Bristol Heart Institute

Newsletter June 2024

World class research at the BHI

Deborah Lawlor reflects on our achievements in 2024 to date

Congratulations to Saadeh Suleiman who has been honoured for “distinguished services to cardiovascular sciences and medicine”.

We held another very successful joint meeting of the BHI and the BHF in February, attended by the Vice Chancellor, Evelyn Welch. The event showcased the breadth of excellent cardiovascular research in Bristol. There were presentations across basic science, translational and clinical research, and population health, including many presentations from PhD students and early career researchers.

Join us for an insightful seminar on June 13th with Danial Grene from Mount Sinai, New York.

We're excited to announce our upcoming Heart Festival on Thursday 13th March 2025 in the Great Hall of the Wills Memorial Building. It will be open to the public to showcase our research as a civic university.

We also congratulate Katie Skeffington on her BHF intermediate Fellowship.

In this issue we spotlight three of our new starters on aspects of their research at Bristol: Daniel Fudulu, Jilau Li and Florence Mouy.

We are grateful to all of you who have contributed to heart research.

Thank you to everyone who has contributed their story to this newsletter.

In this issue:

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University of BRISTOL

Distinguished services honour

Professor Saadeh Suleiman has been honoured by the International Academy for Cardiovascular Sciences (IACS)

We are delighted to announce that Professor Suleiman has been honoured for "distinguished services to cardiovascular sciences and medicine". Professor Suleiman will be presented with the Jan Slezak Award during the forthcoming IACS Honours and Awards ceremony to be held in Bratislava in October 28-30, 2024 (https://iacsworld.com/cv-network-vol-23-no-1-march-2024/).

Professor Saadeh Suleiman is an accomplished academic and researcher with a diverse background. He obtained his education from Bir Zeit University, American University of Beirut, and Essex University. He began his career at An-Najah University in Palestine in 1980, where he played a pivotal role in research development and served as the first Dean of Research and Postgraduate Studies. During his time there, he actively participated in national committees, including the council for higher education and the British Council in East Jerusalem.

He is a founding member of the Bristol Heart Institute which has become one of the top cardiovascular research institutes in the UK. In 2003, the University of Bristol awarded him the higher degree of DSc in recognition of the distinction of his research. Other distinctions include being a member of the team that was awarded the U.K. Hospital Doctor Award for Team of the Year in Surgery and runners up for Cardiovascular Medicine and election to the executive committee of the British Society for Cardiovascular Research.

Additionally, he has been elected as Fellow of the International Academy of Cardiovascular Sciences, Fellow of the European Society of Cardiology, Fellow of the Royal Society of Biology, and Fellow of the Physiological Society. He has published extensively and has been successful at attracting significant funding to support his research, students, and staff. Professor Suleiman has organised and contributed as speaker to a large number of international meetings and has acted as a reviewer for grant giving bodies and journals as well as acting as an external examiner/assessor for national and international academic institutions. He has supervised, mentored, hosted, trained, and examined hundreds of students and researchers at all levels and from different countries worldwide.

Recognising achievements in heart disease

"Seven Wise Cardiac Surgeons of the Golden Decade of the '90s"

Professor Gianni Angelini has been honored by the Greek Parliament for his pioneering work in heart surgery. In a special event at the Old Parliament, seven pioneering cardiac surgeons from the 1990s, including Professor Angelini, were celebrated for their innovative contributions to modern cardiac surgery. The number seven, historically symbolic of great achievements, was central to the event, underscoring the significant advancements these surgeons have made in the field.

… also see next page

From the programme:
Dear colleagues and friends,

We warmly welcome you to the historic symposium "Seven Wise Cardiac Surgeons of the Golden Decade of the '90s" that we proudly organize in the imposing space of the Old Greek Parliament. An event dedicated to those who shaped modern cardiac surgery through their innovations and their dedication to progress. The number seven, from antiquity to the present day, represents much more than a numerical value. From the seven wise men of ancient Greece to the seven pioneering cardiac surgeons of the golden era of the 1990s, the number has been associated with great achievements and breakthroughs. For a few hours, the Old Parliament will host a unique scientific meeting. We will highlight the pioneering work of seven wise cardiac surgeons and honour their contribution to the advancement of science. Consequently, with the contributions of seven leading scientists of the younger generation, we will complete the inspiring journey of cardiac surgery from the past to the present and examine the prospects for the future. Finally, through the dialogue and exchange of ideas between the seven plus seven and the audience, we will cover the totality of the issues involved in dealing with the modern scourge of our time, Coronary Artery Disease.

Gianni Angelini (UK)
Federico Benetti (Argentina)
Antonio Maria Calafiore (Italy)
Tomas Salerno (USA)
Valavanur Subramanian (USA)
Hisayoshi Suma (Japan)
Naresh Trehan (India)

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Recognising achievements in heart disease

… cont'd "Seven Wise Cardiac Surgeons of the Golden Decade of the '90s"

The event honored seven trailblazing cardiac surgeons from the 1990s and engaged in discussions with seven prominent younger scientists.

They delved into the past, present, and future of cardiac surgery, focusing on addressing the contemporary issue of Coronary Artery Disease through an extensive exchange of ideas.

The seven surgeons relaxing at the beach in Mykonos before the award.

From left to right: Salerno, Angelini, Suma, Trehan, Benetti, Subramanian, Calafiore.

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£1 Million award: acute kidney injury cohort study

Prof. Gianni Angelini Leads Study to Recruit 400 Patients Across Four UK Centres

The University of Bristol have been funded £1M from Kidney Research UK to run a cohort study looking at the risk of Acute Kidney Injury (AKI) following cardiac bypass surgery. Led by Prof. Gianni Angelini, the study aims to recruit 400 patients from 4 UK centres.

Patients will have blood and urine samples collected prior and at 3 time points post-surgery which will be analysed for biomarkers which might indicate the likelihood and/or severity of cardiac surgery induced AKI.

This study is part of the larger NURTuRE consortium, which has established the first UK kidney biobank (https://nurturebiobank.org/).

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£1.8 Million NIHR award

Congratulations to Dr Maria Pufulete and Dr Rachel Johnson

CORAL
COENZYME Q10 IN HEART FAILURE

The National Institute for Health Research (NIHR) Health Technology Assessment (HTA) have awarded £1.8m to Dr Maria Pufulete and Dr Rachel Johnson to test whether coenzyme Q10, a nutrient-like substance which can be bought as an over-the-counter food supplement, can improve quality of life in people with heart failure reduced ejection fraction.

The study, currently in set up, aims to recruit 950 people from about 75 GP surgeries in the West of England, South-West Peninsula, East Midlands, North-East and North Cumbria. Study participants will be randomized to receive either coenzyme Q10 or a placebo for one year and followed up through questionnaires and routinely collected health data. Recruitment is due to start in September.

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£2.7 Million award from the NIHR

Congratulations to Dr Maria Pufulete and Dr Ben Gibbison

NIHR | National Institute for Health and Care Research

We are delighted to announce that Dr. Maria Pufulete and Dr. Ben Gibbison have been awarded a £2.7 million grant from the National Institute for Health Research (NIHR) Programme Grants for Applied Research (PGFAR). This significant funding will support their groundbreaking work in developing and evaluating two prehabilitation interventions aimed at optimizing patients before they undergo heart surgery.

One intervention is tailored for patients on the elective pathway, while the other focuses on those on the urgent pathway. These prehabilitation programs are designed to improve patient outcomes by enhancing their physical and mental readiness for surgery, ultimately leading to better recovery and overall health. This award underscores the importance and potential impact of their innovative research in the field of cardiovascular medicine.

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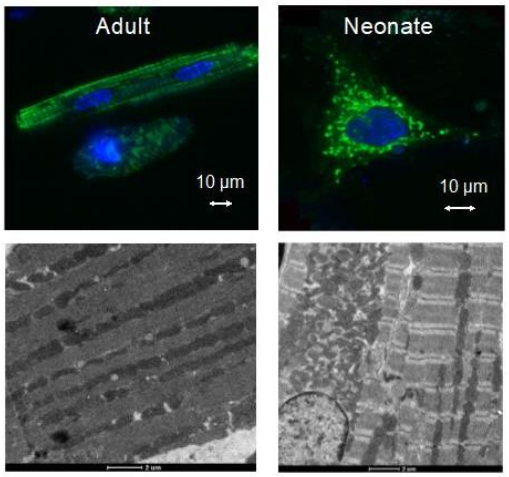
BHF Intermediate fellowship to explore cardioprotection for cyanotic congenital heart disease patients

Dr Katie Skeffington has been awarded £532K for a five-year study

Dr Katie Skeffington, a Senior Research Associate at Bristol Medical School and Bristol Heart Institute, has recently been awarded a 5-year British Heart Foundation Intermediate Basic Research Fellowship (£532K) to work on the optimization of cardioprotective strategies for cyanotic congenital heart disease patients.



Katie completed her PhD in Prof. Dino Giussani's laboratory at the University of Cambridge, where she was involved in a project studying the effect of fetal exposure to chronic hypoxia (low oxygen levels) on the cardiovascular health of the offspring in adulthood.

There are many causes of fetal chronic hypoxia, including pre-eclampsia, placental insufficiency, high-altitude pregnancy and some congenital heart diseases. It is well established that exposure of the heart to chronic hypoxia during fetal life causes alterations in the way the heart develops, predisposing the fetus to a higher risk of cardiovascular disease in adulthood, and Katie's PhD worked on investigating the role of mitochondrial-derived oxidative stress in this process.

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… cont'd

Dr Katie Skeffington has been awarded £532K for a five-year study

Following her PhD, Katie moved to Bristol to join a research programme investigating cardioprotective therapies for paediatric open-heart surgery. There are important developmental differences between paediatric hearts and adult hearts which mean it is not effective to simply extrapolate adult cardioprotective strategies to children. During open-heart surgery, the heart is often arrested to allow the surgeon to operate in a still, bloodless field, however this process of stopping and restarting the heart causes damaging cardiac ischemic reperfusion injury. During the project, which was supervised by Professors Saadeh Suleiman and Massimo Caputo, Katie investigated the use of administration of the drug sildenafil during surgery to reduce cardiac injury.

Work from Bristol and other centers has shown that children with cyanotic congenital heart disease have worse outcomes following surgery than normoxic patients. The mechanisms underlying this are not fully understood, although it is proposed that changes in the fetal stage is likely to contribute to this. Therefore, Katie will use her fellowship to investigate the effect of chronic hypoxia during fetal and early postnatal life on cardiac changes at molecular, structural and functional levels to identify mechanism(s) responsible for predisposing the heart to a greater risk of ischaemic reperfusion injury during open-heart surgery in neonatal and young adult life (the second timepoint is important as many patients will require further surgeries later in life). Katie will use this information to design and begin testing therapeutic strategies specifically optimized for protecting the hearts of cyanotic congenital heart disease patients.

BHF-DZHK-DHF International partnership grant

Research on placental pathology and maternal cardiovascular health using ALSPAC and Dutch cohort data

International Cardiovascular Research Partnership Awards

Professor Abi Fraser has been awarded a British Dutch and German international partnership grant BHF-DZHK-DHF. Using ALSPAC data together with data from a Dutch cohort this will support novel research exploring the role of placental pathology on maternal long term adult cardiovascular disease.

Abi is also the Bristol and epidemiology lead on a large Leducq foundation, led by a US colleague that will bring together international laboratory and population health scientists to determine molecular and genetic mechanisms linking placental health to maternal and fetal cardiovascular health.

International Cardiovascular Research Partnership Awards

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Resilience in research: celebrating achievements and overcoming setbacks

Deborah Lawlor's reflections

All of the above, and many more achievements in recent years, illustrate to me that the University of Bristol conducts outstanding multidisciplinary impactful research integrating clinical, laboratory and population health science.

I was gutted when I got the email to say that we had not been successful in obtaining a BHF Research Excellence Award – something that seems to have alluded Bristo since the first of 4 calls for these awards.

Hell no! but after telling yourself and everyone who is listening why the reviewers have got it wrong, you settle down, regroup and carry on"

I remember asking George Davey Smith and Shah Ebrahim, when I was half-way though my PhD (they were my supervisors) if they ever got over the rejections. I was wondering whether I would be able to cope with that and whether at the end of the PhD I'd be better going back to full-time clinical work. Their response was along the lines of '*Hell no! but after telling yourself and everyone who is listening why the reviewers have got it wrong, you settle down, regroup and carry on*". I am still here and that is because they were right, particularly in indicating the importance of supportive and collaborative colleagues. I feel really lucky and privileged that I do a job that most of the time I love & that's because of the environment and people I get to work with. There is a good chance some of you reading this have had a paper or grant rejected recently – its not great but I would say allow yourself to be angry and frustrated for a bit and then use your energy to regroup with colleagues and work out how to progress.

I think we can and very much should celebrate the research and other successes that has been achieved over the last 5-6 years and should continue to build on the collaborations and innovations that have been supported by the BHF PhD programme led by Alastair Poole and colleagues, The BHF Accelerator Award, the success of which was very much influenced by Emma Hart, Carolina Borges, Giovani Biglino. I also feel that the process of brining people together from different career stages and disciplinary backgrounds further supports new collaborations. This includes a seminar we are hosting with Andrew Mumford and Danial Grene from Mount Sinai New York on rare variant analyses – Details below.

I am really looking forward to seeing you at the Heart Festival in March next year and also at a final Accelerator meeting that we are planning for September to celebrate what we achieved and plans for taking forward new collaborations through different funding sources.

Seminar | Danial Grene from Mount Sinai, New York

Next week: Thursday 13th June 2024

1.00 to 13.00 All welcome Join zoom link 0r in person
Oakfield House 2nd floor seminar room

Abstract: The genetic aetiologies of more than half of rare diseases remain unknown. Standardized genome sequencing and phenotyping of large patient cohorts provide an opportunity for discovering the unknown etiologies. Here we demonstrate our computational approach to rare disease association analysis on the 100,000 Genomes Project dataset, comprising building a compact database, the "Rareservoir", containing rare variant genotypes and phenotypes, and applying our rare disease association method "BeviMed".

In our analysis of protein coding genes, we identified 241 known and 19 previously unidentified associations and subsequently validated associations between (1) loss-of-function variants in the Erythroblast Transformation Specific (ETS)-family transcription factor encoding gene *ERG* and primary lymphoedema, (2) truncating variants in the last exon of transforming growth factor-β regulator *PMEPA1* and Loeys–Dietz syndrome and (3) loss-of-function variants in *GPR156* and recessive congenital hearing impairment. An equivalent analysis of non-coding genes revealed a striking association between rare variants in functional regions of snRNA gene *RNU4-2* and a novel but frequent neurodevelopmental disorder. We will discuss elements of the translational pipeline that follows new gene discovery including opportunities for gaining novel biological insights into common human disease and routes to enhance genetic diagnosis of rare disorders in the clinical genomic medicine service.

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Bristol heart festival

Bristol Heart Institute | Cardiovascular Research for Patients' Benefit

Save the date! Thursday 13th March 2025

The Bristol Heart Institute will be hosting a heart festival in the Great Hall of the Wills Memorial Building.

The day will include a variety of events and activities that should be of interest to the general public to showcase the research work we are doing at the Institute. We will be inviting a number of schools to come along and there will be appropriate activities for various age groups.

There will be public information on how to identify warning signs of stroke and heart attack, debunking myths, yoga, hands-on how to be a heart surgeon or cardiologist, blood pressure measurements, talks and lots more.

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Report on the BHI and BHF joint annual meeting accelerator award

Thursday 22nd February 2024 at the Watershed

- Photos and writeup
- The programme

Bristol Heart Institute | Cardiovascular Research for Patients' Benefit

British Heart Foundation

We were delighted to have had another very successful meeting this year. The event showcased the breadth of excellent cardiovascular research on-going in Bristol. There were presentations across basic science, translational and clinical research, and population health, including many presentations from PhD students and early career researchers.

Our plenary speaker, Dr Sarah Murray has a background in patient care and advocacy. She holds positions in various organizations related to cardiovascular health and surgery, including being Chair of the National PPI group for the BHF Clinical Research Collaborative based at Leicester University, demonstrating her commitment to putting patients at the forefront of medical research and innovation. In addition to her professional roles, Sarah has diverse interests, including beekeeping, fencing coaching, and falconry.

Charli Skinner, the Co-Founder of Soda, also featured, discussing inclusive research practices. Soda focuses on incorporating the insights and experiences of chronically ill, disabled, and neurodivergent individuals into the design of healthcare solutions. Charli's personal lived-experiences and involvement in patient advocacy have driven the formation of Soda, which collaborates with various entities to promote accessible healthcare for all.

Professor Deborah Lawlor provided an update on the BHF accelerator award, and we were pleased to welcome our Vice Chancellor, Evelyn Welch who attended the event once again this year and engaged with students to discuss their research projects.





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Dr Svetlana Mastitskaya

Newly appointed senior lecturer in cardiovascular regenerative medicine

Dr Svetlana Mastitskaya, a newly appointed Senior Lecturer in Cardiovascular Regenerative Medicine, is a cardiovascular neuroscientist and BHF Intermediate Basic Science Research Fellow. Svetlana's research combines expertise in cardiac physiology, autonomic neuroscience, stem cell biology, and in vivo pharmacology. She employs a unique set of cutting-edge techniques, including viral gene transfer and tracing, pharmaco- and optogenetics, in vivo imaging, real-time neurotransmitter detection, biotelemetry, and cardiac electrophysiology applied to in vivo animal models.

Svetlana's work has significantly advanced our understanding of the innate mechanisms of cardioprotection, which involve the recruitment of autonomic reflexes. In her previous research, she demonstrated how vagus nerve activity can be recruited to protect the heart during myocardial infarction (Mastitskaya et al., 2012), preserve cardiac function in heart failure, and improve exercise capacity (Machhada et al., 2020). The signalling pathway from the vagus to the heart is complex and comprises a brain-gut-heart communication axis. Svetlana's research has shown that the cardioprotective action of vagus nerve stimulation on the heart is mediated, at least in part, by an increased release of GLP-1 from the gut (Basalay, Mastitskaya et al., 2016). Stimulation of GLP-1 receptors in the heart leads to the activation of pro-survival signalling pathways and reduces myocardial susceptibility to ventricular arrhythmias (Ang, Mastitskaya et al., 2018).

Svetlana's current research program focuses on the role of cardiac pericytes in the regulation of coronary blood flow in health and disease and how pericyte function can be manipulated to improve cardiovascular health via neuroendocrine mechanisms.

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Spotlight on Daniel Fudulu

Newly appointed consultant senior clinical lecturer in cardiac surgery

Daniel Fudulu has worked as a clinical academic at the Bristol Heart Institute and University of Bristol since 2012, when he started an SHO job in adult cardiac surgery. In parallel to his cardiac surgery training, he completed a PhD in stress response to heart surgery in children at the University of Bristol. He was successfully appointed during national selection to an approved training programme in cardiac surgery in 2017. He always had dedicated research time by being first appointed to an NIHR Academic Fellowship and then to an NIHR Clinical Lectureship.

In addition to his interest in stress research, his research also focused on risk prediction after cardiac surgery and using big data to answer clinically relevant questions in cardiac surgery. His latest research focuses on integrating omics data into clinical machine-learning algorithms to predict outcomes after heart surgery. A pilot study related to this work was also awarded a Clinical Lecturer Starter Grant from the Academy of Medical Sciences.

Daniel has completed his training in cardiac surgery (UK CCT) and has recently been appointed to a substantive consultant senior lecturer position in adult cardiac surgery at the University of Bristol. He will start this position after he returns from an advanced cardiac surgery fellowship in New Zealand in January 2025. Once he returns from New Zealand, his research vision for BHI includes using big data analytics to predict outcomes after cardiac surgery, designing pragmatic clinical trials in heart surgery, and working closely with fundamental sciences colleagues to address basic research questions in cardiac surgery.

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Spotlight on Jilau Li

Research experience from a first year PhD student

Jialu Li, a second-year PhD student at the Bristol Medical School and Bristol Heart Institute, is exploring how the endothelial glycocalyx (eGlx) impacts cardiac ischemia-reperfusion (I/R) injury, often occurring during open heart surgeries like aortic valve replacements and cardiopulmonary bypass. Her research primarily focuses on potential therapies to mitigate I/R injury symptoms, a condition that can affect up to 80% of patients with severe arrhythmic complications post-surgery.

The eGlx, a gel-like coating on endothelial cells, regulates vascular permeability and its damage is linked to adverse vascular responses and swelling. Notably, there is no existing evidence connecting pre-existing eGlx damage directly to myocardial I/R injury. Li's innovative work employs a genetically modified mouse model with the Ext1 gene knocked down to simulate eGlx damage, using the Langendorff system to assess cardiac functions before and after I/R injury.

Her findings aim to determine how eGlx integrity influences cardiac outcomes and to evaluate if specific therapeutic interventions can alleviate reperfusion symptoms. This could pioneer new treatments, addressing the significant clinical challenge where current drug therapies have failed in trials and preconditioning remains the primary strategy.

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Spotlight on Florence Mouy

Cardiology Academic Clinical Fellow

I'm Flo, and I have been working as a cardiology academic clinical fellow (ACF) in Bristol since August. Time does fly, but being in this role has given me the wonderful opportunity to combine my research interests with my clinical training. I have been working in the Bristol CardioNomics Research Group under the supervision of Dr Angus Nightingale and Dr Emma Hart. I'm working on several projects relating to cardiovascular health.

I have been writing a review on the link between hypertension and cerebral perfusion and have submitted an abstract to the British and Irish Hypertension Society 2024 conference on the relationship between age and posterior cerebrovascular variants in hypertension.

Another exciting area of research I am getting involved in is the role of the carotid chemoreflex in heart failure with preserved ejection fraction. There is some preliminary evidence suggesting that inhibiting some of the receptors in the carotid body can improve ventilatory efficiency in these patients, and this is an area of active research in our group. We are currently applying for a grant for a pilot study on this project.

Being in this role in Bristol has enabled me to join a community of like-minded people who are passionate about research. It has been really nice to be able to meet researchers from different groups in Bristol at different events such as the Research Retreat Day for the School of Physiology, Pharmacology and Neuroscience as well as the Research Showcase Day organised by the Clinical Academic Training School in Bristol. I look forward to my ongoing time doing research as part of the Bristol CardioNomics Group.

Our latest publications

From research at the Bristol Heart Institute 2024

•Pradeep Narayan, Tim Dong, Arnaldo Dimagli, Daniel P Fudulu, Jeremy Chan, Shubhra Sinha, Gianni D Angelini. *European Journal of Cardio-Thoracic Surgery*, Volume 65, Issue 2, February 2024, ezae031. Impact of explanted valve type on aortic valve reoperations: nationwide UK experience

•M.C. McNeill, F. Li Mow Chee, R. Ebrahimighaei, G.B. Sala-Newby, A.C. Newby, T. Hathway, A.S. Annaiah, S. Joseph, M. Carrabba, M. Bond; 04 Jan,2024. Substrate stiffness promotes vascular smooth muscle cell calcification by reducing the levels of nuclear actin monomers *JMCC*

•Reza Ebrahimighaei,, Nathalie Tarassova, Samuel C. Bond, Madeleine C. McNeill, Tom Hathway, Hunaid Vohra, Andrew C. Newby, Mark Bond. Volume 1871, Issue 2, February 2024, 119640 Extracellular matrix stiffness controls cardiac fibroblast proliferation via the nuclear factor-Y (NF-Y) transcription factor. *ScienceDirect*

•Jeremy Chan,Pradeep Narayan,Daniel P. Fudulu,Tim Dong,Gianni D. Angelini Trend in mitral valve prostheses of choice and early outcomes in the United Kingdom - International Journal of Cardiology. *Internal journal of cardiology* 2023 Nov 25:131607. doi: 10.1016/j.ijcard.2023.131607. Online ahead of print.

•Amerikos Argyriou1 MBChB MRes, Hunaid Vohra FRCS PhD1, Jeremy Chan MBBS MRCS1,Eltayeb Mohamed Ahmed1 FRCS, Cha Rajakaruna1 FRCS MD Gianni Angelini1 FRCS MD, Daniel Fudulu FRCS PhD1 “Incidence and outcomes of surgical pulmonary embolectomy in the United Kingdom” BJS Accepted (in course of publication).

•Fudulu, D. P., et al; 8 January 2024. "In-hospital outcomes predictors and trends of redo sternotomy aortic root replacements: insights from a UK registry analysis." *Frontiers in Cardiovascular Medicine*

Remember to send details of your latest publications to bcv-info@bristol.ac.uk and add keywords to Pure to ensure publications feed into the BHI feed http://www.bristol.ac.uk/research/institutes/heart/

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