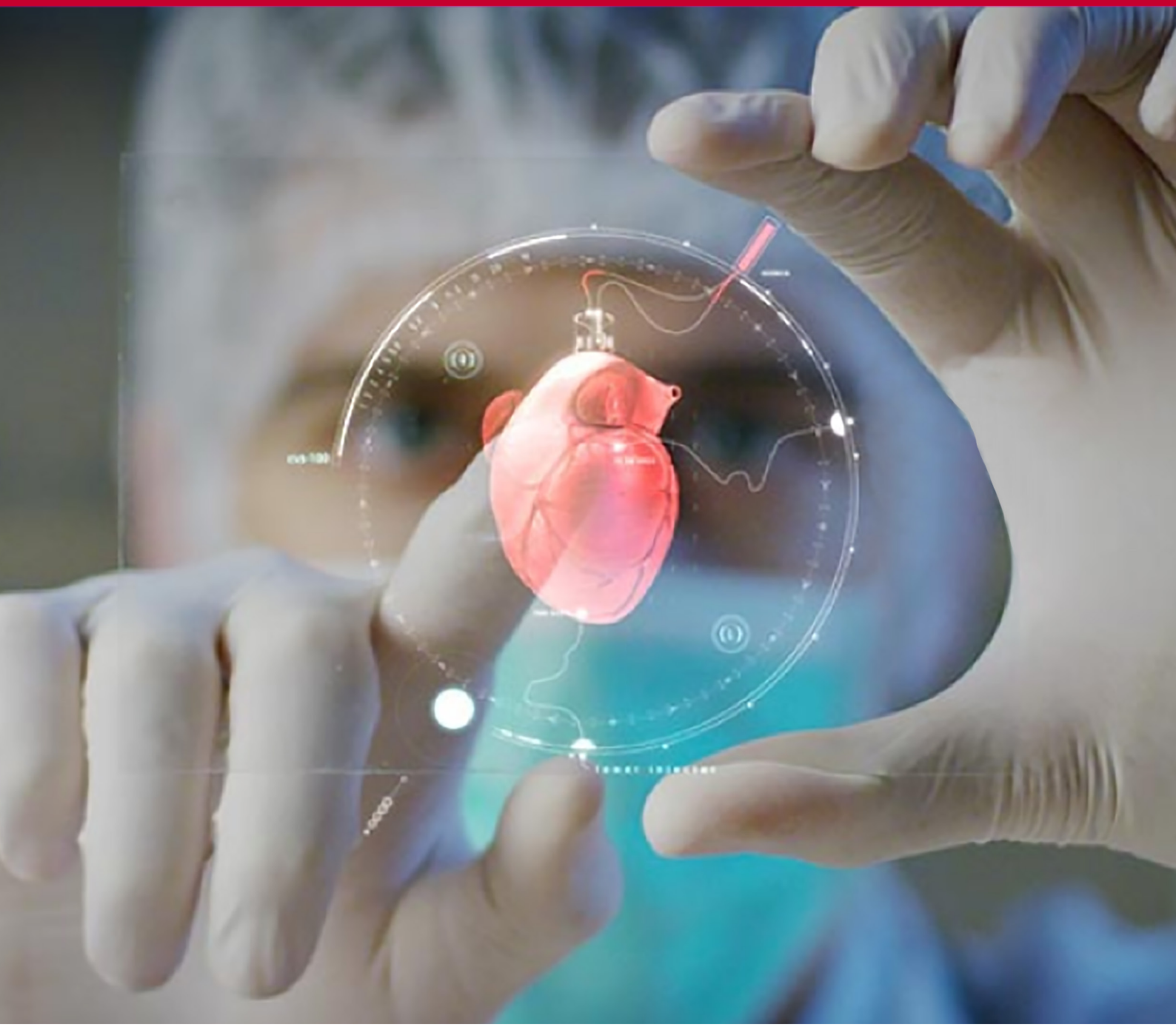
UNIVERSITY OF LEICESTER

7 L COHORT MULTIPLE RANDOMISED TRIALS

A plan to address the research priorities identified by the James Lind Alliance Priority Setting Partnership in Adult Cardiac Surgery.



Funded by

Heart Research UK

HEART SURGERY PRIORITY SETTING PARTNERSHIP

In partnership with

James Lind Alliance
Priority Setting Partnerships

SCTS
Society for Cardiothoracic Surgery in Great Britain and Ireland

CONTENTS

FOREWORD

UK cardiovascular research is world leading in terms of quality and impact. This is attributable to our unique NIHR research infrastructure and funding that makes the NHS the best environment in the world to undertake clinical research, combined with over £100m per year from the British Heart Foundation, the world's largest funder of research into cardiovascular disease.

Cardiac surgery in the UK has the capacity to deliver world class clinical research, and has produced many pivotal trials over the last 5-10 years. However, as a specialty, cardiac surgery is undergoing a period of transition, with increasingly elderly and frail patients referred for surgery, and the continuous development of new less invasive techniques and devices. Continuing to deliver the best personalised care to patients in these circumstances requires high quality evidence based on research.

The research environment is also changing; clinical research is now undertaken by interdisciplinary teams of professionals with diverse skills. Important questions are also often best addressed by national and international networks of researchers. Patients and the public must also be central to all our research activities.

This report describes an approach to cardiac surgery research that will address the changing environment, capitalise on our unique research infrastructure, and result in the best care for our patients. First, we will focus our endeavours on the questions that matter most to patients and clinicians. Patients must be at the centre of our research, and continue as partners and advocates through the lifetime of the research programme. Second, we will come together as a specialty to undertake high quality research in every UK cardiac centre. This research must be interdisciplinary and of the highest quality. Third, we must develop a cohort of young researchers, both trainee surgeons as well as nurses and allied health professionals, who will emerge as research leaders within the next decade. Finally we must create lean, pragmatic research platforms that are attractive to industry partners to enable accelerated technology transfer and device evaluation, as these represent the future of our specialty.

This report we hope will form the basis for a conversation that will enable all stakeholders to contribute to the process, and ensure that we can translate our research priorities into a research programme that will lead to better care for patients.

Professor Gavin Murphy,
BHF Chair of Cardiac Surgery

A NATIONAL CLINICAL TRIALS PROGRAMME IN ADULT CARDIAC SURGERY

RATIONALE

Patients undergoing cardiac surgery in the United Kingdom benefit from the highest quality care. However, as a discipline, cardiac surgery faces multiple challenges. Patients referred for cardiac surgery are increasingly elderly, often with multiple chronic conditions, and require more complex surgery than historical cohorts. In addition, new and potentially better diagnostic tests, less invasive treatments, and devices, are being introduced into clinical care at an accelerating rate. The best way to adapt to these challenges, and to maintain the highest standards of care for patients, is through research. It is only through the generation of high quality evidence that we will be able to direct the best care, to the individual patient, at the right time.

STRATEGY

In 2017, the British Heart Foundation Workshop for Cardiovascular Surgery Research identified priority areas for development:

1. The need for investment in clinical trials research infrastructure.
2. The development of a portfolio of pragmatic trials based on a national priority setting process.
3. The need for investment in academic training.
4. The development of strategic partnerships with industry and universities to facilitate technology transfer and the rapid evaluation of devices.

IMPLEMENTATION

Infrastructure: In 2017, the BHF established a clinical trials funding committee with an emphasis on the delivery of large pragmatic trials. In addition, in 2018, the BHF also established a new Clinical Research Collaborative to coordinate interdisciplinary multicentre trials in cardiovascular disease.

National Priority Setting: In 2017, Heart Research UK funded the James Lind Alliance Priority Setting Partnership in Adult Cardiac Surgery. This identified the Top 10 research priorities for patients, carers and clinicians. These priorities have been converted to research questions that can be answered by clinical trials (see below).

Academic training: In 2017, the Society for Cardiothoracic Surgery in Great Britain and Ireland, along with the Royal College of Surgeons of England's Clinical Trials Initiative funded the training of junior surgeons in clinical trial methodology and the establishment of an Interdisciplinary Research Network of Associate Principal Investigators in every UK cardiothoracic centre. These initiatives will, we hope, nurture next generation of research leaders.

Partnerships: Accelerated technology transfer and strategic partnerships with industry are embedded in the 2018 Life Sciences Sector Deal. Cardiovascular surgery is characterised by rapid technological advancement and innovation and represents an area for further growth in industry funded evaluation of percutaneous and minimally invasive techniques.

THE NEXT 10 YEARS

The UK presents a unique environment for clinical research and innovation in cardiac surgery that will benefit patients and the NHS. The next step is to develop a platform that can deliver a portfolio of clinical trials that address the national research priorities.

PROJECT MILESTONES

James Lind Alliance
Priority Setting Partnerships

Heart Research UK

NOVEMBER 2017

Heart Research UK funds the Heart Surgery Priority Setting Partnership (PSP).

JUNE 2018

Cochrane Heart Group joins the Priority Setting Partnership

DECEMBER 2018

Literature review, duplicate questions combined, already-addressed questions removed. **49** unanswered summary questions identified.

JUNE 2019

Second Survey closes. **492** participants. Questions narrowed down to **21** summary questions.

FEBRUARY 2017

British Heart Foundation identifies the need to develop a consensus around clinical research priorities.

MARCH 2018

Launch of First PSP Survey at Society for Cardiothoracic Surgeons (SCTS) in the UK and Ireland Annual Meeting, Glasgow. @heartsurgerypsp Twitter account launched.

NOVEMBER 2018

First Survey closes. **1080** questions submitted by **629** participants. Duration was 9 months, averaging **70** participants per month.

MARCH 2019

Second Survey launched at SCTS Annual Meeting, Westminster, London.

JULY 2019

Final Workshop, attended by patient, carer and clinician representatives at Leicester.

TOP 10
PRIORITISED QUESTIONS

THE TOP TEN PRIORITIES FOR ADULT CARDIAC SURGERY RESEARCH

1

QUALITY OF LIFE

How does a patient's quality of life (QOL) change (e.g. disability-free survival) following heart surgery and what factors are associated with this?

2

FRAILTY

How can we address frailty and improve the management of frail patients in heart surgery?

3

CHRONIC CONDITIONS

How can we improve the outcomes of heart surgery patients with chronic conditions (obesity, diabetes, hypertension, renal failure, autoimmune diseases etc.)?

4

PREHABILITATION

Does prehabilitation (a programme of nutritional, exercise and psychological interventions before surgery) benefit heart surgery patients?

5

HEART VALVE INTERVENTION

When should heart valve intervention occur for patients without symptoms?

6

SURGICAL METHODS

How does minimally invasive heart surgery compare to traditional open surgery?

7

ORGAN DAMAGE

How do we minimise damage to organs from the heart-lung machine/ heart surgery (heart, kidney, lung, brain and gut)?

8

3D BIO-PRINTING

Can we use 3D bio-printing or stem cell technology to create living tissues (heart valves/heart) and repair failing hearts (myocardial regeneration)?

9

ATRIAL FIBRILLATION

What are the most effective ways of preventing and treating post-operative atrial fibrillation?

10

INFECTION

How do we reduce and manage infections after heart surgery including surgical site/sternal wound infection and pneumonia?

ADDRESSING RESEARCH PRIORITIES USING A COHORT MULTIPLE RCT DESIGN

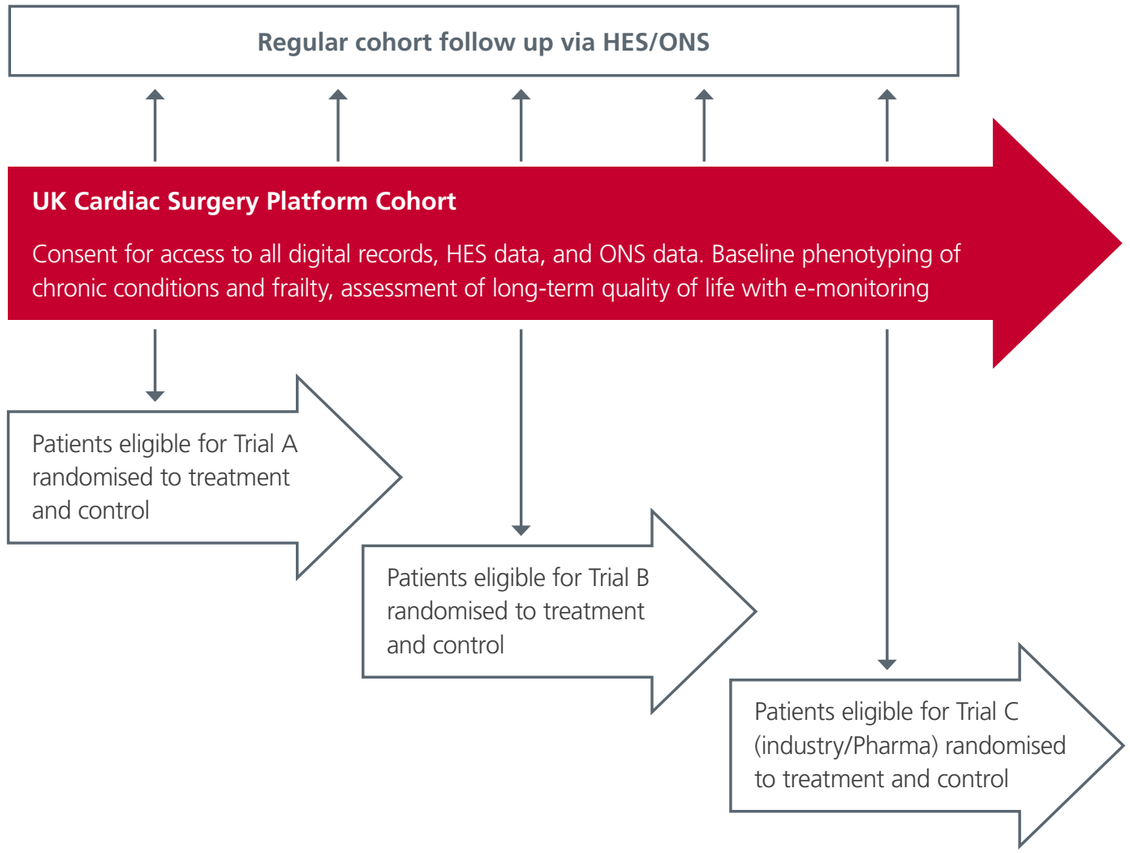
WHAT:

Cohort Multiple RCTs recruit participants to a longitudinal cohort study with long-term follow-up, preferably using routinely collected healthcare data. The cohort also serves to identify those patients who should be eligible for randomisation within individual RCTs of interventions that also utilise the cohort follow-up mechanism to assess outcomes.

WHY:

This approach combines the advantages of traditional RCTs (high quality evidence) and registry data sources (lean, efficient design) and is particularly suited to pragmatic trials.

A COHORT MULTIPLE RANDOMISED TRIALS APPROACH TO ADDRESS THE NATIONAL RESEARCH PRIORITIES IN CARDIAC SURGERY



HOW:

ESTABLISH THE UK CARDIAC SURGERY TRIALS COHORT

A consecutive cohort of adult cardiac surgery patients in every UK unit who will consent to storage of their clinical records including imaging and laboratory data, linkage of their Hospital Episode Statistics and Office of National Statistics data, and agree to remote follow-up using digital data capture from smartphones to measure quality of life, and activity.

Participants will be phenotyped for frailty and chronic conditions at baseline and screening for recruitment to trials of novel tests, devices and interventions.

This work will be supported by the new BHF Cardiovascular Data Science Centre/ Health Data Research UK partnership.

MULTIPLE RCTS

The cohort will serve as a platform to recruit patients to trials of novel diagnostic tests and interventions that aim to reduce the risk of organ failure in the short term (Priority 7), and/or improve long-term outcomes and quality of life (Priority 1). Candidates for novel interventions are Prehabilitaion (Priority 4), minimally invasive surgery (Priority 6), percutaneous devices for valve repair (Priority 19), or surgical site infection prevention (Priority 10). The nature of the cohort platform design will allow evaluation of the interaction between frailty phenotypes and treatment effects within trials, thereby providing evidence for personalised medicine in higher risk cohorts.

COCHRANE COLLABORATION

Cochrane Heart will commission a series of systematic reviews to address the research questions generated by the Priority Setting Partnership. These will define knowledge gaps that can be addressed by RCTs, and inform trial design.

IN SILICO TRIALS

Trials will be modelled *in silico* using existing HES and ONS data. This provides information on patient populations, numbers of eligible patients and sites, event rates for short- and long-term outcomes and unwarranted variation in care. Statistical techniques in causal inference will be used to model treatment effects. Routinely collected health data can also be used to model treatment effects within subgroups, as well as generalisability to the patient population.

PATIENT AND PUBLIC INVOLVEMENT

The programme will build on established PPI networks such as the Priority Setting Partnership Steering Committee, Aortic Dissection Awareness, The UK Mini Mitral Trial, the National Cardiac Benchmarking Collaborative, and patient groups affiliated to the British Heart Foundation and Heart Research UK.

MIXED METHODS EVALUATION

The NIHR Research Design Service will advise on the development of an integrated mixed methods approach to these trials. This will directly inform decision makers and commissioners as to the value of implementation of new treatments and tests.

Process: Process evaluations within these trials will assess the fidelity and quality of implementation of interventions, clarify causal mechanisms, and identify contextual factors associated with variation in outcomes.

Behaviour: The QUINTET approach will be used to enhance participation by medical staff, recruitment of participants, adherence, and follow-up.

Quality of life: Long-term quality of life will be assessed during follow-up using a smartphone app. This facilitates message reminders to complete the assessments, and enables direct, secure, data transfer to trial databases.

Health economics: Hospital Episode Statistics were originally designed for audit and billing and allow health technology assessments to evaluate cost effectiveness.

CLINICAL TRIALS UNITS

Methodological support will be provided by researchers from the UKCRC Accredited Clinical Trials Units in Bristol, Oxford, Newcastle, Leicester, and Leeds.

GOVERNANCE

The BHF Clinical Research Collaborative will host governance committees. The Executive of the Society for Cardiothoracic Surgery will host an oversight committee. An external oversight committee will be composed of an international panel of leading clinical researchers.

ADDED VALUE

Interdisciplinary research networks: In the UK cardiothoracic surgery trainees, nurses and allied health professionals have formed an interdisciplinary research network of associate principal investigators who are participating in multiple research projects. This initiative will attract, train and develop the next generation of clinical researchers. It has already identified young researchers who are currently undergoing training in research methods as part of the Royal College of Surgeons Clinical Trials Initiative. It is envisaged that these individuals will lead the UK Cardiac Surgery Trials Cohort and associated trials in future.

Technology Transfer and Strategic Partnerships with Industry: The UK Cardiac Surgery Cohort will be attractive to device manufacturers and will facilitate the evaluation and introduction of new technologies.

Translational Research: The BHF NIHR Cardiovascular Partnership brings together the BHF Centres of Research Excellence and Research Accelerators with the NIHR Biomedical Research Centres that have cardiovascular themes. Areas of potential synthesis include the rapid translation of successful early stage trials to evaluation of clinical and cost effectiveness, as well as potentially reverse translation through the collection of human tissue biopsies for early phase research and molecular phenotyping.

Professor Gavin Murphy, who commissioned the Heart Surgery PSP, operates with a colleague during a cardiac surgery procedure at Glenfield Hospital, Leicestershire.

FORMULATING RESEARCH QUESTIONS

PRIORITY 1

How does a patient's quality of life (QOL) change (e.g. disability-free survival) following heart surgery and what factors are associated with this?

PRIORITY 2

How can we address frailty and improve the management of frail patients in heart surgery?

PRIORITY 3

How can we improve the outcomes of heart surgery patients with chronic conditions (obesity, diabetes, hypertension, renal failure, autoimmune diseases etc.)?

PRIORITY 4

Does prehabilitation (a programme of nutritional, exercise and psychological interventions before surgery) benefit heart surgery patients?

Rationale: The four top research priorities address the most commonly expressed concerns of patients and clinicians: How do we identify and stratify often elderly patients with multiple chronic conditions where their cardiac disease is considered an indication for surgery? These conditions can contribute to frailty, a poorly defined condition not incorporated in existing risk scores. Frail patients and those with multiple comorbidities often do not experience the long-term benefits of surgery that underpin existing treatment guidelines. Personalised interventions that target these conditions, or treatments stratified by objective markers of frailty may have patient benefits.

Evidence gap: Systematic reviews [1, 2] report low to moderate certainty as to the long-term benefits in quality of life following cardiac surgery, due primarily to poor data, non-random attrition in existing trials, and poor validation of existing quality of life metrics in non-coronary artery disease populations.

POTENTIAL RESEARCH QUESTIONS

- What is the best tool to assess Quality of Life (QOL) in specific cardiac surgery disease?
- What modifiable factors can be targeted to improve QOL.
- Are there important QOLbenefits in elderly patients who undergo cardiac surgery?
- What is the long-term comparison in terms of QOL between surgical and interventional approach?

No treatment guideline makes specific recommendations as to the management of chronic conditions affecting the lungs, kidneys, or other organ systems, in patients referred for cardiac surgery. Guidelines do make recommendations as to the perioperative management of diabetes, however these are of low certainty [3].

A review of AHA and ESC guidelines for the treatment of ischaemic heart disease and valvular disease identifies class I level B recommendations for frailty. These recognise the need for frailty assessment in guiding clinical practice, but there is no consensus as to which score or thresholds can inform treatment decisions [4].

POTENTIAL RESEARCH QUESTIONS

- Can we identify specific frailty phenotypes that do not derive benefits from surgery versus other treatments?
- Are there specific pre-surgery interventions that can be targeted to patients with chronic conditions or frailty
- Do specific surgical techniques (e.g. minimally invasive surgery), or percutaneous approaches improve outcomes in populations with chronic diseases?
- Are pre-surgery interventions feasible in non-elective surgery?
- Does prehabilitation improve outcomes in frail patients?
- What are the best nutritional strategies for prehabilitation?
- Does prehabilitation have long-term benefits?
- Should we design prehabilitation programs specific to patient groups and type of cardiac surgery?

PRIORITY 5

When should heart valve intervention occur for patients without symptoms?

Rationale: People with severe valve disease take years to develop symptoms that include shortness of breath, chest pain, or even sudden death. Some patients may never develop symptoms at all. Major heart surgery is a very good treatment for patients with symptoms but can cause complications and is often associated with prolonged recovery. The dilemma is therefore: should we operate in everyone when valve disease is severe to avoid the risk of heart failure and death or wait until symptoms develop so that patients are spared unnecessary major surgery?

Evidence gap: Recommendations for valve interventions in asymptomatic patients are of low certainty [4, 5]. Advancements in medical therapy, new risk stratification tools such as cardiac Magnetic Resonance Imaging, and changes in the diagnostic criteria of severity create new areas of uncertainty to be addressed by research in the future.

POTENTIAL RESEARCH QUESTIONS

- Can B-type natriuretic peptide (BNP) levels guide the timing for intervention on the aortic valve?
- Is aortic flow peak velocity an adequate criterion to plan surgery on asymptomatic patients?
- Does mid-wall myocardial fibrosis findings at cardiac magnetic resonance (CMR) have a role in the timing of surgery in asymptomatic patients with severe aortic valve disease?
- Does longitudinal strain measurement have a role in the timing of surgery in asymptomatic mitral valve regurgitation?

PRIORITY 6

How does minimally invasive heart surgery compare to traditional open surgery?

Rationale: New techniques have been developed that allow surgery to be performed through smaller incisions, or without the use of the heart lung machine. These operations reduce the extent of the surgical incision, but they are technically more challenging and therefore have potential additional risks. Whether these operations are better than traditional open surgery or new percutaneous techniques and devices is unclear.

Evidence gap: Minimally invasive procedures have been shown to limit perioperative bleeding and blood transfusion in trials. However, there is uncertainty as to the clinical benefits to patients from minimally invasive valve or endovascular treatments of aortic disease [6, 7].

POTENTIAL RESEARCH QUESTIONS

- Is minimally invasive surgery clinically or cost effective?
- What is the optimal communication strategy to present the choice between minimally invasive and traditional surgery to the patients?
- What are the requirements for the provision of specialised minimally invasive cardiac surgery services?
- Is there a difference in long-term QOL between minimally invasive and traditional surgery?

PRIORITY 7

How do we minimise damage to organs from the heart-lung machine/ heart surgery (heart, kidney, lung, brain and gut)?

Rationale: Organ injury or failure affecting the heart, lung, brain, or kidneys, complicates up to 50% of all cardiac surgery operations and costs the NHS £125m per year.

Evidence gap: Organ protection is a major theme in cardiac surgery research and strategies tailored to optimise this outcome are considered in all major guidelines [3-5, 8-10]. However, despite decades of research, the pathogenesis of these conditions remains poorly understood and effective organ protection interventions are not in widespread use.

POTENTIAL RESEARCH QUESTIONS

- Does pre-surgery optimisation of chronic kidney, lung, or metabolic diseases reduce post-surgery lung and kidney injury or infection.
- Do personalised perioperative treatment algorithms based on enhanced monitoring of tissue oxygenation or vascular function during surgery prevent organ injury.
- Are there pharmacological strategies or other interventions (fluid restriction, enhanced recovery, extracorporeal circuit modification) that attenuate the effects of surgery on organ function.
- Can novel myocardial protection strategies improve clinical outcomes.
- Which perfusion strategy should we adopt for aortic dissection?

PRIORITY 8

Can we use 3D bio printing or stem cell technology to create living tissues (heart valves/heart) and repair failing hearts (myocardial regeneration)?

Rationale: 3D printing in combination with stem cell technology offers the potential for surgical prosthesis that have enhanced durability, low thrombogenicity, and plasticity. This would reduce the requirements for repeated procedures over the lifetime of the patient, as well as both the need for anticoagulation and risk of thrombosis.

Evidence gap: No RCTs were identified regarding 3D bio-printing using the tailored search strategy we adopted. Systematic reviews identified a total of 1907 participants in 38 trials on stem cell therapy for chronic ischaemic heart disease (CHD) and 2732 participants in 41 trials on stem cell treatment for acute myocardial infarction (AMI) [11, 12]. These trials did not demonstrate efficacy however there were important design limitations in all of these trials that limited interpretation. The most effective mode of stem cell delivery was not resolved by these trials.

POTENTIAL RESEARCH QUESTIONS

This research is still largely in the early translational phase in cardiac surgery and no specific research questions that could be addressed by pragmatic clinical trials were identified.

PRIORITY 9

What are the most effective ways of preventing and treating post-operative atrial fibrillation?

Rationale: New onset atrial fibrillation can occur in about 30% of people undergoing heart surgery where it is associated with morbidity including stroke, prolonged hospitalisation, and increased healthcare costs. There are no effective interventions that prevent or reduce the frequency of postoperative atrial fibrillation.

Evidence Gap: The evidence in favour of both pharmacological and non-pharmacological prophylaxis is low because of the quality and the heterogeneity of the data, and choice of the best individualized intervention for patients is still problematic [13]. Moreover, recommendations for management of anticoagulation in postoperative atrial fibrillation in the EACTS guidelines are still class IIa level C [3].

POTENTIAL RESEARCH QUESTIONS

- Do preoperative lifestyle interventions such as weight loss or exercise have a role in postoperative atrial fibrillation prevention?
- Does attenuating the inflammatory response to surgery reduce post-operative atrial fibrillation?
- Is rhythm control or rate control the optimal management strategy in every patient subgroup?
- Is surgical ablation safe and effective in longstanding persistent atrial fibrillation?
- Is hybrid (endocardial + epicardial) atrial fibrillation ablation superior to surgical and transcatheter interventions?
- What is the optimal management of post-operative atrial fibrillation in heart failure patients?

PRIORITY 10

How do we reduce and manage infections after heart surgery including surgical site/sternal wound infection and pneumonia?

Rationale: The 2017 Public Health England SSI report (PHER 2017) stated that the incidence of SSIs in UK cardiac surgery centres was 3.8% following coronary artery bypass grafts (CABG) and 1.7% in non-CABG operations. This is associated with a 10-fold increase in mortality, a six-fold increase in the risk of readmission to hospital. In the UK the annual costs of treating in SSIs in cardiac surgery is approximately £30m. Likewise, pulmonary complications such as lower respiratory tract infection can lead to prolonged ICU and hospital stay and result in a six-fold increase in mortality.

Evidence Gap: The Cardiothoracic Interdisciplinary Research Network has recently completed a Cochrane systematic review of trials of interventions to prevent or reduce surgical site infections in cardiac surgery. Identified evidence gaps related to choice of preoperative skin antiseptic, antibiotic prophylaxis duration and choice, dexamethasone effect on wound healing, dressing removal time, and benefits of microbial sealants. Evidence on the prevention of post-surgery lower respiratory tract infection has developed in largely non-cardiac surgical settings.

POTENTIAL RESEARCH QUESTIONS

- How effective is preoperative skin antisepsis in preventing surgical infection?
- What is the optimal ventilation management to prevent postoperative pneumonia?
- How do we manage steroid therapy in the perioperative period to avoid complication on wound healing?
- Do microbial sealants prevent surgical site infection?
- Which interventions should be part of a care bundle to prevent surgical site infection in cardiac surgery?
- What is the optimal surgical antibiotic prophylaxis and duration?
- Are interventions to prevent infection applicable to hybrid cardiac surgery procedures?

BIBLIOGRAPHY

1. Huffman MD, Karmali KN, Berendsen MA, Andrei AC, Kruse J, McCarthy PM, et al. Concomitant atrial fibrillation surgery for people undergoing cardiac surgery. The Cochrane database of systematic reviews. 2016(8):Cd011814.
2. Sibilitz KL, Berg SK, Tang LH, Risom SS, Gluud C, Lindschou J, et al. Exercise-based cardiac rehabilitation for adults after heart valve surgery. The Cochrane database of systematic reviews. 2016;3:Cd010876.
3. Sousa-Uva M, Head SJ, Milojevic M, Collet JP, Landoni G, Castella M, et al. 2017 EACTS Guidelines on perioperative medication in adult cardiac surgery. Eur J Cardiothorac Surg. 2018;53(1):5-33.
4. Nishimura RA, Otto CM, Bonow RO, Carabello BA, Erwin JP, Guyton RA, et al. 2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Circulation. 2014;129(23):e521.
5. Falk V, Baumgartner H, Bax JJ, De Bonis M, Hamm C, Holm PJ, et al. 2017 ESC/EACTS Guidelines for the management of valvular heart disease. European journal of cardio-thoracic surgery : official journal of the European Association for Cardio-thoracic Surgery. 2017;52(4):616-64.
6. Abraha I, Romagnoli C, Montedori A, Cirocchi R. Thoracic stent graft versus surgery for thoracic aneurysm. Cochrane Database of Systematic Reviews. 2016(6).
7. Kirmani BH, Jones SG, Malaisrie SC, Chung DA, Williams RJ. Limited versus full sternotomy for aortic valve replacement. The Cochrane database of systematic reviews. 2017;4:Cd011793.
8. Erbel R, Aboyans V, Boileau C, Bossone E, Bartolomeo RD, Eggebrecht H, et al. 2014 ESC Guidelines on the diagnosis and treatment of aortic diseases: Document covering acute and chronic aortic diseases of the thoracic and abdominal aorta of the adult. The Task Force for the Diagnosis and Treatment of Aortic Diseases of the European Society of Cardiology (ESC). European heart journal. 2014;35(41):2873-926.
9. Hiratzka LF, Bakris GL, Beckman JA, Bersin RM, Carr VF, Casey DE, et al. 2010 ACCF/AHA/AATS/ACR/ASA/SCA/SCAI/SIR/STS/SVM guidelines for the diagnosis and management of patients with Thoracic Aortic Disease: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines, American Association for Thoracic Surgery, American College of Radiology, American Stroke Association, Society of Cardiovascular Anesthesiologists, Society for Cardiovascular Angiography and Interventions, Society of Interventional Radiology, Society of Thoracic Surgeons, and Society for Vascular Medicine. Circulation. 2010;121(13):e266.
10. Sousa-Uva M, Neumann FJ, Ahlsson A, Alfonso F, Banning AP, Benedetto U, et al. 2018 ESC/EACTS Guidelines on myocardial revascularization. Eur J Cardiothorac Surg. 2019;55(1):4-90.
11. Fisher SA, Doree C, Mathur A, Taggart DP, Martin-Rendon E. Stem cell therapy for chronic ischaemic heart disease and congestive heart failure. Cochrane Database of Systematic Reviews. 2016(12).
12. Fisher SA, Zhang H, Doree C, Mathur A, Martin-Rendon E. Stem cell treatment for acute myocardial infarction. Cochrane Database of Systematic Reviews. 2015(9).
13. Arsenault KA, Yusuf AM, Crystal E, Healey JS, Morillo CA, Nair GM, et al. Interventions for preventing post-operative atrial fibrillation in patients undergoing heart surgery.The Cochrane database of systematic reviews. 2013(1):Cd003611.

NEXT STEPS

It is proposed that researchers in the UK undertake a programme of world leading clinical trials in adult cardiac surgery that address these research priorities.

DISSEMINATION

The Priority Setting Partnership dissemination plan includes the production of a short report that will be shared via social media, newsletters, websites, and via presentations at conferences and workshops. A full report will be drafted for publication in a peer-reviewed journal. All of the non-clinical members of the Priority Setting Partnership have committed to further dissemination activities within their own networks and these individuals will support the PPI components of the proposed trials programme.

FUNDERS

This document will be shared with NETCC, the British Heart Foundation, the Medical Research Council, Heart Research UK and other funders with the intention of informing commissioning and funding calls.

RESEARCHERS

The Priority Setting Partnership has included representatives of Cochrane Heart who have developed a parallel programme of systematic reviews to identify evidence gaps related to the Priority Setting Partnership research priorities.

It is also envisaged that the research priorities will guide the development of research programmes and prompt research groups to address the resulting research questions in future proposals.

PARTNERSHIPS

The success of this proposal will require successful partnerships with the NIHR Research Design Service, the British Heart Foundation Clinical Research Collaborative, the NIHR BHF Cardiovascular Partnership, the BHF Cardiovascular Data Science Centre/Health Data Research UK partnership, the Clinical Research Networks, Patient and Public Groups affiliated to British Heart Foundation, and the Royal College of Surgeons of England Surgical Trials initiative.

INDUSTRY

The medical directors of technology companies who provide devices for cardiac surgery will be approached for advice on the design of the cohort to ensure buy-in for this initiative.

INTERNATIONAL COLLABORATIONS

The Cardiothoracic Surgical Trials Network in North America are now midway through their second 5-year programme of pragmatic multicentre RCTs. Their executive group have expressed an interest in joint projects. Clinical researchers in Australia have also indicated their desire to undertake joint projects.

ACKNOWLEDGEMENTS AND DISCLAIMER

This report is based on a James Lind Alliance (JLA) priority setting process, which was commissioned and funded by Heart Research UK for adults involved in cardiac surgery. The views expressed in the publication are those of the author(s) and not necessarily those of the Heart Research UK, British Heart Foundation, James Lind Alliance, the NIHR, its arm's length bodies or other government departments.

REPORT AUTHORS

- Professor Gavin Murphy BHF Chair of Cardiac Surgery, University of Leicester, Society for Cardiothoracic Surgery in Great Britain and Ireland, Academic and Research Committee Chair
- Dr Riccardo Abbasciano, Clinical Research Fellow, University of Leicester
- Miss Bethany Tabberer, Clinical Trials Administrator, University of Leicester
- Mrs Tracy Kumar, Senior Research Manager, University of Leicester
- Mr Hardeep Aujila, Clinical Trial Co-ordinator, University of Leicester
- Mrs Florence Lai, Statistician, University of Leicester

If you have any queries or comments about this work, please contact:

gjm19@leicester.ac.uk

Further information about the project can be found at:

www.le.ac.uk/heart-surgery-psp

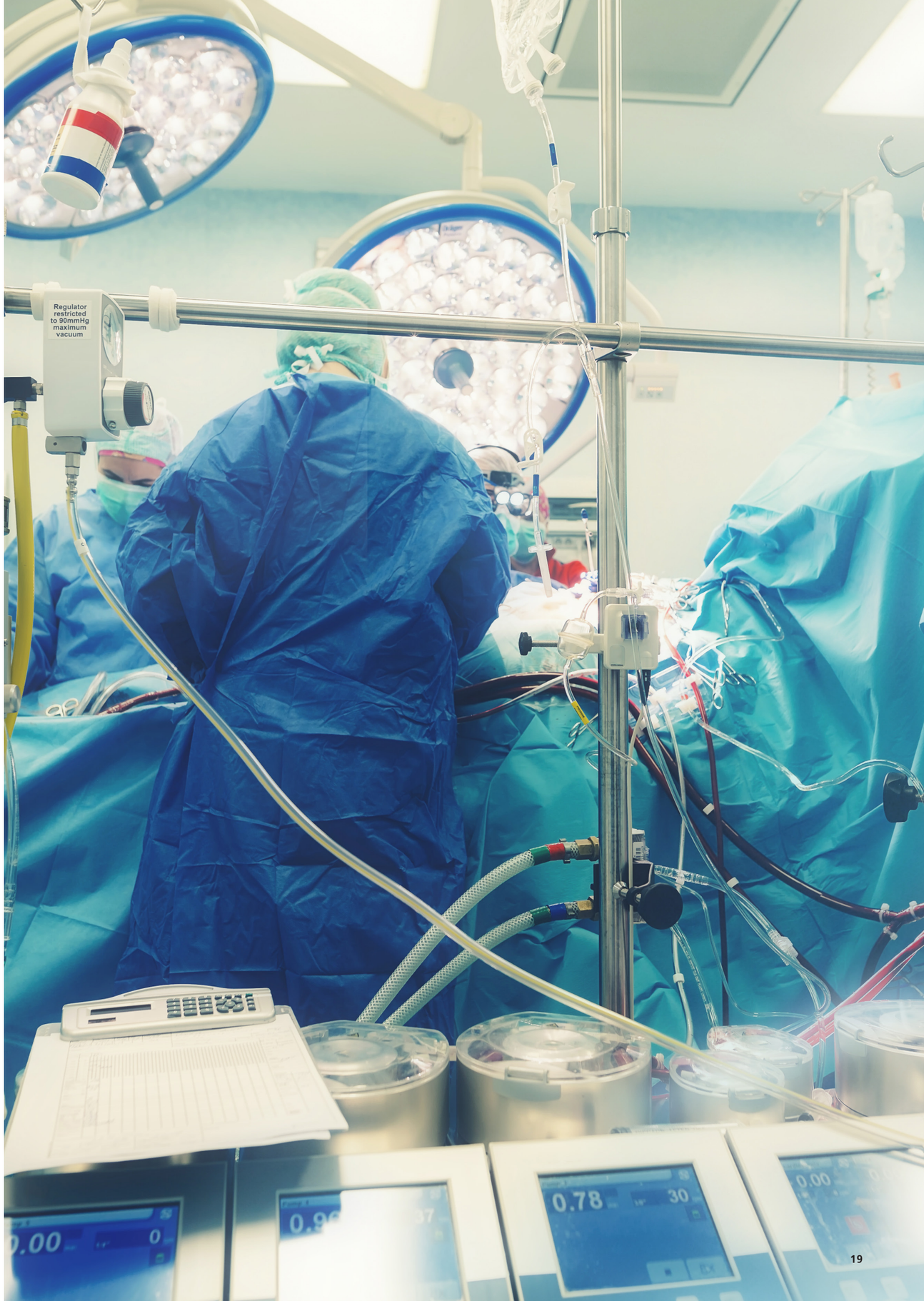
MEMBERS OF THE PSP STEERING GROUP WERE:

- Anthony Locke, Leicestershire Cardiac Surgery Patient and Public Involvement Group, NIHR Senior PPI panel
- Peter Read, Leicester Cardiac Surgery PPI Group
- Trevor Fernandes, Cardiovascular Care Patients (CPPUK) and Wider Community Patient Links
- Richard Fitzgerald*, (CPPUK) and Wider Community Patient Links (deceased)
- Zena Jones, Patient Representative, Health Watch County Durham
- Jonathan Stretton-Downes, Six Times Open
- Grace Stretton-Downes, Family Member Representative
- Professor Gavin Murphy BHF Chair of Cardiac Surgery, University of Leicester, Society for Cardiothoracic Surgery in Great Britain and Ireland, Academic and Research Committee Chair
- Mr Enoch Akowuah, Consultant Cardiac Surgeon, James Cook Hospital, Middlesbrough, member of the British Cardiac Society, Heart Valve Clinical Studies Group
- Professor Mahmoud Loubani, Hon Professor of Cardiothoracic Surgery, University of Hull
- Professor Julie Sanders, Director Clinical Research, Quality and Innovation, St Bartholomew's Hospital
- Professor John Pepper, Professor of Cardiothoracic Surgery, Imperial College London
- Professor Andrew Klein, Mackintosh Professor of Anaesthesia, Royal Papworth Hospital NHS Trust, Association of Cardiothoracic Anaesthesia Research Subcommittee Chair
- Professor Rod Stables, British Cardiovascular Society, Academic and Research Committee Chair
- Carol Akroyd, East Midlands Centre for Black and Minority Ethnic Health & Collaboration for Leadership in Applied Health Research Prevention Theme Manager
- Harpal Ghattoraya, Research Delivery Manager, NIHR Clinical Research Network (CRN)
- Mr Peter Braidley, Consultant Cardiac Surgeon, Sheffield University Hospitals, Heart Research UK Trustee
- Dr Nazish Khan, Principal Pharmacist Cardiac Services, The Royal Wolverhampton Hospitals NHS Trust
- Ms Katherine Cowan (PSP Chair, JLA Senior Adviser), The James Lind Alliance (JLA)
- Mrs Tracy Kumar, Senior Research Manager, University of Leicester
- Mrs Florence Lai, Statistician, University of Leicester
- Mrs Clare Gillies, Lecturer in Medical Statistics, University of Leicester
- Mrs Selina Lock, Research Information Advisor, University of Leicester

ADMINISTRATIVE TEAM

- Mrs Sue Page, PA to Professor Gavin Murphy, University of Leicester
- Mr Hardeep Aujla, Clinical Trial Co-ordinator, University of Leicester
- Miss Bethany Tabberer, Clinical Trials Administrator, University of Leicester
- Carrie Ackrill, Heart Surgery PSP Administrator, University of Leicester

The Project Team and Steering Group members would like to thank Richard Fitzgerald for his contribution to the Heart Surgery PSP until his passing in 2019.



UNIVERSITY OF LEICESTER

Heart Surgery PSP Project Team
Department of Cardiovascular Sciences
Clinical Sciences Wing
Glenfield Hospital
Leicester LE3 9QP

t: +44 (0)116 258 3021
e: heartsurgerypsp@leicester.ac.uk
w: www.le.ac.uk/heart-surgery-psp

TRI/7792_10/19