South Wales and South West
Congenital Heart
Disease Network

DRAFT Research Strategy

GIG CYMRU NHS WALES

NHS

Background

Enhancing patient care through research is a key objective of the many studies being conducted within South Wales and the South West Congenital Heart Disease Network. It is widely accepted that aA research active culture can bring a host of benefits for patients, clinicians and the NHS. Research drives innovations, enables better and more cost-effective treatments and creates opportunities for staff and patients. The NHS England CHD Service Specification and Standards 2016 acknowledges the benefits of research within networks and in section G states that Congenital Heart Disease Networks must:

- have, and regularly update, a research strategy and programme that documents current and planned research activities in the field and the resource needed to support the activity and objectives for development.
- include a commitment to working in partnerships with other specialist surgical (Level 1), cardiology (Level 2) centres, and local (Level 3) centres, as appropriate, in research activity which aims to address issues that are important for further development and improvement of clinical practice, for the benefit of patients.
- demonstrate close links with one or more academic departments in higher education institutions.
- Where they wish to do so, patients should be supported to be involved in trials of new technologies, medicines etc.

The standards for all centres within the network (Level 1, 2 and 3) state that all centres should participate in research (G1).

Purpose

Within the South Wales and South West CHD network there is a vast arrange of academic and clinical trials research being conducted, with well-established links between members organisations and the academic institutions in the region. The purpose of this strategy is to sign post to existing key research strategies in its member organisations and to provide a programme of research activity that documents current and planned CHD research activities within the network. This programme of research activity will be updated on an annual basis and presented to the Clinical Governance Group, which has delegated responsibility for research from the Network Board. An update on research in the network will also be included in the SWSW CHD Networks Annual Report. The research strategy and programme of activity, as well as other useful research links, will be made available on the SWSW CHD Network website https://www.swswchd.co.uk/en/page/research-useful-links.

Research within the Congenital Heart Disease Network South Wales and South West

Key Research links across the Network			
	NHS provider	**Academic/Research Institutions**	**Research policies/strategies**
Level 1 centres	**UH Bristol Foundation Trust** Research and Innovation Department **BHI Research Team-** Adult Cardiology research, Adult Cardiac Surgery research **BRCH Cardiac Research Team** - The Cardiac Research Nursing Team, which has been in existence for 6 years, consists of 2.9 WTE and draws together cardiac research studies under one umbrella to ensure a single approach for families. Fetal research – tbc **Women & Childrens Divisional Research Leads-** Professor Ramannan, Professor Adam Finn and Natalie Fineman (research nuse)	Bristol University – Clinical Research and Imaging Unit British Heart Foundation Congenital Research Programme (led by Professor Massimo Caputo) Bristol NIHR Biomedical Research Center	UH Bristol research and innovation strategy please click here **NIHR**; https://www.nihr.ac.uk/
Level 2 centres	**Professor Orhan Uzun** leads the Paediatric Cardiac Units research programme	Cardiff University	https://www.healthandcareresearch.gov.wales/policy-and-strategy/
Level 3 centres	tbc	Exeter University	

CHD Network South Wales and South West rolling research programme – 2018/19

Currently Recruiting

No	Name of study	Key aims	Principle investigator	Expected finish date	For further information
1	INVITE	The effectiveness on post-operative recovery of using 'off pump' self-expanding tissue valves (IPVR) versus 'on pump' conventional tissue valves (PVR) for pulmonary valve replacement: a pilot randomised controlled trial (RCT).	Mr AJ Parry	October 2018	Paediatric Cardiac Research Team 0117 342 8889
2	SAXOPHONE	The objectives of this study are to assess the following in paediatric subjects with congenital or acquired heart disease requiring chronic prophylactic anticoagulation: □ the safety of apixaban □ apixaban PK, PD (by measuring FX using chromogenic assay), and anti-FXa activity □ the effects of apixaban versus VKA or LMWH on QOL measures □ the efficacy of apixaban for thromboprophylaxis (exploratory aim) □ biomarkers that may reflect anticoagulant efficacy or risk of thrombosis □ the effects of apixaban on bone density	Dr RP Martin	28/02/2021	Paediatric Cardiac Research Team 0117 342 8889
3	THERMIC 3	The hypothesis to be tested is that compared to ICBC, IWBC improves myocardial metabolism and reduces early morbidity in children undergoing open heart surgery. We will quantify the effectiveness of IWBC compared to ICBC both with respect to an objective measure of myocardial damage using serum cTnT levels and with respect to a range of secondary outcomes.	Mr SC Stoica	31/07/2020	Paediatric Cardiac Research Team 0117 342 8889
4	PEACOCK	We aim to study the stress response to cardiac surgery and cardiac catheterisation in children and babies.	Prof Angelini	01/08/2020	Paediatric Cardiac Research Team 0117 342 8889
5	STEM CELL	The aim of this project is to upgrade the valved-conduits and patches commonly used in reconstructive CHD	Prof Caputo	30/06/2020	Paediatric Cardiac Research

		surgery, by creating biomaterials/medical devices endowed with potential to grow, remodel and regenerate the failing right ventricle in vivo. We will test different cell products, including autologous stem cells from neonatal heart and bone marrow and blood, and cardiovascular cells derived from autologous induced pluripotent cells, to verify the optimal regenerative component within the medical device. We shall then use an in vivo CHD piglet model to test the new devices for proof of concept of feasibility and efficacy. If feasibility and efficacy is demonstrated we will perform a first-in-human clinical trial, comparing bio-engineered and conventional scaffolds for reconstruction of the right ventricular outflow tract and pulmonary arteries which will be the subject of future applications for regulatory approval.			Team 0117 342 8889 m.caputo@bristol.ac.uk
6	TRECCA	The immediate aims of TRECA are to evaluate the potential for MMIs to improve the quality of decision making about participation in healthcare trials involving children and adolescents with long-term conditions, and to assess the impact on trial recruitment and retention. The long-term aim of the project is to increase the available clinical evidence base for the treatment of children and adolescents with long-term conditions	Mr SC Stoica	31/07/2020	Paediatric Cardiac Research Team 0117 342 8889
7	TUB	Comparison between temperature sensing urinary catheter and rectal temperature probes for measurement of core body temperature in children undergoing open heart surgery.	Mr SC Stoica	31/07/2020	Paediatric Cardiac Research Team 0117 342 8889
8	Outcome Monitoring in Cardiac Surgery (OMACS)	Monitoring short, medium and long term outcomes in heart surgery patients.	Lucy Culliford	March 2026	lucy.culliford@bristol.ac.uk
9	Gabapentin in Post Surgery Pain (GAP)	Effectiveness and safety of Gabapentin versus placebo as an adjunct to multimodal pain regimens in surgical patients.		November 2020	sarah.baos@bristol.ac.uk

In Follow-up Phase (active recruitment completed)

No	Name of study	Key aims	Principle investigator	Expected finish date	For further information
1	Injectable Valve Implantation Trial (INVITE)	Comparing conventional pulmonary valve replacement with Injectable valve replacement.	Rachael Heys	February 2021	rachael.heys@bristol.ac.uk

In Results Phase

No	Name of study	Key aims	Principle investigator	Status	For further information
1	THERMIC 2	An RCT to compare normothermic (35-37°C) and hypothermic (28°C) CPB for the repair of common congenital cardiac pathologies. It is expected that this work will provide important information to improve strategies of CPB perfusion and therefore decrease the inevitable organ damage that occurs during the non-physiological body perfusion with extracorporeal circulation in paediatric cardiac surgery.	Prof Caputo	Accepted for publication in HEART journal	Paediatric Cardiac Research Team 0117 342 8889
2	DECISION	We anticipate that testing for blood clotting abnormalities in children before or after cardiac surgery will confer benefit by helping to reduce excessive bleeding and transfusion of allogeneic blood components after cardiac surgery. The potential benefits of testing for blood clotting abnormalities is two-fold; a) test results may enable us to improve selection of the best treatment products in children with blood clotting abnormalities, and, b) test results may enable us to prevent the use of unnecessary treatments in children who do not have blood clotting abnormalities. The study objectives are as follows: Objective 1: to describe the prevalence of the different types of blood clotting abnormality in children before and after cardiac surgery. Objective 2: to estimate the association between (a) the laboratory test results and clinical concern about bleeding (CCB) after cardiac surgery, and (b) different types of blood clotting abnormality and clinical concern about bleeding after cardiac surgery. Objective 3: to estimate the diagnostic accuracy of ROTEM tests vs. reference laboratory tests for the different types of blood clotting abnormality identified (a) before and (b) after cardiac surgery. Objective 4: to investigate the agreement between the treatment recommended by	Dr A Mumford	Awaiting results	Paediatric Cardiac Research Team 0117 342 8889

		the results of the reference tests and the treatment recommended by the ROTEM test results.			
3	OXIC 2	A prospective randomised controlled trial, a comparison between normoxic (normal for a cyanotic child: 70-100 mmHg) and standard (high for a cyanotic child (relatively hyperoxic): 150-200 mmHg) CPB prior to the ischaemic cardioplegic arrest for children undergoing surgery for congenital cyanotic heart disease.	Proff Caputo	Awaiting results	Paediatric Cardiac Research Team 0117 342 8889
4	AIMS	In this study we wish to translate the pre-clinical, neonatal and paediatric work into a randomised clinical trial to investigate whether the ARB Irbesartan can reduce aortic dilatation in patients with Marfan Syndrome (MFS) compared to placebo.	Dr AG Stuart	Presented at European Society of Cardiology. Full publication to follow.	Paediatric Cardiac Research Team 0117 342 8889

British Heart Foundation Congenital Heart Disease Research Program

The team (led by Prof Massimo Caputo and encompassing engineers, basic scientists and clinicians) has strong and active collaborations in Bristol (across the BHI and within the University), in the South West, nationally and internationally. The program is also linked to the Bristol NIHR Biomedical Research Center 2018-2022.

There are four main strands to the team's research:

1. Imaging-based research

Using imaging data in CHD and ACHD patients to better understand aspects of their pathophysiology, this includes both retrospective and prospective work, making use of large imaging database but also collecting state-of-the-art imaging data prospectively in patients.

- Using statistical shape modelling to better characterize the morphology of the aortic aortic arch in presence of CHD (BAV, CoA)
- Studying aortic and pulmonary hemodynamics using 4D cardiovascular magnetic resonance (CMR) imaging (BAV, TOF, TGA)
- Evaluating ventriculo-arterial coupling non-invasively by means of CMR-derived wave intensity analysis including calculating vessel distensibility
- Integrating information from different imaging modalities, e.g. CMR + stress echo

Publications include:

- Sophocleous et al. EJCTS 2019 (https://www.ncbi.nlm.nih.gov/pubmed/30380029)
- Neumann et al. Physiol Measur 2018 (https://www.ncbi.nlm.nih.gov/pubmed/30192235)
- Sophocleous et al. JCDD 2018 (https://www.ncbi.nlm.nih.gov/pubmed/29671812)

2. 3D (bio)printing

Established a 3D Lab with the support of The Grand Appeal (The Grand Appeal 3D Bio-Printing Unit) at the Clinical Research & Imaging Centre (CRIC Bristol).

- Exploring uses of 3D printing technology, e.g. decision-making, training/teaching, counselling and research
- Refining workflow for producing CHD models, including industrial collaboration (3DLifePrints) supported with MRC grant
- Multiple collaborations (e.g. BHF grant with GOSH) and exploring new applications (foetal model is collaboration with Prof Luciani's team in Verona)
- International standing: 3D+ Special Interest Group of the Society of Cardiovascular Magnetic Resonance (SCMR)

Publications include:

- Lee et al. BMJ Open 2019 (https://www.ncbi.nlm.nih.gov/pubmed/30852545)
- Biglino et al. BJR 2018 (https://www.ncbi.nlm.nih.gov/pubmed/30325646)
- Biglino et al. IJAO 2019 (in press)
- Biglino et al. Front Pediatr 2017 (https://www.ncbi.nlm.nih.gov/pubmed/29034225)

3. Tissue engineering

Research geared toward creating living material made by cellularized grafts that, once implanted into the heart, would grow and remodel in parallel with the recipient organ, avoiding repeated surgical corrections for failed grafts (big clinical problem in CHD). Research focuses both on exploring feasibility of engineering clinical-grade living autologous replacement grafts using different cell types and developing scaffolds suitable for cardiovascular tissue engineering applications and *in vivo* usage.

Publications include:

- Iacobazzi et al. Tissue Eng Part A 2018 (https://www.ncbi.nlm.nih.gov/pubmed/29054134)
- Swim et al. Tissue Eng Part A 2018 (https://www.ncbi.nlm.nih.gov/pubmed/30284966)

4. Clinical studies and creation of CHD databases

Clinical studies and the collection of clinical data, including the creation of databases, with a vision to link data of different scales, from clinical variables to 'omics'. This includes creating REDCap databases and linking clinical data and clinical follow-up with imaging (echo, MRI, exercise) and 'omics', including on-going analysis of microRNA profiling and proteomics. We have conducted two major control randomised trials, supported by the BHF and NHIR-BRU Bristol, comparing normothermic vs hypothermic (THERMIC) and hypoxic vs normoxic (OXIC) CPB in paediatric patients.

Publications include:

- Caputo et al. Heart 2018 (https://www.ncbi.nlm.nih.gov/pubmed/30322847)
- Heys et al. BMJ open 2019 (https://www.ncbi.nlm.nih.gov/pubmed/30944136)
- Stoica et al. JTCVS 2019 (in press)

Patient and public engagement/involvement (PPI/E)

The team also has a strong focus on exploring and incorporating patients' views, including collaborating on a national touring exhibition exploring cardiovascular anatomy and disease (www.insidetheheart.org, PI Dr Giovanni Biglino) that was realized in 2018 and offered great opportunity for additional events and interactions with patients and the general public at various events.

Publications include:

- Biglino et al. Cardiovasc Diagn Ther 2019 (https://www.ncbi.nlm.nih.gov/pubmed/30881882)
- Biglino et al. Medical Humanities 2018 (https://www.ncbi.nlm.nih.gov/pubmed/30337338)