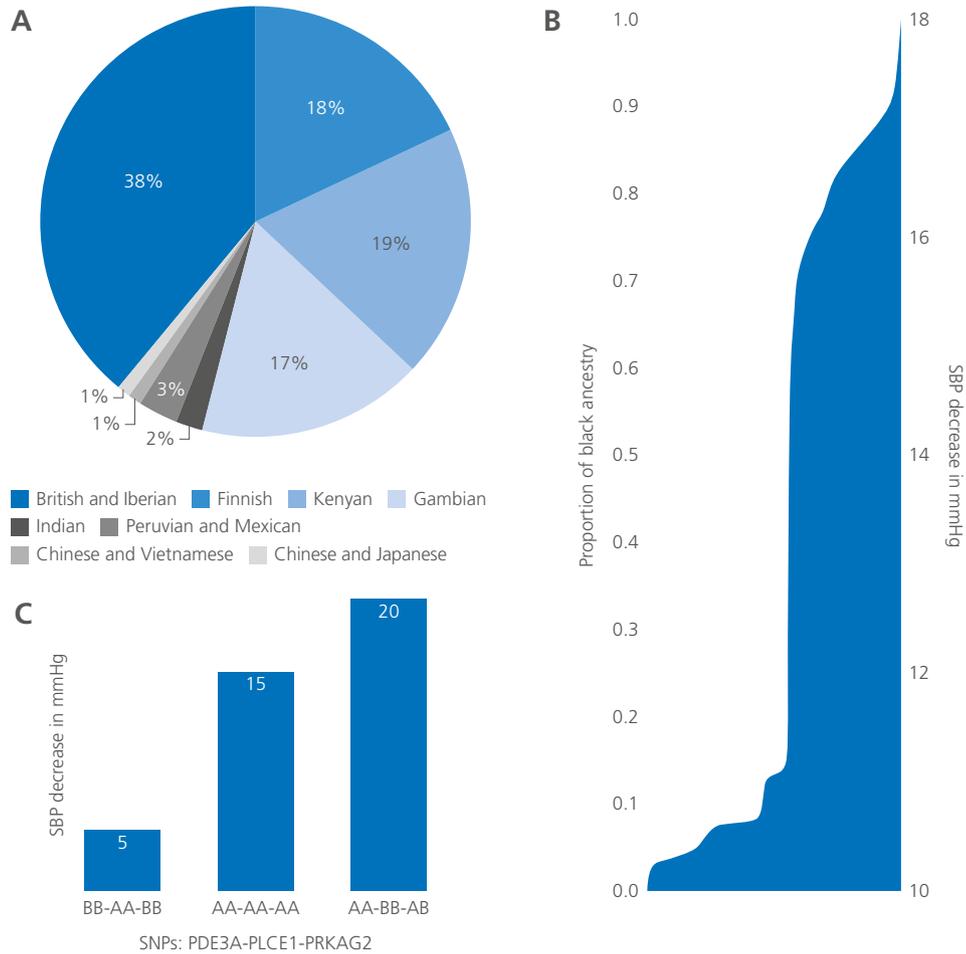
High blood pressure (hypertension) is the single largest cause of death and disability in the world. Although a healthy lifestyle is important, most people with hypertension require drug treatment. There are many different drugs used for hypertension but there is a large variation from one person to another in their response to each type of drug. Finding the right drug or combination of drugs for an individual often involves time-consuming “trial and error” and is frustrating for patients. In the AIM HY programme (The Ancestry and biological Informative Markers in the stratification of Hypertension), we are trying to find ways of predicting which drug(s) will work best in individual patients so that we can avoid the trial and error approach. We have identified genetic markers that differ in patients of different ethnicity and are now carrying out a clinical trial to test whether these can be used to match the right drugs to patients. This may be particularly important in some ethnic minority groups who we know respond less well to some of the commonly used drugs.

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18 Blood Pressure in Healthy Humans is Regulated by Neuronal NO Synthase. Shabeeh H, Khan S, Jiang B, Brett S, Melikian N, Casadei B, Chowienczyk PJ, Shah AM. *Hypertension* 2017;69(5):970–976.

19 Impaired neuronal nitric oxide synthase-mediated vasodilator responses to mental stress in essential hypertension. Khan SG, Geer A, Fok HW, Shabeeh H, Brett SE, Shah AM, Chowienczyk PJ. *Hypertension* 2015;65(4):903–909.

**Figure 41** | Using genetics to match the drug to the patient in hypertension



A: Genetic markers can be used to find the genetic ancestry of patients – the proportion of genes they have inherited from ancestors from certain populations. B: The blood pressure lowering effect of many drugs relates to people’s genetic ancestry (here the amount of African ancestry). C: Much of the variation in drug response can be predicted by just a few gene variants (or SNPs) which could be used to select which drug to use based on an individual person’s genetics.



Creating networks

# Creating networks

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## King's Health Partners Cardiovascular

Our vision for King's Health Partners Cardiovascular is to provide excellent care for patients, along with academic excellence and clinical innovation, to create a truly "world-class" service. By working with a wide range of partners, including service providers, health professionals, patients, patient representatives, academics and commissioners we seek to develop a new type of clinical academic network. The principal objective of the new model of care is to put the patient at the centre of all pathways and improve care across the whole pathway from the most specialist quaternary services to care in secondary, community and primary care settings.

Current clinical networks for cardiovascular services in south east London and Kent are generally informal and often based on historical arrangements. Our vision is to harmonise and improve these networks, and to modernise them by making best use of new advances in diagnosis and treatment and innovative changes in clinical practice, for example, those based on

digital technology and data science. We would like to see rapid translation of new advances to benefit patients throughout the network. In addition, the clinical academic network will provide a platform for workforce education and training. Critical to our success will be a distributed leadership model and engaging clinicians at all levels. With all these factors, we will create breakthroughs in the way our patients receive care and the excellent outcomes achieved; more care can be delivered closer to patients' homes, and patients will only need to travel to larger centres for the most complex treatments.

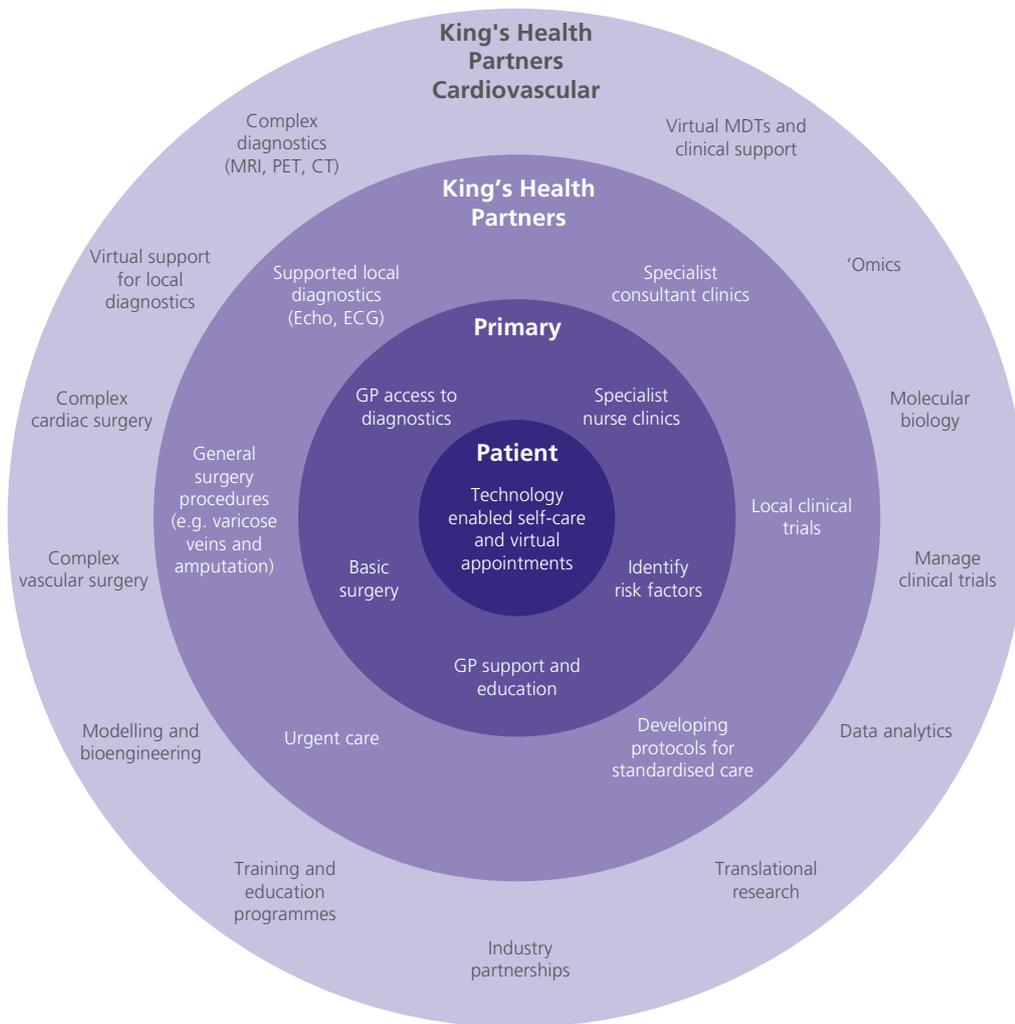
The network will bring together all stakeholders to develop a cardiovascular service that:

- improves patient outcomes and satisfaction;
- provides equity of access for patients;
- uses robust clinical evidence, expertise and leadership to drive strategic planning and commissioning decisions;

- reduces variation in service delivery, including direct service improvement opportunities;
- provides more of the right care in the right place by the right people;
- rapidly translates innovations in care;
- makes best use of new developments in IT, digital technology, clinical informatics and data science;
- focuses on prevention;
- integrates education and training resource across the network; and
- provides best overall value for money for care across the health system.

King's Health Partners cardiovascular will combine clinical and academic excellence and provide the opportunity to completely transform the provision of care using a value based healthcare approach for our population across a large integrated network in south east London, Kent and potentially further afield.

**Figure 42 | Patient-centred model of care in the clinical academic network**



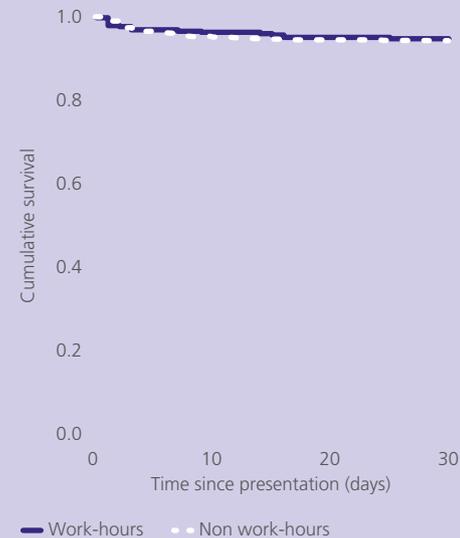
## Case study: Development of King's Health Partners' heart attack services

King's College Hospital and Guy's and St Thomas' NHS Foundation Trusts both provide a 24/7 primary angioplasty service for heart attack patients. This is a life-saving alternative to clot-busting drugs. It involves having a tiny balloon inserted under local anaesthetic and then inflated to clear the blocked artery carrying blood to the heart. Prior to 2007, the proportion of people receiving the gold-standard primary percutaneous coronary interventions (PPCIs) for ST-elevation myocardial infarction (STEMI) in England was less than 20% – one of the worst in Europe.

**The cardiac networks have since delivered the transformation required to deliver PPCI to over 99% of patients suffering STEMI, as well as the improvement in other operational metrics e.g. door-to-balloon time that can impact outcomes. The service delivers excellent outcomes for patients both in normal working hours and at weekends/night time (see Figure 43).**

Despite being a key part of national policy, the service required local implementation, working across organisational boundaries such as the ambulance services, the district general hospital, the PPCI centre and rehabilitation services. A key driver for change has been the publication of performance-related data from the Myocardial Ischaemia National Audit Project (MINAP).

**Figure 43 | 1,120 consecutive patients**





The physical and mental  
healthcare interface

# The physical and mental healthcare interface

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The mind and body are inseparable. We are committed to caring for physical and mental ill health across the cardiovascular interface in an integrated manner, with eight Mind and Body Champions across King's Health Partners Cardiovascular.

## Mental well-being in patients with cardiovascular conditions

Acute and chronic cardiac conditions and treatments – such as heart attacks, heart failure, cardiac surgery, implantation of defibrillators – are frequently accompanied by significant anxiety and depression. Failure to adequately diagnose and manage co-existent mental health problems leads to multiple re-admissions, poor quality of life and difficulty in controlling the physical health problem.

## IMPARTS

The Integrating Mental & Physical Healthcare: Research, Training and Services (IMPARTS) programme improves mental healthcare provision within medical settings across King's Health Partners. IMPARTS is provided through five components: outcome assessment/informatics, care pathways, self-help materials, research, and training/education.

IMPARTS is currently embedded in 12 cardiovascular clinics as well as in certain inpatient services, strengthening the screening for significant mental health issues. Early work performed through the IMPARTS programme shows that:

- 6.1% of patients with adult congenital heart disease have probable major depressive disorder and 9.7% have probable generalised anxiety disorder;

- 27.8% of inpatients and 9.6% of outpatients with endocarditis have probable major depressive disorder.

Cardiovascular-specific resources developed through IMPARTS include:

- Overcoming your Fear of Needles in Adult Congenital Heart Disease;
- Breathlessness and Anxiety in Adult Congenital Heart Disease – both adopted by the national charity, the Somerville Foundation;
- Coping After Endocarditis (short and long versions).

## 3DLC (three dimensions of long-term conditions) programme

Psychological support is especially important in patients with long-term conditions and is currently implemented in the adult congenital heart disease, heart failure, cardiac rehabilitation, complex blackouts, and long-term venous ulcer services. In the heart failure service, community-based psychologists work closely with nurse specialists and GPs as well as providing individual support.

## Cardiovascular health in patients with severe mental illness

Patients with mental illness have significant morbidity and mortality related to cardiovascular disease. Patients with persistent anxiety often present with chest pain and may undergo unnecessary investigations for physical heart disease. Many drugs used to treat severe psychosis and similar conditions have significant cardiovascular side-effects.

- King's Health Partners Cardiovascular runs a dedicated service for patients on anti-psychotic drugs who are suspected of having disturbances of heart rhythm and/or function;
- Working alongside the Psychosis Clinical Academic Group, we are establishing a routine ECG assessment service for patients admitted with acute mental health problems and/or initiated on new drugs.



Value based healthcare

# Value based healthcare

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## Infective endocarditis – a holistic approach

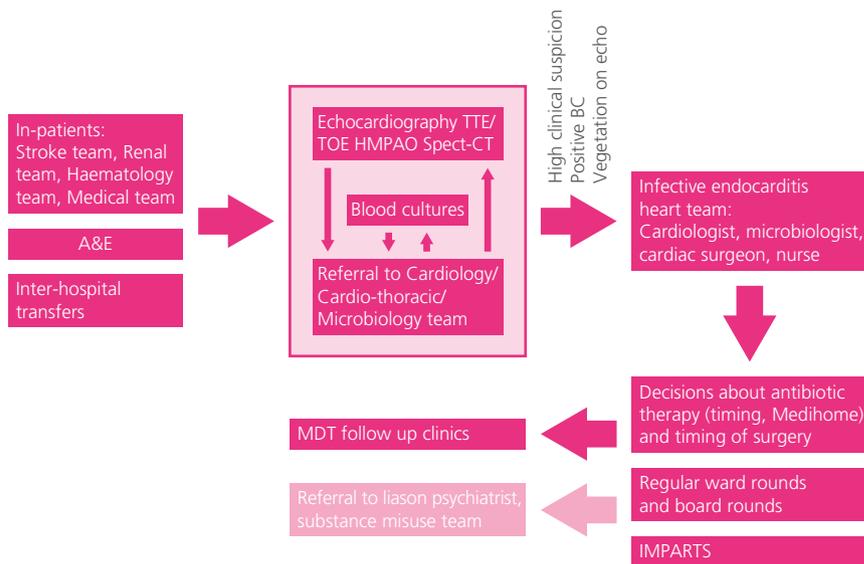
Infective endocarditis (IE) is associated with substantial morbidity and poor survival, with 14–22% in-hospital and up to 40% one-year mortality rates. Prompt diagnosis and antibiotic therapy and early surgical intervention, when indicated, has been shown to improve patient outcomes.

At the end of 2012 we introduced the value based approach to treatment of patient with Infective Endocarditis. We established multidisciplinary working groups, consisting of clinicians (cardiologist, microbiologist, cardiac surgeon, nurses) and non-clinicians (managers, financial specialist, IT specialist and patients). From March 2013, we started to collect information prospectively and have a fully functional multidisciplinary IE team (see Figure 44).

To improve patient outcomes and value of our care, our aim is early identification of patients with suspected IE, early optimise antimicrobial therapy and finally to refer them for early cardiac surgery if indicated. In addition, we introduced a routine use of web-based screening interface (IMPARTS) for patient-reported mental and physical outcome measures and embedded in routine clinical practice.

**175 patients with infective endocarditis were treated between 2010 and 2015. In this time period thanks to the value based MDT approach, we managed to reduce time from the suspicion of IE to valve surgery from eight days to five days. This was associated with a reduced duration of inpatient stay by 17% from 30 days to 25 days and an improved in-hospital and one-year mortality from 20% to 13% and 30% to 23%, respectively.**

**Figure 44 | MDT approach to IE**



**When to refer a patient to IE team (DH-site) referrals from cardiology/microbiology/CT SpRs**

1. All confirmed IE cases
2. Possible IE
3. Inconclusive cases with high clinical suspicion

**When to refer a patient to IE team (PRU-site) referrals from cardiology/microbiology consultant**

1. Complicated IE (HF, abscess, embolic complications, high embolic risk) early transfer and management on DH site – if haemodynamically unstable direct referrals to on-call CT/Cardiology team
2. Non-complicated IE managed on PRU site after discussion with IE team
3. Possible IE, inconclusive cases with high clinical suspicion

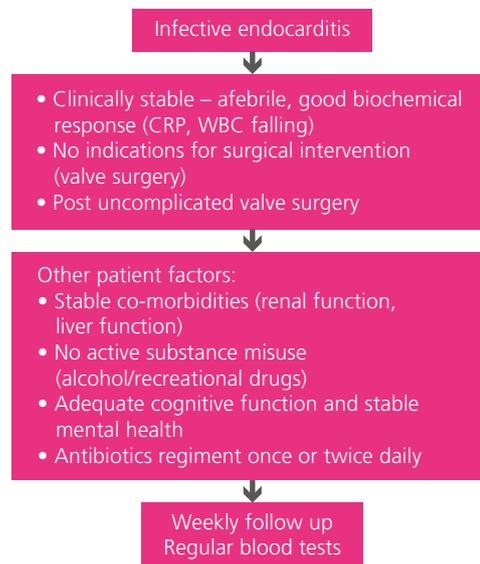
**In the last 3 years, the in-hospital mortality for medically (8%) and surgically (9%) treated IE has substantially reduced.**

Our care for patients with IE does not finish in-hospital. We have established follow up IE clinics, where patients are reviewed after their discharge or while being on outpatient parenteral antimicrobial therapy (OPAT). OPAT has been shown to be efficacious, safe and cost-effective for a variety of infections but data regarding managing IE with out of hospital parental antibiotics is limited. Critical for OPAT in IE patients is safety and regular evaluations by the IE team. Patients suitable for OPAT are identified using the algorithm in Figure 45.

## Mind and body

About 30% of patients with infective endocarditis have significant psychological distress (anxiety or depression) at presentation. After completion of treatment about 17% still require some support and specialist help. As such we provide continuous patient support by enabling patients direct access to CNS/consultants, patient information leaflets and health advice.

**Figure 45 |** Algorithm to identify patients suitable for OPAT<sup>20</sup>



<sup>20</sup> Inception of the 'endocarditis team' is associated with improved survival in patients with infective endocarditis who are managed medically: findings from a before-and-after study. Kaura A, Byrne J, Fife A, Deshpande R, Baghai M, Gunning M, Whitaker D, Monaghan M, MacCarthy PA, Wendler O, Dworakowski R. *Open Heart* 2017; 4(2):e000699.



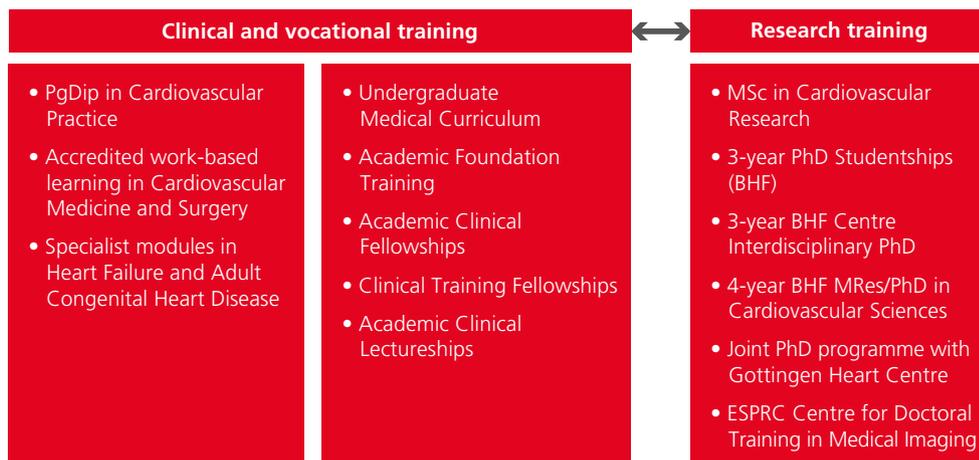
Education and training

# Education and training

King's Health Partners Cardiovascular provides an extensive and distinctive range of postgraduate scientific research training (PGR) programmes (see Figure 46). We have a strong track record of training and mentoring early career non-clinical and clinical academic fellows, and the School of Cardiovascular Medicine and Sciences holds an Athena Swan Silver Charter Award.

We also provide NHS-based educational activities including the coordination and delivery of training for specialist registrars in cardiology, cardiac surgery, vascular surgery and clinical pharmacology; as well as the training of clinical scientists and specialist nurses.

**Figure 46** | Overview of education and training delivered by King's Health Partners Cardiovascular



## Development of new programmes/consolidation of programmes

The education oversight committee has representatives who lead education for undergraduates and postgraduates in the faculties of nursing and medicine within King's College London and are embedded in the Cardiovascular Educational Academy responsible for work-based learning at Guy's and St Thomas' NHS Foundation Trust and King's College Hospital NHS Foundation Trust.

The undergraduate medical curriculum has been reorganised and a new vascular teaching block has replaced the previous arrangement which focussed teaching around a single consultant (the "firm"). The new curriculum went live in October 2018 with teaching that is grounded on the physiology, pathology and pharmacology of the heart and blood vessels. The formal lectures and learning by watching clinical practise are organised over four, eight-week blocks and accommodate 420 students per year. The curriculum is coordinated by King's Health Partners Cardiovascular over Guy's and St Thomas' NHS Foundation Trust, King's College Hospital NHS Foundation Trust and Queen Elizabeth Hospital, Lewisham and Greenwich

NHS Trust campus and is preceded by one week of introductory lectures. We:

- Train 420 medical students per year in cardiovascular medicine;
- Award prize scholarships to encourage the brightest medical students to devote one year to a Bachelor of Science Degree in Cardiovascular Biology;
- Offer a range of intercalated Bachelor of Behavioural Science degrees tailored to medical students' interests.

The postgraduate taught medical curriculum delivers training in all the cardiovascular specialties. Training is divided into traditional and integrated tracks. The integrated track combines traditional clinical training with academic training and allows trainees to devote up to 50% of their time to research and teaching. We accommodate 10 integrated academic trainees with a recent expansion achieved through winning posts in competition across specialties and geographic regions.

We offer training for established specialists in various aspects of advanced care including surgery and diagnostic imaging. For example, PCR London Valves, is the world's largest educational meeting dedicated to valvular heart disease with a global faculty and greater than 2,500 participants. The King's Health Partners teams include the Principal Course Director and senior members of the Programme Board. The combined clinical teams have extensive experience of live case demonstrations to global audiences exceeding 10,000 and transmit innovative procedures live at the most prestigious international meetings in interventional cardiology.

At King's Health Partners we:

- offer training in all aspects of cardiology and cardiac and vascular surgery;
- protect 3 and 6 months blocks each year from clinical activity for trainees to have dedicated training in research;
- train overseas specialists in all aspects of cardiology;
- host PCR London Valves.

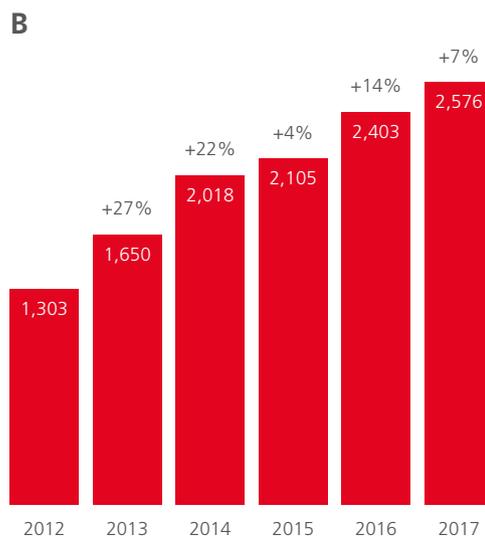
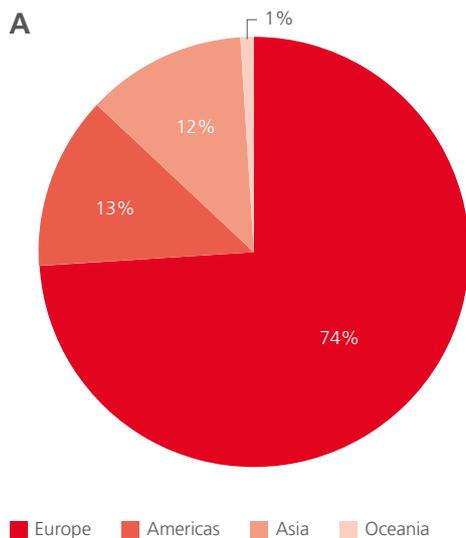
The postgraduate taught non-medical curriculum is evolving very rapidly to enable us to modernise our workforce, introduce seven day working and reduce the burden on medical staff in King's Health Partners Cardiovascular. The training is mainly provided in the workplace through partnerships between the hospitals

and the university that accredit a mixture of classroom, online and "on-the-job" learning. These schemes allow non-medics to adopt roles traditionally viewed as medical by learning how to assess patients, prescribe drugs and perform surgery under standardised conditions. The portfolio of courses we have developed and plan to develop dovetail with one another to allow students to become advanced practitioners and work independently in defined subspecialties with high workloads.

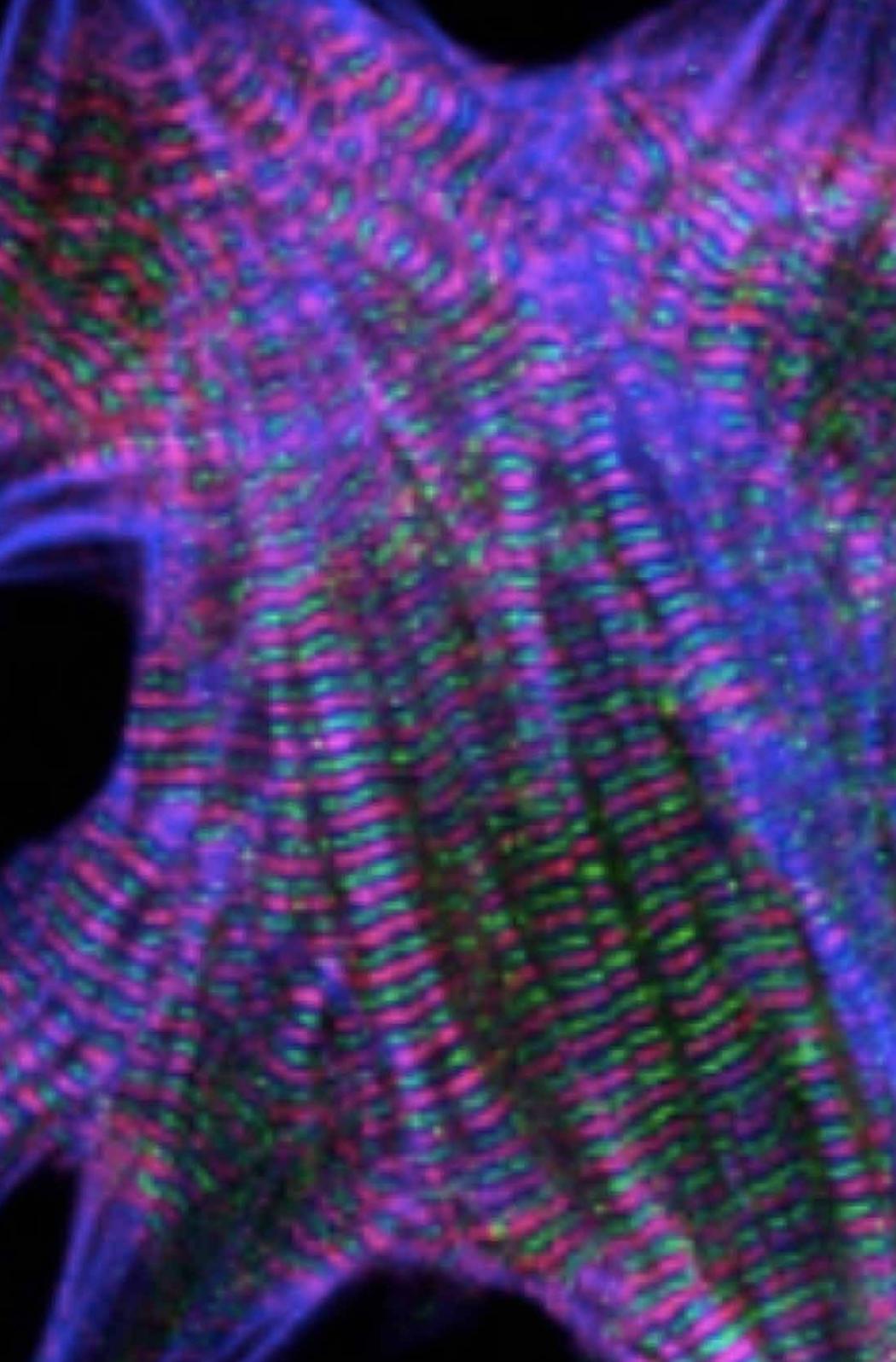
- Offer innovative courses in Heart failure, Advanced Assessment Skills for Non-Medical Practitioners and Principles of Cardiovascular Medicine leading to a Masters in Science;
- Teaching integrated with the Florence Nightingale School of Nursing, ranked number one in the UK;
- Formal and approved structures to supervise and accredit workplace-based learning.

We offer a range of postgraduate research courses for medical and non-medical staff. These occur at Masters and Postgraduate Doctoral Degree Levels. The Masters courses often progress to Doctorate level and involve blended learning with rotation through different laboratories and research projects to provide "tasters". These laboratories may be overseas since we have strategic research grants and formal training links with several external universities and award Postgraduate Doctoral Degrees jointly with the University of Göttingen.

**Figure 47** | PCR London valves is the world's largest and leading meeting dedicated to education and training in minimally invasive valve surgery. Currently it has fostered two subsidiary meetings PCR Chengdu China Valves (n=900) and PCR Tokyo Valves (n=800) in which King's Health Partners Cardiovascular is closely involved.



- Wide portfolio of Postgraduate Doctoral Degree programmes including 4-year programmes in the British Heart Foundation centre and Medical Research Council doctoral training centre that promote interdisciplinary research and reciprocal joint training at overseas centres of excellence;
- In 2018 we had 35 medics and 108 scientists studying for Postgraduate Doctoral Degrees.



Research

# Research

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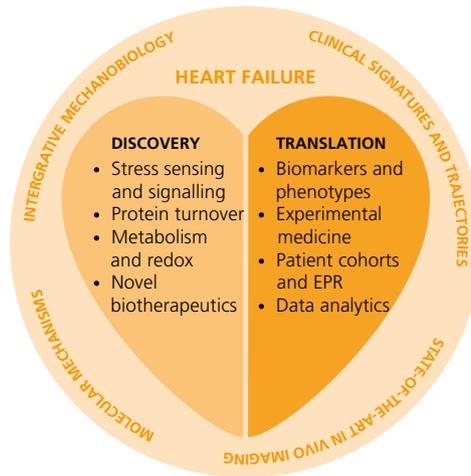
King's Health Partners Cardiovascular research activities are centred around the King's British Heart Foundation Centre of Research Excellence and the National Institute for Health Research Biomedical Research Centre. The King's British Heart Foundation Centre was established through a national competition in 2008 and competitively renewed in 2014 and 2018. It has to date received the highest amount of funding of any UK British Heart Foundation Centre.

Our mission is to improve outcomes for patients with cardiovascular conditions through research-led discovery and innovation, including:

- Improved prevention, diagnosis and monitoring (through imaging, biomarkers, genetic risk, modelling and data science);
- New therapies and therapeutic targets (through expertise in basic and translational cardiovascular science and experimental medicine);
- Clinical innovation such as novel minimally-invasive procedures, novel devices, imaging-guided interventions and personalised treatment.

The British Heart Foundation Centre nurtures a critical mass of multi-disciplinary scientists within a highly collaborative state-of-the-art environment to facilitate internationally-leading research programmes with clear translational potential (Figure 48). It has a particular focus on heart failure but also delivers world-class research in other areas such as muscle cell biology, cardiac regeneration, cardiovascular biomarkers, drug discovery, *in vivo* cardiovascular imaging and vascular disease. Leading edge technologies that are applied to cardiovascular disease include proteomics, genetics, *in vivo* imaging, molecular biophysics, structural biology, super-resolution microscopy, stem cell modelling and others. The British Heart Foundation Centre attracts the most talented individuals to training programmes and careers in cardiovascular science and academic medicine.

**Figure 48** | An illustration of the integrative approach to research that is deployed within the King's British Heart Foundation Centre through a critical mass of multi-disciplinary expertise and state-of-the-art underpinning technologies.



## Some facts and figures about King's Health Partners cardiovascular research

- >100 independent principal investigators including 5 British Heart Foundation Professors;
- Current research grant income of over £114 million since 2014;
- Since April 2014, Centre PIs have published >700 peer-reviewed papers;
- 29 new group leaders appointed since 2014;
- Number one recipient of British Heart Foundation research funding in the UK (see Tables 1 and 2);
- 13 Programme Grants, five Foundation Leducq Transatlantic Networks of Excellence, three European Research Council Advanced Investigator Awards and three British Heart Foundation Translational Awards;
- Approximately £10m research funding within the Biomedical Research Centre cardiovascular theme;
- Dedicated cardiovascular Clinical Research Facility;
- 28 patents filed since 2014 leading to two spinout companies;
- World-leading "Field weighted citation index", an internationally recognised metric that describes the quality of research publications (based on the number of citations as compared to the average number of citations weighted for the specific research field) (see Figure 49);
- 48% of research was rated internationally-leading and 45% internationally competitive in the last UK research assessment exercise (REF 2014);
- Research publications in all the top basic and clinical scientific journals (e.g. Nature, Science, Nature Medicine, Cell, NEJM, JAMA, Lancet, JCI, Nature Genetics, Nature Cell Biology, PNAS).

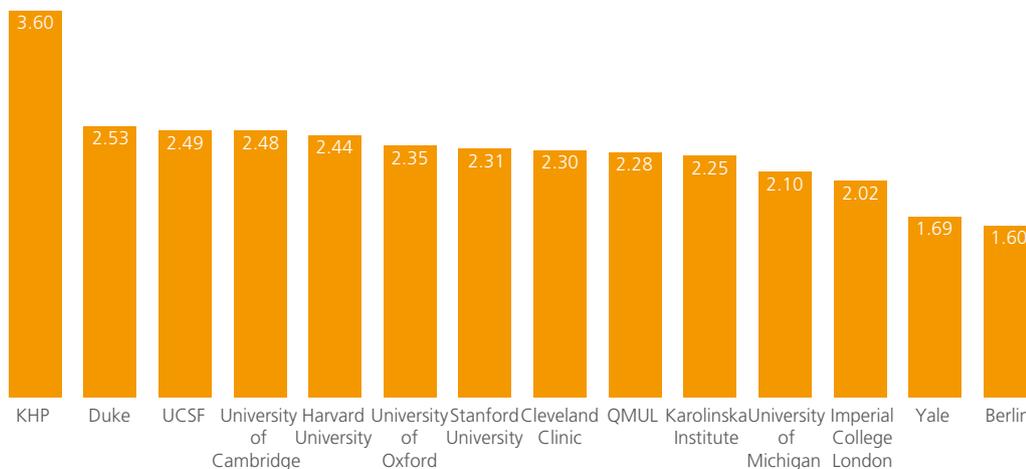
**Table 1** | Total British Heart Foundation funding for research in 2016–17, by institution (number of awards given to the top 10 institutions)

Institution	Number of awards
King's College London	26
University College London	25
Imperial College London	23
University of Oxford	18
University of Edinburgh	15
University of Leeds	15
University of Bristol	14
University of Cambridge	11
University of Glasgow	10
University of Manchester	9

**Table 2** | Total British Heart Foundation funding for research in 2016–17, by institution (amount awarded to the top 10 institutions)

Institution	Amount awarded (£m)
King's College London	14.0
University of Oxford	11.0
Imperial College London	8.4
University of Leeds	6.7
University College London	6.3
University of Leicester	5.9
University of Edinburgh	5.9
University of Cambridge	5.4
University of Bristol	4.2
University of Glasgow	3.3

**Figure 49** | Field-weighted citation index as a marker of research quality, comparing King's Health Partners Cardiovascular (orange) with other cardiovascular leading national and international institutions



Source: King's Health Partners internal analysis.

## Research partnerships

We collaborate closely with other foci of excellence within King's Health Partners, such as the Randall Centre in the School of Basic and Translational Biomedical Sciences, the School of Biomedical Engineering and Imaging Sciences and others. These interactions are promoted through joint PhD studentships and short-term grant awards.

International partnerships include major initiatives with the Heart Centre Göttingen (Germany) and the University of Pennsylvania Division of Cardiovascular Medicine (USA).

We also have many strategic partnerships with industry and pharma in order to enhance the translational potential of our research and to drive clinical innovation.

## Research training and mentorship

King's Health Partners Cardiovascular provides a vibrant research and training environment that attract numerous high calibre scientists, early career researchers and students, thus developing the research leaders of the future. There are currently:

- Five prestigious externally-funded Senior Research Fellowships;
- 13 Intermediate (early career) Research Fellowships;
- 35 Clinical PhD Trainees;
- 108 non-clinical PhD students.

Basic scientists and clinical PhD Fellows work side by side and gain experience from the integration of skill sets across the spectrum of work. There is a strong focus on mentoring and career development of junior staff. The King's College London School of Cardiovascular Medicine and Sciences holds an Athena Swan Silver Award.

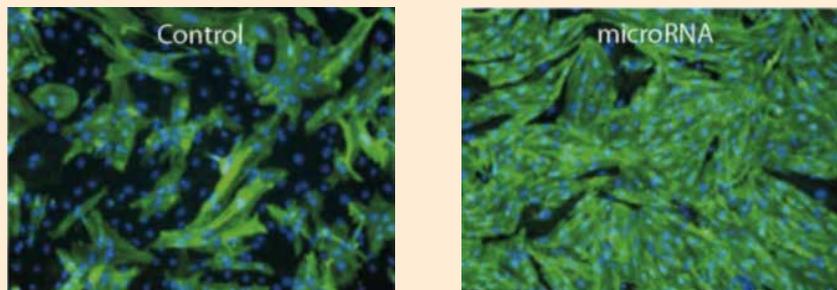
## Regenerating the heart

Cardiac injury due to heart attacks results in irreversible death of heart muscle cells, which are replaced by scar tissue. This commonly leads to heart failure. Current treatments can slow progression of heart failure but do not cure it.

Our latest senior international recruit, Mauro Giacca, Professor of Cardiovascular Sciences, is a world leader in cardiac regenerative medicine with a focus on developing new therapies for cardiovascular disorders such as heart failure.

Formerly the Director General of the United Nations International Centre for Genetic Engineering and Biotechnology (ICGEB) in Trieste (Italy), Professor Giacca has identified novel biological agents that promote heart regeneration by stimulating healthy heart muscle cells to multiply and thus replace the scarred portions of the heart. These novel agents are microRNAs, which are short stretches of nucleic acids that can simultaneously target multiple proteins and therefore an entire process – such as muscle cell division. These microRNAs can be synthesized and used as potential drugs and have been found experimentally to promote heart repair and markedly improve function after heart attacks. The aim over the next few years is to develop this advance into a unique treatment for humans.

**Figure 50** | Heart muscle cells treated with specific microRNAs (right) show an increase in division and cell number



MicroRNA therapy stimulates uncontrolled cardiac repair after myocardial infarction in pigs. Gabisonia K, Prosdocimo G, Aquaro GD, Carlucci L, Zentilin L, Secco I, Ali H, Braga L, Gorgodze N, Bernini F, Burchielli S, Collesci C, Zandona L, Sinagra G, Piacenti M, Zacchigna S, Bussani R, Recchia FA, Giacca M. *Nature* 2019. In press.

## Selected research highlights

### Cardiac myosin-binding protein C – a novel biomarker of heart injury

Research lead: Professor Michael Marber

Direct Comparison of Cardiac Myosin-Binding Protein C with Cardiac Troponins for the Early Diagnosis of Acute Myocardial Infarction. Kaier TE, Twerenbold R, Puelacher C, Marjot J, Imambaccus N, Boeddinghaus J, Nestelberger T, Badertscher P, Sabti Z, Giménez MR, Wildi K, Hillinger P, Grimm K, Loeffel S, Shrestha S, Widmer DF, Cupa J, Kozuharov N, Miró O, Martín-Sánchez FJ, Morawiec B, Rentsch K, Lohrmann J, Kloos W, Osswald S, Reichlin T, Weber E, Marber M, Mueller C. *Circulation* 2017;136(16):1495–1508

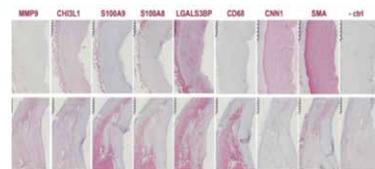
There are over 2.2 million attendances to Emergency Departments in England per year, with 10% of these attributed to chest pain. A minority of these will have heart attacks and it is therefore important to identify these patients as rapidly as possible so that others who do not have a serious cardiac problem can be discharged. The current blood test (troponin) that is used to rule out heart attacks can only do this after several hours in most patients. The King's Health Partners team have identified cardiac myosin binding protein C (cMyC) as a diagnostic biomarker that rises and falls much more quickly than troponin and can therefore rule out heart attacks quicker and more accurately. In a study of nearly 2,000 patients who presented with chest pain in hospitals across Europe, published in the journal *Circulation*, Professor Marber's team confirmed that cMyC can correctly exclude a heart attack in twice as many people as the troponin test. They are now working to develop a point-of-care diagnostic device that could be used in emergency departments, potentially saving the NHS millions of pounds and patients countless hours of waiting in hospital.



### A proteomics-based signature for the prediction of cardiovascular disease

Research lead: Professor Manuel Mayr

Extracellular matrix proteomics identifies molecular signature of symptomatic carotid plaques. Langley SR, Willeit K, Didangelos A, Matic LP, Skroblin P, Barallobre-Barreiro J, Lengquist M, Rungger G, Kapustin A, Kedenko L, Molenaar C, Lu R, Barwari T, Suna G, Yin X, Iglseder B, Paulweber B, Willeit P, Shalhoub J, Pasterkamp G, Davies AH, Monaco C, Hedin U, Shanahan CM, Willeit J, Kiechl S, Mayr M. *Journal of Clinical Investigation* 2017;127(4):1546–1560



The identification of people who are high risk of cardiovascular complications, such as heart attacks and strokes, is an important aim for cardiovascular prevention. Current methods rely simply on “risk factors” such as smoking and high blood pressure and the measurement of blood cholesterol, but are imperfect. In this study published in the *Journal of Clinical Investigation*, the King's Health Partners team led by British Heart Foundation Professor Manuel Mayr used state-of-the-art proteomics and genetics approaches to analyse tissue specimens from patients who had undergone surgery for carotid narrowings. They were able to identify a molecular signature of “unstable plaques”, that is, narrowings that are more likely to cause complications. The team then developed a test based on 4 blood biomarkers that was able to predict the occurrence of cardiovascular complications in two separate European populations. This is a very promising approach to improve cardiovascular risk prediction, which will now be further refined and developed.

### A new bioinformatics tool for the diagnosis of patients with genetic heart disease

Research leads: Professors Mathias Gautel and Franca Fraternali

TITINdb – a computational tool to assess titin's role as a disease gene. Laddach A, Gautel M, Fraternali F. *Bioinformatics* 2017; 32(21):3482–3485



Dilated cardiomyopathy is a type of heart failure that is often caused by gene mutations. It has recently become evident that there are hundreds of genetic variants in a protein called titin, which is the largest protein in the body and forms an important structural element in heart muscle. However, many apparently normal healthy people also have some of these variations in the titin gene. Because titin is a very large gene, it is very unclear which of these variants are disease-causing mutations and which ones are just an innocent variant (the analogy would be normal gene variants, e.g. those that affect eye colour). British Heart Foundation Professor Gautel, a world-leading expert in titin and genetic heart disease, along with Professor Fraternali

(a bioinformatician), was able to develop a web-based tool (TITINdb) which allows the classification of titin variants as disease-causing or normal as well as predict the impact of the variant. This tool is now freely available around the world for any inherited heart disease specialist to use.

### **Blood pressure regulation by nerves – a new target for treatment?**

Research lead: Professor Ajay Shah

Blood Pressure in Healthy Humans is Regulated by Neuronal NO Synthase. Shabeeh H, Khan S, Jiang B, Brett S, Melikian N, Casadei B, Chowienczyk PJ, Shah AM. *Hypertension* 2017;69(5):970–976



High blood pressure remains one of the most important causes of cardiovascular disease worldwide and there is a need for more effective treatments. In a world-first study in humans, the team led by British Heart Foundation Professor Shah along with Professor Phil Chowienczyk made the surprising discovery that a crucial regulator of blood pressure in healthy people is a chemical called nitric oxide released by nerves surrounding blood vessels. The nitric oxide is produced by an enzyme called nNOS and when the team used an inhibitor of nNOS, they found that blood pressure was increased by a surprisingly large amount. They also found that the nNOS pathway is defective in many patients with hypertension, suggesting that this abnormality may be contributing to the high blood pressure. This discovery fundamentally changes the way we view the regulation of blood pressure. Until now the majority of blood pressure drugs have focussed on other pathways. Establishing that nerves releasing nitric oxide influence blood pressure provides a new target for drugs and could eventually lead to more effective treatments for patients.

### Developing new drugs for cardiovascular disease

Research lead: Professor Phil Eaton

Proof of Principle for a Novel Class of Antihypertensives That Target the Oxidative Activation of PKG Ia (Protein Kinase G Ia). Burgoyne JR, Prysazhna O, Richards DA, Eaton P. *Hypertension* 2017;70(3):577–586

Most medicines that are used to treat cardiovascular disorders work by targeting important cellular pathways that are involved in the disease process. One such disease pathway involves a protein enzyme called PKG (protein kinase G). It is known that PKG is involved in conditions such as hypertension, cardiac hypertrophy, heart failure and stroke but there are currently no drugs that target PKG. The team led by Professor Eaton has identified the precise molecular mechanisms involved in the activation of PKG. In their latest work, they have now developed the first drug that is able to activate PKG and demonstrated proof-of-concept in laboratory studies that this drug can have beneficial effects on blood pressure. This is a crucial step in the development of a new class of medicines that could be used to treat cardiovascular disorders.

### 1-year outcomes after transcatheter aortic valve implantation in the SOURCE 3 registry

Research lead: Professor Olaf Wendler

SOURCE 3: 1-year outcomes post-transcatheter aortic valve implantation using the latest generation of the balloon-expandable transcatheter heart valve. Wendler O, Schymik G, Treede H, Baumgartner H, Dumonteil N, Neumann FJ, Tarantini G, Zamorano JL, Vahanian A. *European Heart Journal* 2017;38(36):2717–2726

Transcatheter aortic valve implantation (TAVI) has developed from a procedure for patients who are unsuitable or too high risk for conventional surgery into a treatment option even for intermediate risk elderly patients. This study in the *European Heart Journal* led by Professor Wendler of the King's Health Partners TAVI team presents the European results of the latest generation balloon-expandable SAPIEN 3 valve in nearly 2000 patients across 80 centres and 10 European countries. The mean age of the treated patients was 81.6 years. One year after TAVI, the all-cause mortality was 12.6%, cardiovascular mortality 8.0%, stroke 3.1%, disabling stroke 1.4%, and rate of new pacemakers 13.2%. On multivariable analysis, the main predictors of mortality were poor kidney function and a worse cardiac state before TAVI. Valve function remained very good in the vast majority of patients, without significant leaking. This study confirms that TAVI using the latest generation valves is an increasingly safe and effective treatment for severe aortic stenosis.

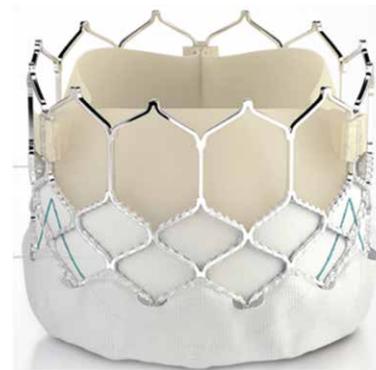


Image: Edwards SAPIEN 3™ Transcatheter heart valve. © Edwards Lifesciences Corporation 2018

### **Cost effectiveness of implementing the new NICE guidelines on ruling out acute heart failure using plasma NT-proBNP levels**

Research lead: Dr Gerry Carr-White

A cost effectiveness study establishing the impact and accuracy of implementing the NICE guidelines lowering plasma NTproBNP threshold in patients with clinically suspected heart failure at our institution. Webb J, Draper J, Rua T, Yiu Y, Piper S, Teall T, Fovargue L, Bolca E, Jackson T, Claridge S, Sieniewicz B, Porter B, McDiarmid A, Rajani R, Kapetanakis S, Rinaldi CA, Razavi R, McDonagh TA, Carr-White G. *International Journal of Cardiology* 2018; 257:131–136

Plasma NT-proBNP levels below a threshold are used to rule out heart failure (HF) in patients who present with breathlessness and suspected HF. The 2014 National Institute of Clinical Excellence (NICE) guidelines on the management of acute HF updated previous guidelines and lowered the NT-proBNP threshold from 400pg/ml to 300pg/ml, based on trials performed in other countries. In this study, the King's Health Partners HF team led by Dr Carr-White examined the diagnostic and economic implications of using this new threshold in a large unselected "real-world" UK population. Nearly 2,000 consecutive patients with clinically suspected HF were included in the study, of whom 84% (1,683) had a NTproBNP >400pg/ml and of which 35% had a final confirmed diagnosis of HF. Lowering the threshold to 300pg/ml would have involved screening an additional 61 patients but would have identified only one new patient with HF. This would have involved additional costs of approximately £42k per new HF patient. This study highlights the importance of analysis of treatment and guideline recommendations in unselected "real-world" populations.

### **Radiation-Induced DNA Damage in Doctors Performing X-ray guided procedures**

Research lead: Professor Bijan Modarai

Radiation-Induced DNA Damage in Operators Performing Endovascular Aortic Repair. El- Sayed T, Patel AS, Cho JS, Kelly JA, Ludwinski FE, Saha P, Lyons OT, Smith A, Modarai B; Guy's and St Thomas' Cardiovascular Research Collaborative. *Circulation* 2017;136(25):2406–2416

The increasing use of minimally-invasive procedures performed under X-ray fluoroscopy has led to concerns about radiation exposure to the operators who may perform many such procedures every year. One of the most well recognised consequences of excessive radiation exposure is damage to DNA in cells and tissues which could predispose to cancer. This study investigated operators performing endovascular aortic repair (EVAR), a minimally invasive alternative to open aortic aneurysm/dissection surgery. The vascular surgery team led by Professor Modarai looked for evidence of DNA damage in circulating blood cells of operators before, during and after EVAR. They found significant evidence of DNA damage in blood cells immediately after certain complex procedures although this improved 24 hours later. Interestingly, the blood of different operators had different susceptibility to the same

radiation dose. They also found that shielding of the operators' legs (in addition to the normal upper body protection) prevented the DNA damage. The study highlights the importance of safeguarding the health of medical professionals as well as patients during new high-tech procedures.

### **Genetics of arterial stiffening with aging in the Twins UK cohort**

Research lead: Professor Phil Chowienczyk

Arterial stiffening is a heritable trait associated with arterial dilatation but not wall thickening: a longitudinal study in the twins UK cohort. Cecelja M, Jiang B, Keehn L, Hussain T, Silva Vieira M, Phinikaridou A, Greil G, Spector TD, Chowienczyk P. *European Heart Journal* 2018; 39(24):2282–2288

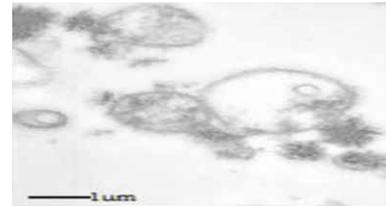
As we age, our arteries become stiffer and this is a major contributor to age-related cardiovascular complications such as hypertension and heart failure. On the other hand, thickening of the arteries relates to the risk of heart attacks. It is not clear to what extent stiffening and thickening are determined by conventional cardiovascular risk factors (such as smoking and high cholesterol) and how much is determined by genetic factors. The King's Health Partners team led by Prof Chowienczyk are studying the vascular changes that occur with ageing in the Twins UK cohort, a unique collection of hundreds of genetically identical twins in which it is possible to determine the relative contributions of genetics versus environmental influences. Detailed measurements of vascular properties were performed several years apart in 762 female twins. In this study published in the *European Heart Journal*, the authors found that 55% of the change in vascular stiffness with aging was heritable (i.e. likely to be genetically-determined) whereas only 8% of the change in vascular thickening was heritable. The important conclusion is that different aspects of vascular aging are determined by different factors. The genetic factors that influence progression of vascular aging are now being determined by the team.



### **Effect of anticoagulants on vascular calcification**

Research lead: Professor Cathy Shanahan

Prothrombin Loading of Vascular Smooth Muscle Cell-Derived Exosomes Regulates Coagulation and Calcification. Kapustin AN, Schoppet M, Schurgers LJ, Reynolds JL, McNair R, Heiss A, Jahnke-Dechent W, Hackeng TM, Schlieper G, Harrison P, Shanahan CM. *Arteriosclerosis, Thrombosis and Vascular Biology* 2017;37(3):e22–e32



Progressive calcification of arteries occurs in patients with diabetes, kidney disease, and in older individuals and contributes to problems in many parts of the body, e.g. the heart, kidneys, aorta and legs. Professor Shanahan, a world-leading expert on vascular calcification has previously found that small vesicular structures called exosomes released by vascular smooth muscle cells initiate the process of vascular calcification. In this study, the group investigated how exosomes regulate calcification. After undertaking a proteomic analysis of exosomes, they identified the presence of several coagulation factors in the exosomes. They then found that some of these coagulation factors could inhibit the effect of exosomes to cause calcification. The commonly used drug, warfarin, is a potent inhibitor of these coagulation factors and the group's findings suggest that warfarin could contribute to accelerated calcification in patients receiving this drug. This possibility should now be directly investigated in patients.

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