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Case Studies

OHMR Cardiovascular Research Capacity Program
Interim Evaluation

Prepared by Urbis for Agency for Clinical Innovation

May 2025

Agency for Clinical Innovation

NSW GOVERNMENT

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aci.health.nsw.gov.au

AGENCY FOR CLINICAL INNOVATION

1 Reserve Road St Leonards NSW 2065
Locked Bag 2030, St Leonards NSW 1590
Phone +61 2 9464 4666
Email **aci-info@health.nsw.gov.au** | **aci.health.nsw.gov.au**

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Contents

Acronyms and abbreviations

Term	Meaning
AF	Atrial fibrillation
CHD	Congenital heart disease
CMR	Cardiac Magnetic resonance
CVD	Cardiovascular disease
FWCI	Field Weighted Citation Impact
MRFF	Medical Research Future Fund
NAD	Nicotinamide adenine dinucleotide
PDGF	Platelet Derived Growth Factor
PSC-CM	Pluripotent stem cell derived cardiomyocytes
VT	Ventricular tachycardia
WHO	World Health Organisation

Background

OHMR cardiovascular research capacity program interim evaluation

The Cardiovascular Research Capacity Program (the Program) is a ten year (2018 – 2028), $150 million, NSW Government investment in cardiovascular research in NSW (1). The Program aims to build cardiovascular research capacity in NSW to drive scientific discoveries, support the development of innovative therapies, and ultimately improve health outcomes for patients with cardiovascular disease (CVD) (1).

The Office for Health and Medical Research (OHMR) engaged the Agency for Clinical Innovation (ACI) to conduct the interim evaluation of the Cardiovascular Research Capacity Program (1).

The objectives of the evaluation are to

- assess how well the Program, and its individual grant types, has been implemented to date
- assess outcomes of the funded grant research projects based on evidence to date
- assess the impact of the Program on the CVD research community to date
- capture the total costs of the Program and generate an early assessment of net social benefit of the Program for NSW (2).

Case studies

As part of the evaluation, ACI engaged Urbis to conduct eight case studies with selected grant projects (1). The purpose of the case studies is to capture in depth evidence about the likelihood for funded projects to contribute to the Program long-term outcomes, including for priority populations, and generate a net social benefit for NSW (1).

The outcome focus areas for the case studies are

- knowledge advancement
- capability building
- policy and practice
- health and community impact
- economic benefits (2).

The following report presents the eight case studies, and the outcomes generated under each project against the focus areas.

Methodology

The case studies employed a mixed-methods approach to collect and triangulate evidence. The case studies are informed by the following key data sources.

Data source and timing	Details
Document and data review March 2025	Urbis conducted a rapid review for each grant project using grant report data and survey responses. This data was analysed and used to inform the development of the discussion guides tailored to each grant project. Urbis also conducted a rapid review of other relevant program documentation (such as evaluation and grant guidelines) to inform discussion guide development and case study structure.
Interviews with grant recipients March 2025	Urbis conducted eight interviews with grant recipients (n=8). Interviews were one hour and held online over Microsoft Teams. Following each interview, Urbis analysed the data collected in the discussion along with the data analysed in the document and data review to develop findings for the case studies.

Limitations

The following limitations should be taken into consideration when reading this report:

- As some of the research discussed is basic science, and some projects are still being undertaken, recipients were not always able to identify outcomes that have occurred to date, particularly outcomes further along the research translation pathway (translation to practice). As such, recipients at times hypothesised on potential outcomes that could be generated in the future. These have been included and indicated.
- These case studies reflect outcomes as at the time this report was written (May 2025). For many projects outcomes will increase over time. For example, economic benefits via additional grants may increase, or treatment or savings or guideline changes may be yet to materialise. Citations will also increase over time- as such Field Weighted Citation Impact is a reflection of citation impact as at May 2025. Outcomes should be understood in this context.
- Each case study represents a unique piece of research. As such, case studies are not intended to be comparable. Outcomes differ between case studies, and not all case studies will show outcomes in each outcome area. This does not indicate a research project's level of success, rather, it indicates where outcomes are relevant or not.

Case Study 1: Cardioprotective effects of the pneumococcal polysaccharide vaccine

Project Summary

Grant recipient: Professor John Attia	**Grant type: Clinician Scientist Grant; Round 1; Health services research**
Funding received: $600,000 (May 2019 – December 2023)	**Other CVD Research Capacity Program grants received by recipient:** Investigator Development Grant (2020-2022)

Key outcomes generated:

Publication metrics – Four publications with an average FWCI of 1.04 have been published.[1] Findings have been shared at multiple conferences (number not known).

Economic benefit – $100,000 in additional funding leveraged.

Knowledge advancement – The research provided a robust result demonstrating the pneumococcal vaccine does not contribute a cardioprotective effect in humans, closing this knowledge gap.

Capability building – Two researchers involved on the project have gone on to become university faculty staff through their contributions and experience gained.

The research problem

The question as to whether the pneumococcal Pneumovax vaccine[2] also has a cardioprotective effect (i.e. it protects against heart attacks and strokes) has, for some time, been present due to a body of research showing this effect in mice. However, whether the effect translates to humans has until recently remained unanswered. Although observational human data supported this effect, there was no randomised controlled trial. If it were to translate to humans, this would have major implications for the prevention of CVD.

Research aims

This research had one aim, to establish whether the cardioprotective effect of the pneumococcal vaccine seen in mice can translate to humans. This required a national, multicentre, randomised controlled trial to test the effect of the vaccine in humans.

[1] Average FWCI for the four publications calculated by averaging FWCI scores as given by Scopus.

[2] The pneumococcal Pneumovax vaccine targets pneumococcal disease; a bacterial infection (3). Up until July 2020, the Australian National Immunisation Program recommended the pneumococcal vaccination age for healthy, non-Indigenous adults be 70 years old (previously 65 years old) and that the vaccine change from Pneumovax to Prevenar for this age group (4,5).

Research findings

The research found that the cardioprotective effect of the pneumococcal vaccine seen in mice did not translate to humans. The antibodies that were thought to mediate the cardioprotective effect were present at one month but had disappeared by two years, and there were no differences between the group that received the vaccine and the group that didn't in terms of any of the surrogate markers of CVD (such as cholesterol or glucose markers). Linked data of CVD events also showed no ultimate difference between the groups.

While the result was negative, it was a robust negative, meaning the finding is considered reliable due to the robustness of the methods used. The research was the first and only test of the cardioprotective effect of the vaccine in humans internationally, and as such, has provided a clear answer to this long unanswered question.

Outcomes generated

Knowledge advancement

New knowledge generated by the funded project

The research found that the pneumococcal vaccine does not have cardioprotective properties in humans.

Increased publication reach and quality

The knowledge generated has been shared in several ways. The surrogate measures were published at two and four years, and the recruitment experience, method, and protocol were also published. The findings of the research have recently been submitted for publication.

Additionally, findings have been shared at multiple conferences.[3]

Four publications have been published from this research. These are:

Publication	Citations (Scopus)	FWCI (Scopus)
"Rationale and design of a randomized controlled trial of pneumococcal polysaccharide vaccine for prevention of cardiovascular events: The Australian Study for the Prevention through Immunization of Cardiovascular Events (AUSPICE)", American Heart Journal, 2016	35	1.54
"Generation of cardio-protective antibodies after pneumococcal polysaccharide vaccine: Early results from a randomised controlled trial", Atherosclerosis, 2022	11	1.46

[3] The grant recipient was not able to provide details on these conferences, including number of conferences or names of conferences.

"Evaluating recruitment strategies for AUSPICE, a large Australian community-based randomised controlled trial", Medical Journal of Australia, 2019	13	0.70
"Persistence of Detectable Anti-Pneumococcal Antibodies 4 Years After Pneumococcal Polysaccharide Vaccination in a Randomised Controlled Trial: The Australian Study for the Prevention through Immunisation of Cardiovascular Events (AUSPICE)", Heart Lung and Circulation, 2023	2	0.46

Policy and practice

Changes to policy and clinical practice

There was no change to policy and clinical practice coming from the project.

New treatments used in clinical care

The development of treatments is not relevant to this project.

The grantee suggested that the data generated could possibly be used to develop a more robust immune response. This is because the research showed that antibodies do occur from the vaccine, though they disappear by two years. The grantee suggested that another researcher might be able to take these findings and pursue ways to make the vaccine more antigenic. However, the grantee was not currently exploring this, nor planning to.

Prevention practices

The pneumococcal vaccine does not contribute a cardioprotective effect, and therefore is not being progressed into any preventative measure.

Health and community impact

Potential to reduce burden of disease

As the cardioprotective effect was not found, the research has not contributed to reducing burden of disease for priority populations.

Economic benefits

Impact on funded researchers' career's progression

The grant recipient reported that the grant had allowed them to continue and complete research that had been started under previous NHMRC funding. The NHMRC funding had initially been granted to fund a large scale randomised clinical trial over five years to test the effect of the pneumococcal vaccine in humans. However ethical approval and recruitment processes took much longer than expected and expended much of this funding. Obtaining the Clinician Scientist grant meant that the research could be completed, and the work established under the NHMRC grant was not wasted. It also provided funding for additional research beyond what was initially allowed through the NHMRC grant. This included

surrogate measures to be studied that could provide insight into any short-term changes generated by the vaccine, as final outcomes couldn't be measured for six to seven years. However, having the capacity to study surrogate measures in the interim meant papers could still be published from this research project. In these ways, receiving the funding was critical to the grant recipient's career as it allowed their body of research to be finalised.

The grant recipient is now retired so there is no further relevant career outcomes following this project.

Impact on NSW cardiovascular disease research capacity

The research leveraged a second CVD grant (Investigator Development Grant) worth $100,000 which supported the inclusion of testing for surrogate measures. This was supported through an international collaboration with a researcher based in the US, who conducted the testing for surrogate measures.

Potential for commercialisation of research outputs and revenue forecast

Commercialisation was not relevant to this research.

Economic benefits from improved patient care

Economic analysis undertaken by the research team suggested that had the vaccine been shown to contribute a cardioprotective effect, one vaccination would have reduced an individual's risk of heart attack and stroke by 25 per cent. This would have meant notable impact on quality of life years gained and related economic benefits from avoided health care costs (100 per cent vaccine coverage was associated with additional mean cost saving of $179 and a mean quality of life year gain of 0.0075 per person over 10 years) (6). However, as the cardioprotective effect was not found these benefits were not realised.

The grant recipient was not able to comment on the costs that have been avoided by not increasing the vaccine uptake to a broader age bracket. The pneumococcal vaccine is at no cost to the individual regardless, so there is no avoided cost to the individual. Economic analysis undertaken by the research team suggested the current 50 per cent uptake could increase to up to 100 per cent uptake if the results were positive and increased uptake recommended. Hence, it could be assumed that cost of increased rollout for the health system would increase similarly.

Capability building

The funding was used to attract a PhD pharmacy student who wrote their PhD on the project, contributed to writing the research protocol, and published some of the surrogate outcome papers. This student has since received their PhD and is on the University of Newcastle faculty.

Additionally, a research nurse engaged on the project used the experience gained from this research to assist on a number of other studies undertaken at the Hunter Medical Research Institute.

Case Study 2: Developing novel treatments to improve heart failure and myocardial infarction outcomes

Project summary

Grant recipient: Associate Professor James Chong	**Grant type:** Clinician Scientist Grant; Round 1; Basic science
Funding received: $750,000 (May 2019- June 2022)	**Other CVD Research Capacity Program grants received by recipient:** Investigator Development Grant (2020-2021); Early Mid-Career Researcher (Round 4)

Key outcomes generated:

Publication metrics – 47 publications have been published from this research with average impact factor of 6.658.[4] Findings were shared at 13 national and international conferences.

Economic benefits – Additional funding leveraged off this research is over $7 million. The research has contributed to Westmead's growth into a heart research hub.

Knowledge advancement – Two novel therapies for heart attacks have been tested in pig models and are progressing toward clinical trials.

The research problem

Myocardial infarctions, or heart attacks, can lead to heart failure and are a significant cause of death in Australia (7). This is because heart attacks cause scarring of the heart muscle, and the scar tissue can't function as normal heart muscle (8). Treatment of heart attack includes immediate measures to salvage the parts of the heart muscle at risk of scarring, however, this treatment is not always adequate and patients frequently progress to heart failure (7).

Research aims

The purpose of the project was to develop novel therapies to reduce the costs associated with death and illness from heart attacks and resulting scarring. It involved two aims:

- Aim 1: Pluripotent stem cell derived cardiomyocytes (PSC-CM). Pluripotent stem cells can be differentiated into any cell type - in this case, cardiomyocytes, the heart's muscle cells (9,10). Aim 1 explored growing cardiomyocytes from pluripotent stem cells. The rationale for growing heart cells was that eventually this might result in a therapy where the damaged heart muscle can be replaced with the lab grown heart muscle.

[4] Average impact factor calculated from the average of Impact factors for the 47 publications as provided by grant recipient in their CV.

- Aim 2: Platelet Derived Growth Factor (PDGF). PDGF are peptides that play a role in wound healing, tissue repair, and cell growth (11,12). Aim 2 explored PDGF as a novel treatment for heart repair following heart attack. The grant recipient had undertaken previous research regarding the therapeutic potential of PDGF but needed funding to progress the concept into the next phase by testing on large animal models. This grant allowed for testing in a pig model.

Research findings

Through Aim 1, the project identified which cells would engraft into a host heart best, the PSC-CM with the lowest cardiac arrythmias after engraftment, and that cardiac arrhythmias from PSC-CM are due to subpopulations of atrial and pacemaker-like cells that can be removed to make the product safer.

Under Aim 2, the project found PDGF increases heart function for three months in a pig model, showing that the benefits of PDGF therapy are enduring in a large animal model.

Outcomes generated

Knowledge advancement

New knowledge generated by the funded project

The research made considerable progress in developing novel therapies for heart attack and heart failure; in Aim 1, PSC-CM, and Aim 2, PDGF.

In testing the PDGR therapies on pig models, an important step was made in progressing these treatments along the knowledge translation pathway. This is because it enabled testing in large animal (pig) models as the next step after the grantee's previous research testing in small animal (mouse) models. The grant recipient reported that for the therapies to progress further along the knowledge translation pathway and eventually be implemented in practice, clinical trials would need to be undertaken dependent on TGA approval.

Following this project, funding was received to progress the PSC-CM to clinical trials. The grant recipient estimated that, should evidence continue to show this as an appropriate treatment, in approximately ten years it could become an approved therapy. Similar trials occurring internationally support the likelihood of this eventuality.

As noted below in Economic Benefits, the research team has since shifted the development of the full-length protein to focus on a peptide mimetic of this product instead. In vitro and in vivo rodent testing has been performed for this, and patents have been filed.

Increased publication reach and quality

The research has resulted in 47 publications. The top five publications by FWCI are:

Publication	Citations (Scopus)	FWCI (Scopus)
"Cellular heterogeneity of pluripotent stem cell-derived cardiomyocyte grafts is mechanistically linked to treatable arrhythmias", Nature Cardiovascular Research, 2024	10	7.39
"Mechanistic Insights and Knowledge Gaps in the Effects of Radiation Therapy on Cardiac Arrhythmias", International Journal of Radiation Oncology Biology and Physics, 2024	1	6.26
"Vascular cells improve functionality of human cardiac organoids", Cell Reports, 2023	44	5.55
"NETosis and thrombosis in vaccine-induced immune thrombotic thrombocytopenia", Nature Communications, 2022	55	4.19
"Clinical Pathway for Coronary Atherosclerosis in Patients Without Conventional Modifiable Risk Factors: JACC State-of-the-Art Review", Journal of the American College of Cardiology, 2023	29	3.55

Additionally, the grant recipient was invited to share findings at 13 talks at national and international meetings, which have involved scientists, clinicians, and at times clinical trialists and policy makers.[5] These were:

- 2024 November- Westmead Health and Innovation District Conference "Transformative Healthcare Innovations and Commercialisation of Research" (Panel discussion).
- 2024 September- 30th Annual Congress of The Transplantation Society, Istanbul, Türkiye. "Regenerative Medicine in Cardiology"
- 2024 September- Children's Medical Research Institute Seminar Series, Sydney, Australia. "New Therapies for Heart Regeneration".
- 2024 August- Cardiac Society of Australia and New Zealand Annual Scientific Meeting, Perth, Western Australia, Australia. "Next generation heart failure therapies".
- 2024 May - Invited plenary, "Manipulating cell product before and after engraftment arrhythmias to solve engraftment arrhythmias", 8th Annual NIH Progenitor Cell Translational Consortium Cardiovascular Bioengineering Symposium, Houston, Texas, USA.

[5] The grant recipient was unable to assess which conferences were the most impactful nor provide attendance details.

- 2023 December - CIRCE, Cardiovascular Conversations, Madrid, Spain “Cellular therapies to treat Cardiovascular Diseases”.
- 2023 October - Centenary Institute, Sydney, NSW, Australia “Developing new therapies to repair and regenerate the damaged heart”.
- 2023 September - Baker Heart and Diabetes Institute, Melbourne, Vic, Australia “Developing new therapies to repair and regenerate the damaged heart”.
- 2023 August - Cardiac Society of Australia and New Zealand Annual Scientific Meeting, Adelaide, SA, Australia. “iPSCs and Cardiac Repair”.
- 2023 May - NIH/Keio University Cardiovascular Bioengineering Symposium, Kyoto Japan. “Protein and peptide therapeutics for repair of the infarcted heart”.
- 2023 February - New South Wales Cardiovascular Research Network ECR event. “Grants for success: lessons learned from writing and reviewing grants”.
- 2022 November - Sydney-Seoul Research Network Webinar Series. “Mechanism and treatment of pluripotent stem cell derived cardiomyocyte graft arrhythmias”.
- 2022 June - NIH/DZHK Cardiovascular Bioengineering Symposium, Gottingen Germany. “Pluripotent stem cell derived cardiomyocyte graft arrhythmia mechanism and treatment”.

Policy and practice

Changes to policy and clinical practice

Changes to clinical policy are not a focus of this research.

The grant recipient did however note some potential implications for clinical practice. Eventually, it is hoped that the therapies could become an alternative treatment option offered in clinical practice, and that in providing these options, the approach to treating heart failure could shift from a current reliance on heart transplant and toward a regenerative approach that rebuilds the existing heart. This was highlighted in the context of Australia’s ageing population and the increasing demand for effective treatments for heart attack and failure. The grant recipient was not able to provide an estimated timeframe for this to occur.

New treatments used in clinical care

As described above, the project has made progress in developing novel therapies. Though they have not yet been implemented in clinical care, steps are being taken to progress toward clinical trials in the hope that they will one day be implemented in clinical care.

Prevention practices

Outcomes for prevention practices are not relevant for this project. The PSC-CM therapy is intended for application where the heart is already failing, and similarly the PDGF therapy targets heart attack patients who already have significant injuries following heart attacks.

Health and community impact

Potential for improvement in care or outcomes for priority populations and related comorbidities or diseases

Generally, these therapies will provide particular benefit for older people who tend to experience heart failure at a higher rate. The grant recipient identified that accessing a heart transplant typically takes time and is high cost.[6] Importantly, in addition, many patients are not ever eligible for heart transplant. If the PSC-CM were available, it would mean an ongoing supply of heart muscle cells to address this demand, and patients wouldn't need to wait for transplants to become available, therefore accessing treatment quicker.

The grant recipient suggested that the PDGF therapy could likely particularly benefit patients from regional areas. This is because these patients don't have the same access to 24-hour angioplasty[7] compared to those in metropolitan areas, which means they are more likely to experience significant heart attacks.

The research targets and offers improved outcomes for patients with an 'untreatable' disease. This is because the therapies developed could provide an alternative option to patients who would otherwise have no other treatment option if they were not valid candidates for heart transplants.

Economic benefits

Impact on funded researchers' career progression

The grant recipient identified that the grant allowed them to subsequently gain almost $5 million in MRFF funding for the PSC-CM clinical trial, which was considered a significant step in progressing the research program. The recipient noted that because the grant allowed for funding to support a program of work rather than a single project, they were able to progress both lines of research (PSC-CM and PDGF) and build momentum that was otherwise unlikely to have occurred.

Impact on NSW cardiovascular disease research capacity

The following funding was leveraged:[8]

- MRFF grants, $4,978,369 (to take the PSC-CM into the next phase with a clinical trial), $998,838 and $450,000
- Medical Research Future Fund Stem Cell Mission $977,183
- Australian Stroke and Heart Research Accelerator Project Grant, $250,000
- National Heart Foundation Vanguard Grant, $150,000
- Therapeutic Innovation Australia Pipeline Accelerator Grant, $50,000.

[6] The grant recipient was not able to provide a time period for which patients wait before receiving heart transplant, as it is extremely variable and dependent on matching and patient characteristics. They were also not able to comment on cost specifically, but referenced the following "in 2020, the average cost of a heart transplant in the United States before insurance was $1,664,800" (13).

[7] Angioplasty is a procedure to open blocked coronary arteries to minimise risk of heart attack (14)

[8] The grant recipient was not able to comment on the extent to which the funded project specifically contributed to this funding being leveraged.

The grant recipient felt that Westmead had grown significantly as a heart research hub and precinct through receiving grants, including the MRFF Stem Cell Mission grant.

Potential for commercialisation of research outputs and revenue forecast

Efforts are currently being made toward commercialisation. For the PSC-CM therapy, a provisional patent was filed in 2023 on the discovery of the PSC-CM with the lowest cardiac arrythmias.

After receiving the Clinician Scientist grant, commercialisation efforts were made for the PDGF therapy using a full-length protein. After receiving feedback that full length proteins are difficult to produce for the large scale required for clinical therapeutics, the research team instead created peptides, small fragments of the full-length protein that can mimic its functions. This has recently been tested in rodents and a provisional patent was filed in 2022.

Economic benefits from improved patient care and reduced burden of disease

Heart failure and heart attacks are two of the largest causes of morbidity and mortality in NSW, Australia and around the world. The grant recipient suggested that if both PDGF and PSC-CM treatments show evidence of effectiveness and are integrated into practice, they would lead to improved patient care and reduce the burden of disease related to illness and death following heart attack. They were not able to provide a dollar estimate.

Capability building

The research group included four research assistants, six exchange students and undergraduates, 19 Doctor of Philosophy and Masters students and four postdoctoral students. Two honours research students received supervision through this project. Four PhD students were finalists for the Ralph Read prize, and one PhD student was the first author of a published paper.

The grant recipient reported that OHMR grant-supported training and researcher development[9] is likely to have a compounding effect, where supported researchers are going on to provide training to other colleagues and widening cardiac research capability across the Westmead hub.

[9] The grant recipient was not able to quantify a dollar value for the training and development supported through this grant.

Case Study 3: Translating genomics to clinical care of patients with inherited heart disease

Project summary

Grant recipient: A/Professor Richard Bagnall	**Grant type:** Senior Scientist Grant; Round 1; Clinical medicine & science
Funding received: $750,000 (May 2019 - June 2022)	**Other CVD Research Capacity Program grants received by recipient:** Investigator Development Grant (2020-2021); Senior Researcher (2022-ongoing)

Key outcomes generated:

Publication metrics – 17 publications have been published from this research with an average FWCI of 2.17.[10] The research has been presented at eight national and international conferences.

Economic benefits – Additional funding leveraged from this research totals over $3 million. The grant recipient has established themselves as an expert in their field through this research, and since progressed significantly in their career to Associate Professor and head of CVD Research at the Centenary Institute.

Knowledge advancement – Methods by which to improve genetic testing for heart disease have been identified and shared.

Clinical practice – Newly identified variants are now included on genetic testing panels.

The research problem

Inherited heart diseases are a collection of heart muscle diseases and abnormal heart rhythm disorders that can lead to heart failure and sudden death (15). If a person is diagnosed with inherited heart disease, family members can be tested and clinically monitored to reduce this risk (15). However, genetic testing outcomes can be improved. Commercial genetic testing, at the time of the research, was limited to screening the protein coding regions of genes only, which only represent one per cent of the DNA (15).

Research aims

The research aimed to improve genetic testing outcomes for patients with inherited heart diseases. It involved three aims:

- Aim 1: To identify causes of inherited heart disease by identifying variants in non-coding regions of DNA. Given that genetic testing has tended to look at the protein coding regions of DNA only, it was hoped that expanding to non-coding regions would enable the identification of more variants.

[10] Average FWCI calculated by averaging the FWCI of each of the 17 publications as given by Scopus.

- Aim 2: To use RNA sequencing to identify genetic causes of inherited heart disease. It was proposed that the addition of RNA-based genetic analysis to DNA-based genetic testing could find additional genetic causes of inherited heart disease when compared to DNA-based genetic testing alone.
- Aim 3: To use functional analysis to assess the variants identified through RNA sequencing. This was needed to confirm that the identified variants cause the disease.

Research findings

Additional genetic causes of inherited heart disease were identified in non-coding regions of DNA. It was demonstrated that extending genetic testing to the non-coding regions of DNA can increase the diagnostic yield. Up to 10 per cent of people with inherited heart disease were found to have non-coding variants (over 100 variants were identified).

The research found suspected variants using RNA sequencing, and demonstrated how functional assessment of suspected variants can help determine their pathogenicity.

Outcomes generated

Knowledge advancement

New knowledge generated by the funded project

A new diagnostic method has been established. The research has tested and provided evidence to support genetic testing in non-coding regions of DNA and using RNA analysis.

Patient-specific cell models of heart disease were also developed. Blood cells from patients with inherited heart disease were cultured in a cocktail of growth factors that redirect them to grow into heart cells. These patient-specific heart cells represent a disease-in-a-dish. These can be used by the research team to measure their electrical rhythm, how they beat, and how medications interact with them to better understand heart disease mechanisms and the potential for medications to treat them.

Increased publication reach and quality

17 publications have been published from this research.

The top five publications by FWCI include:

Publication	Citations (Scopus)	FWCI (Scopus)
“Recommendations for clinical interpretation of variants found in non-coding regions of the genome”, Genome Medicine, 2022	112	11.88
“Concealed Cardiomyopathy in Autopsy-Inconclusive Cases of Sudden Cardiac Death and Implications for Families”, Journal American College of Cardiology, 2022	33	4.32
“"Concealed cardiomyopathy" as a cause of previously unexplained sudden cardiac arrest”, International Journal of Cardiology, 2020	43	3.90

"Genetic Basis of Childhood Cardiomyopathy", Circulation: Genomic and Precision Medicine, 2022	22	2.62
"Whole genome sequencing delineates regulatory, copy number, and cryptic splice variants in early onset cardiomyopathy", NPJ Genomic Medicine, 2022	19	2.08

The research has been presented at eight national and international conferences, listed below.[11]

- 2023 "Splice-site variants in genetic heart disease", CSANZ Genetics Council Symposium, Australia. (Invited oral presentation)
- 2022 "Genetic basis of childhood cardiomyopathy", CSANZ Annual Meeting Gold Coast, Australia. (Oral presentation)
- 2022 "An atypical splicing variant", Institute of Bioinformatics and Precision Medicine, Sydney (Invited oral presentation)
- 2022 "Genome Sequencing", ICCG Brisbane, Australia. (Invited oral presentation)
- 2022 "Essentials of Genetic Testing", ICCG Brisbane, Australia. (Invited oral presentation)
- 2021 "RNA Sequencing Workshop", HGSA (Invited case presentation)
- 2021 "Using genomics to improve care of people with inherited heart disease", Institute of Bioinformatics and Precision Medicine, Sydney (Invited oral presentation)
- 2020 "Insights from genome sequencing in sudden cardiac death and cardiomyopathies", CSANZ Annual Meeting, Virtual (Invited oral presentation)

Policy and practice

Changes to policy and clinical practice

The grant recipient attributed the inclusion of variants on genetic testing panels to the collective impact of the research completed under this funding, as well other international research that supports the findings. They identified this as a cumulative effect; the research done under the grant has helped contribute to the broader evidence base for the validity of these variants.

For example, the disease-causing variants identified through this research have been published in manuscripts and uploaded to the publicly available ClinVar database, which publishes aggregated information about genomic variations and supporting data (16). 347 variants have been submitted to ClinVar, however the grant recipient was not able to specify how many were submitted during the three-year study, as they are continually updated and the data entry date is not recorded. The inclusion of the variants on ClinVar provides evidence for whether a variant is responsible for disease. This can help worldwide efforts to classify the clinical relevance of genetic variants.

The findings regarding the identified variants have also been shared with at least 10 genetic test providers in Australia, Europe and USA. Providers, having found the same genetic variants, have sought further information from the grant recipient so they can compare clinical presentations and strengthen

[11] The grant recipient was unable to assess which conferences were the most impactful nor provide attendance details.

confidence that the variant is the cause of the disease. The findings are regularly discussed with genetic testing providers through the Australian Genomics: Cardiovascular Genetic Disorders Flagship. Additionally, guidelines for clinical diagnostic practice when interpreting non-coding variants have been developed and published (17).

Similarly, the grant recipient identified that some of their published research was included in the successful 2022 application to the Medical Scientific Advisory Council, which (in addition with other published research) demonstrated why genetic testing for cardiomyopathy and inherited arrythmia syndromes should be funded under Medicare. Prior to this, genetic testing had to be funded through research studies or the individual. The grant recipient noted that Medicare funding had made genetic testing for cardiomyopathy and inherited arrythmia syndromes more accessible to Australians.

Sometimes, a disease might have similar features to an inherited disease, or the diagnosis might not be so clear for a clinician. Through the grantee's research identifying additional variants and contributing evidence to improve genetic testing precision (by testing non-coding regions), patients can now receive more accurate diagnoses and subsequently more precise treatments.

New treatments used in clinical care

The development of treatments as an outcome was not a specific focus of project.

However, to prove the pathogenicity of the variants, the research team designed oligonucleotides, blocking agents that are put into heart cells to block the variant effect. The grant recipient also identified their potential as a therapeutic treatment. The research team is not currently pursuing its therapeutic potential, but it may be explored in the future.

Prevention practices

The project identified new genetic causes of inherited heart disease in non-coding regions of DNA which are now looked for by clinical genetic testing centres, contributing to a higher diagnostic yield. This means more people are likely to receive an accurate diagnosis. Finding the genetic cause means family members who have inherited the disease-causing variant can be targeted for earlier intervention of prevention strategies (for example, implantation of defibrillator or reproductive interventions).

Health and community impact

Potential for improvement in care or outcomes for priority populations and related comorbidities or diseases

Inherited heart diseases are more likely to impact children and young people than other heart diseases, and can be a cause of sudden cardiac death amongst this age group (17). Improved genetic testing with higher diagnostic yield means more children and young people can receive genetic diagnosis and receive monitoring, preventive intervention and treatment, thereby improving care and health outcomes for this group.

Additionally, the project contributed to improved access to accurate diagnosis for the patients involved in the study by offering free genetic testing. Through the grant, the project paid for genetic testing for approximately 100 NSW patients who might not otherwise have been able to afford to pay (at the cost of $400 per patient; total $40,000) (15).

Potential for improvement in care for related comorbidities was not identified as an outcome for this grant project.

Economic benefits

Impact on funded researcher's career progression

The grant recipient described the grant as a 'lifeline' for their career, emphasising it provided the capacity needed to start pursuing the research questions they wanted to pursue whereas previously they had not had that capacity. The recipient framed it as a 'big boost' for their career stage and emphasised that the grant is a significant opportunity for researchers at all career stages. Particularly as the recipient had come to NSW from overseas, they had not been eligible for many other grants until they gained citizenship. This grant was an exception because the recipient had only been a contributing investigator on previous grants (due to visa restrictions) and was researching other people's ideas. This grant was the first one after they gained citizenship where they were the lead researcher. They were able to establish their own group with their own research lines of enquiry.

Since receiving the funding and building up a body of related research, the grant recipient has been able to establish their expertise in genetic testing in non-coding regions of DNA. Other researchers are now including them in their applications for other related grants.

Following receiving the grant, they have been promoted to Associate Faculty and to Associate Professor, and have also become head of CVD research the Centenary Institute. They described the grant funding, and the research that has followed it, as 'stepping stones to [this] recognition'.

Impact on NSW cardiovascular disease research capacity

Other funding leveraged through this research include:

- MRFF 2021 Genomics Health Futures Mission: $2,997,498
- Australian Government Research Training Program Fellowship: $107,850
- Australian Genomics Cardiovascular Genetic Disorders Flagship Research Grant: $18,000.

Potential for commercialisation of research outputs and revenue forecast

Commercialisation of research outputs was not considered relevant for this project.

Economic benefits from improved patient care and reduced burden of disease

There is potential for the burden of disease to be reduced, because finding the genetic cause means family members who have inherited the disease-causing variant can be targeted for earlier intervention. It also means that if a genetic cause is not found, the burden of disease is reduced as those not at risk don't need to be involved in clinical screening, allowing the health system to focus this effort on those who do.

The recipient suggested that this contribution to improved patient care had potential economic benefits, but were unable to provide a dollar estimate.

Capability building

The recipient spoke to how the funding had grown the capacity of early career researchers. For example, the grant funding was used to pay for a research assistant who was able to publish a few publications directly from the funded research. This research assistant then used these publications to apply for two scholarships (Cardiac Society of Australia and New Zealand and Sydney University); both of which were awarded. Similarly, this grant part-paid for a researcher to analyse genome sequencing data. This researcher has also published data from this research and subsequently begun a prestigious PhD with a scholarship from the Heart Foundation. In both these cases the grant recipient noted the research helped build the researchers' track record, which has supported them in furthering their research careers.

Case Study 4: Working towards a genetic diagnosis for the majority and identifying the benefits

Project summary

Grant recipient: Professor Sally Dunwoodie	**Grant type:** Senior Scientist Grant; Round 1; Basic science
Funding received: $750,000 (July 2020 - June 2022)	**Other CVD grants received by recipient:** Senior Researcher (2022-ongoing)

Key outcomes generated:

Publication metrics – There have been 17 publications from this research, with an average FWCI of 1.52.[12] Research findings have been shared at 15 national and seven international presentations.

Economic benefits – Additional funding leveraged through the research totals over $15.5 million for NSW based researchers. Four researchers involved in the funded project received six fellowships, and two researchers were able to go on to build independent research careers. The grant recipient received the 2025 CVRN Ministers Award.

Knowledge advancement – Additional genetic causes of congenital heart disease (CHD) were identified, and linked data were developed to determine the incidence of CHD in NSW.

Policy and practice – The identification of new genetic causes of CHD has added to the evidence base supporting these genes as variants, including via inclusion on PanelApp Australia. Increased knowledge of these variants and support for their validity means more patients are likely to be tested for them, providing important information to inform patient care.

The research problem

Congenital heart disease (CHD) refers to structural abnormalities of the heart, aorta or other large blood vessels which are present at birth and change the normal flow of blood to the heart (18). CHD is the most common form of birth defect in Australia, affecting one in 100 Australian children, and some forms of CHD can be complex and life-threatening (18). Though CHD is common and its impacts can be severe, there have been knowledge gaps regarding its causes and prevalence.

The research responded to the need for further knowledge into the causes and prevalence of CHD, specifically regarding genetic causes of CHD, and CHD incidence across NSW.

[12] Average FWCI for the 17 publications calculated by averaging FWCI as given by Scopus.

Research aims

The research involved the following key aims:

- Aim 1: To genetically diagnose CHD in patients by identifying mutations in genes 'known' to cause CHD. This involved whole genome sequencing of DNA from patients and their parents and identifying gene variants based on the genes known, at the time, to cause CHD. The purpose was to provide genetic diagnosis for families.
- Aim 2: To identify 'new' CHD causing genes and establish how they cause CHD. This involved the same method as in Aim 1, however identification of variants looked at all genes of the genome, rather than those known to cause CHD, to identify further variants. Once the suspected variants were identified, they were then tested in mice to determine whether they cause CHD. The purpose was to identify a broader range of gene variants that could be included in genetic testing.
- Aim 3: To establish methods to quantify nicotinamide adenine dinucleotide (NAD) and related metabolites. Previous research undertaken by the grant recipient had identified a link between low levels of NAD caused by gene variants, birth defects, and miscarriage in families and in mouse models. This prompted the question as to whether low NAD levels in women might generally cause additional cases of miscarriage and birth defects including CHD. Aim 3 established an effective method by which to quantify the metabolites in the NAD pathway; a crucial step required before this research and related interventions could be further explored in clinical studies.
- Aim 4: To establish the incidence of CHD in NSW through linked data. This involved a collaboration with Sydney University and the NSW Centre for Health Record Linkage to access de-identified data for all births with CHD in NSW in the last 20 years, including hospital records, parental demographic data, education data, and services accessed. The purpose was to map the patient journey over their lifetime and identify where incidence of CHD is highest.

Research findings

Under Aim 1, families with CHD received a genetic diagnosis as variants were identified in known CHD-causing genes.

Under Aim 2, additional genetic causes of CHD were identified. This means that there are an expanded number of genetic variants that can be used in genetic diagnosis for CHD.

Under Aim 3, methods were established to effectively quantify NAD and related metabolites in humans and mouse models. The implications of this are discussed further below.

Under Aim 4, the incidence of CHD in NSW was established (by region and severity).

Outcomes generated

Knowledge advancement

New knowledge generated by the funded project

Under Aim 2 additional genes have been identified that cause CHD. This knowledge is used globally to increase the genetic diagnostic rate for CHD.

Under Aim 3, new methods were established to effectively quantify NAD and related metabolites in humans and mouse models. Using these methods, the research team has since undertaken other studies to identify baseline NAD levels and to test which types of vitamin B3 (a vitamin that affects NAD levels) are effective in improving NAD levels. The grantee hypothesised that when these findings are further developed through clinical trials, there is potential for them to inform interventions to prevent birth defects, as vitamin B3 could be taken to bring a woman's levels of NAD to baseline before becoming pregnant, thus reducing adverse pregnancy outcomes. Though this outcome has not yet been achieved, the research undertaken in Aim 3 has set up the evidence needed to progress this along the knowledge translation pathway.

Under Aim 4, the incidence of CHD in NSW was established (by region and severity). This is a new dataset that did not exist previously. It has since been further developed in other research not funded under this grant (see below to Potential to reduce burden of disease).

Increased publication reach and quality

New knowledge generated from the project has since been disseminated. Data generated have been made available via publication in 17 articles in international journals.

The top five publications by FWCI are:

Publication	Citations (Google Scholar)	FWCI (Scopus)
"A metabolic signature for NADSYN1-dependent congenital NAD deficiency disorder", Journal of Clinical Investigation, 2024	8	5.68
"A Curated Database for Congenital Heart Disease Genes", Circ Genom Precis Med., 2022	26	4.37
"Whole genome sequencing in transposition of the great arteries and associations with clinically relevant heart, brain and laterality genes", American Heart Journal, 2021	15	1.99
"Functional genomics and gene-environment interaction highlight the complexity of Congenital Heart Disease caused by Notch pathway variants", Human Molecular Genetics, 2020	51	1.97

"Bi-allelic Mutations in NADSYN1 Cause Multiple Organ Defects and Expand the Genotypic Spectrum of Congenital NAD Deficiency Disorders", American Journal of Human Genetics, 2020	47	1.92

Research findings have been shared at 15 national and seven international presentations. These were:

- December 2025 - "NAD Deficiency disrupts embryogenesis", Indian Developmental Biology Society India (approx. 300 attendees)
- May 2025 – "NAD Deficiency disrupts embryogenesis", Keystone Metabolism, USA (number of attendees unknown)
- Nov 2024 – "Identifying causes of congenital heart disease", Australian Functional Genomics Network, Melbourne (approx. 150 attendees)
- July 2023 – "Impact of functional genomics on rare disease", International Congress of Genetics, Australian Genomics Summit, Melbourne (approx. 200 attendees)
- June 2023 – "NAD Deficiency disrupts embryogenesis", Australian Society for Medical Research Conference (plenary), Newcastle (approx. 60 attendees)
- June 2023 – "NAD metabolism and the importance of extra–embryonic tissues in mammalian development", Gordon Research Conference Developmental Biology, Massachusetts, USA (approx. 150 attendees)
- June 2023 – "Environmental factors that mediate or disrupt mammalian embryogenesis", Gordon Research Seminars in Developmental Biology (plenary), Massachusetts, USA (approx. 150 attendees)
- Nov 2022 – "NAD deficiency disrupts embryogenesis", Developmental Metabolism and the Origins of Health and Disease, West Sussex, UK (approx. 50 attendees)
- June 2022 – "Embedding functional genomics in clinical research", Curating the Clinical Genome meeting, USA (approx. 100 attendees)
- May 2022 – "Genetic and Environmental causes of congenital heart disease", Hunter Cell Biology Meeting, Newcastle (approx. 200 attendees)
- April 2022 – "Congenital Heart Disease: a diverse research approach to explain causes and outcomes", UNSW Cardiovascular Symposium (approx. 100 attendees)
- Aug 2021 – "Genetic and environmental causes of congenital heart disease", Basic Science Lecture, Cardiac Society of ANZ, Adelaide (approx. 150 attendees)
- May 2022 - "Congenital heart disease", International Clinical Cardiovascular Genetics (ICCG) Conference, Brisbane (approx. 150 attendees)
- Nov 2020 – "Assaying variant function in cardiovascular disease", Australian Functional Genomics Conference, Melbourne (approx. 100 attendees)
- July 2020 – "Preparing a successful, cross-disciplinary Synergy Grant – our approach, concerns and considerations", Cardiac and Vascular Health Clinical Academic Group Annual Meeting (approx. 150 attendees)
- Dec 2019 – "Gene discovery in congenital heart disease", ANCVDB Annual Meeting, Adelaide (approx. 100 attendees)

- Oct 2024 – “Congenital malformation: Identifying causes, disease mechanisms, and opportunities for possible prevention”, Alumni annual Lecture, University of Queensland, Brisbane (approx. 200 attendees)
- Nov 2022 – “Gene mutations, metabolites and congenital heart disease”, Hunter Medical Research Institute, Newcastle (approx. 150 attendees)
- Oct 2020 – “Identifying genetic and environmental factors causing developmental defects in humans and mice”, School of Biomedical Sciences, University of Melbourne (approx. 60 attendees)
- Sept 2020 – “Identifying genetic and environmental factors causing developmental defects in humans and mice”, Baker IDI- Heart Research Institute, Melbourne & Sydney (approx. 100 attendees)
- June 2020 – “Identifying genetic and environmental factors causing developmental defects in humans and mice”, Biological Sciences, Monash University (approx. 50 attendees)
- May 2020 – “Identifying genetic and environmental factors causing of congenital heart disease”, Cardiovascular Research Centre, Mount Sinai Medical School, New York, USA (approx. 30 attendees)

Policy and practice

Changes to policy and clinical practice

Population-level data showing CHD incidence is now available through the establishment of the linked data undertaken under Aim 4. Although no policy impacts have been realised yet, there is potential for these data to inform CHD policy concerning service provision, as it quantifies CHD incidence geographically and service usage patterns across NSW.

Additional new variants identified through Aim 2 are now included on PanelApp Australia, an open, online platform enabling the recording and sharing of genes known to cause disease. The grant recipient noted that published grant research partly contributed to this evidence base and allowed for their inclusion on PanelApp. In practice, this means that patients will be able to be diagnosed more readily, as there are a broader range of genes recognised as valid to search for in genomic testing. Clinicians are able to access PanelApp to see what genes are associated with CHD and order this genomic testing for patients with CHD. Though statistics on numbers of clinicians that have accessed this information via PanelApp are not publicly available nor known by the recipient, available research indicates that as at May 2022, PanelApp Australia had 63,901 panel downloads for various conditions, not just CHD (19).

New treatments used in clinical care

The research has not contributed to new treatments being used in clinical care. As discussed above, the research team is working to progress the findings under Aim 3 to eventually develop a new intervention, however this has not yet been developed and implemented.

Prevention practices

As described above, Aim 2 led to the identification of additional variants that cause CHD, meaning there is now a broader range of variants that families can be tested for. Additionally, the families involved in Aim 1 were provided genetic diagnosis of CHD. In these ways, both Aims 1 and 2 have or will enable more families to access genetic diagnosis. When families have a genetic diagnosis, they have access to

information that they can use to make informed reproductive choices and minimise the likelihood of a child being born with CHD.

For example, genetic testing can provide parents information on the likelihood of any future children carrying the variant for CHD. If the variant is present in one child, but not in the parents, this means the variant wasn't inherited and that the next child would have the same likelihood as the baseline population of receiving the variant. Knowing whether the variant is inherited, and therefore knowing the likelihood of any future children carrying the variant, means that families can make informed reproductive choices if they wish (for example, parents could choose to undertake preimplant genetic testing to assist in selecting an embryo without the variant).

Health and community impact

Potential for improvement in care or outcomes for priority populations and related comorbidities or diseases

Children are a priority population targeted in this research. CHD is present at birth and can have a significant impact on the early life of a child. There is potential for improved care for children and their families, as families involved in the study have received genetic diagnosis. Knowing the genetic cause of CHD could provide prognostic value for the patient with CHD. The recipient suggested that the clinical geneticists and cardiologists who referred patients to the study would be able to incorporate the genetic diagnosis into the care of these patients (for example, as described below).

As a result of families and future patients accessing genetic diagnosis there is the potential for improvement in care for related comorbidities. This is because some gene variants are associated with both CHD and other conditions such as cardiomyopathy, arrhythmia or cancer, meaning people with these variants are predisposed to these other conditions later in life. If gene variants are detected that are also associated with other conditions, these conditions can be monitored for, and preventative measures implemented.

Potential to reduce burden of disease

The research has the potential to contribute to reducing the burden of disease in the following ways.

- Aims 1 and 2: If a gene is identified, and this gene is also known to be associated with additional disease, as described above, preventative measures can be taken to address risk of developing this disease, therefore reducing burden of disease.
- Aim 3: As described above, the recipient hypothesised that when the findings of Aim 3 are further established through clinical trials, there is potential for these to inform interventions to prevent birth defects. A woman's levels of NAD could be brought to baseline before becoming pregnant, thus reducing adverse pregnancy outcomes. This has the potential to reduce burden of disease by preventing birth defects in children and reducing rates of miscarriage.
- Aim 4: Findings from Aim 4 have been incorporated into further research, including one study that will soon be published demonstrating a correlation between the incidence of ADHD and CHD in children. The recipient hypothesised that this could assist clinicians supporting families of children with CHD to diagnose ADHD earlier. This could support access to early interventions for children, therefore reducing the burden of disease associated with a lack of diagnosis and early support. Though this

particular research was not funded under this grant, it was informed by the establishment of linked data from Aim 4 research.

Economic benefits

Impact on funded researchers' career's progression

The grant recipient noted that receiving the grant was valuable to their career as it provided leverage to receive further, larger grants, listed below.

Impact on NSW cardiovascular disease research capacity

The recipient reported they were successful in leveraging several further grants. The research under Aims 1 and 2 led to a NHMRC Project grant worth $2.8 million over 5 years. All researchers involved were NSW based.

The research under Aims 1,2, and 4 led to a NHMRC Synergy grant $5 million over 5 years and, again all researchers involved were NSW based. This NHMRC Synergy grant is funding research which has built on the findings of Aim 4, adding additional data linkage across other states and territories to further establish CHD incidence.

The research results also contributed to three researchers (including the recipient) receiving NHMRC Investigator Grants totalling ~$7.7 million.

Capability building

The four researchers who worked on the CVD Senior Scientist funded project went on to receive six fellowships from the NHMRC and/or OHMR Cardiovascular Research Capacity Program Grants. Collectively, this included two NHMRC Investigator Grants, and two OHMR Cardiovascular Research Capacity Program EMCR Grants.

The two OHMR Cardiovascular Research Capacity Program EMCR Grants (above) enabled two researchers to be recognised as group leaders in their research, to build independent research careers after maternity leave, and to continue their work while based in NSW.

The grant recipient received the 2025 CVRN Ministers Award.

Case Study 5: Improving women's cardiovascular health after hypertensive pregnancy

Project summary

Grant recipient: Associate Professor Amanda Henry	**Grant type:** Early Mid-Career Researcher Grant; Round 3; Clinical medicine & science
Funding received: $449,562 (February 2022 – February ongoing)	**Other CVD Research Capacity Program grants received:** None

Key outcomes generated:

Publication metrics – One publication has been published, with one citation and FWCI of 9.36. More publications are expected to follow once research findings are finalised. The research has been shared at four conferences.

Economic benefits – The research has led to further collaborations worth over $3 million in additional grant funding.

Policy and practice – The research has contributed to the grant recipient's expertise as a researcher working in women's health after hypertensive pregnancy. Their expertise has been sought out to inform several national and international guidelines and resources on this topic.

Capability building – The funding to employ midwifery staff in research roles (total 0.8 FTE) brought research capability into involved hospitals and supported one midwife to progress to a clinical midwifery consultant role. The capability of several undergraduate and post-graduate students has been built through their involvement in this research.

The research problem

High blood pressure diseases in pregnancy affect at least 1 in 20 NSW pregnancies (20). High blood pressure in pregnancy, or hypertensive pregnancy, increases risk of CVD including heart attack and stroke, as well as other health problems (20). Despite these risks to women's health, knowledge of these issues is low amongst women and their healthcare providers, and early intervention or education programs to improve heart health after hypertensive pregnancy could be strengthened (20).

Research aims

This project explores women's health after hypertensive pregnancy, and knowledge of health after hypertensive pregnancy in South East Sydney LHD. The project has two aims:

- Aim 1**:** A prospective cohort study[13] following women at 3-4 years post pregnancy to assess their health outcomes. This study is following on from a previous randomised controlled trial that had involved three methods of follow-up and lifestyle behaviour change for women in the first year following hypertensive pregnancy. Under the CVD Early Mid-Career Researcher Grant, the

[13] A prospective cohort study is a longitudinal, observational study that observes exposure and health outcomes as they progress over time amongst the cohorts studied (21).

prospective cohort study is looking at the same cohort (approx. n=250) studied in the previous randomised trial. This research has two purposes. The first is to collect data to provide a 'snapshot' of women's health outcomes at 3-4 years post hypertensive pregnancy, as this is a period that has not been well studied. The second purpose is to assess the effectiveness of the methods of follow up and lifestyle behaviour change that were implemented in the previous study by assessing the cohort's ongoing health outcomes. At the time of writing, final follow-up visits with these women were being conducted, and it was planned that data collection would be finalised mid-2025 before analysis and publication of findings.

- Aim 2: The second aim is in relation to closing knowledge gaps of women and healthcare providers around health after hypertensive pregnancy. This has drawn on previous research from the research team that mapped the educational gaps and needs of women and care providers. Under the CVD Early Mid-Career Researcher Grant, the data from the previous research was used to develop an educational package, which provided women (approx. n=120) and their care providers (n=16) resources for health after hypertensive pregnancy. Both the women and their care providers also received reminders for follow-up appointments. Interviews and questionnaires are being conducted at baseline, 6- and 12-months post-partum to assess the impact of receiving the educational package and reminders on the women's health indicators, and on their knowledge regarding health after hypertensive pregnancy.

Research findings

The research was still being conducted at the time of writing, so the final data collection and analysis is yet to be finalised. This means the overall effectiveness of the interventions studied is not yet known.

Emerging findings have been identified for both research focuses. Qualitative data from the cohort study highlights the trauma experienced by women due to the complications at birth of hypertensive pregnancy, and the resulting impacts on their mental health over the three to four years following hypertensive pregnancy. It shows that the women faced some difficulty in adhering to a healthy lifestyle following hypertensive pregnancy, however data for health outcomes is still being finalised and the extent to which women managed behaviour change is not yet known.

Preliminary findings under Aim 2 indicate that the intervention (educational package and reminders) had improved women's understanding of health post hypertensive pregnancy, but there has been less impact generated for behavioural change and the reduction of women's cardiovascular risk factors. However, data is still being finalised and so these findings are not complete.

Outcomes generated

Knowledge advancement

New knowledge generated by the funded project

No prototypes have been developed.

Increased publication reach and quality

The research led to a scoping review looking into post-partum care and the gaps in post-partum care. This has recently been published (January 2025). At the time of writing, the article had received one

citation and had a FWCI score of 9.36 (Scopus). More publications are predicted to follow once the research has been finalised.

Additionally, the research has been presented by PhD researchers involved in the work at multiple conference presentations:[14]

- October 2024: "Improving post-HDP transitions from hospital to primary care", Australian/Aotearoa NZ Preeclampsia Research Network, Pre- congress Day, ISOM-SOMANZ Joint Congress, Sydney (oral presentation).
- October 2024: "Improving healthcare provider capacity to implement evidence-based care following Hypertensive Disorders of Pregnancy", ISOM-SOMANZ Joint Congress, Sydney (oral presentation). This presentation won a SOMANZ travel award.
- October 2024: "Improving healthcare provider capacity to implement evidence-based care following Hypertensive Disorders of Pregnancy", HiPPP-EMCR (health in preconception, pregnancy and postpartum Early-Mid-Career Researcher) conference, MOH St Leonards and online. This presentation won student award for best presentation.
- October 2024: "Mental health after HDP", Australian/Aotearoa NZ Preeclampsia Research Network, Pre- congress Day, ISOM-SOMANZ Joint Congress, Sydney (oral presentation).

Learnings regarding the implementation of the educational package study have been shared internationally. A research group in Ireland is similarly aiming to improve knowledge gaps and follow-up for women post hypertensive pregnancy. The research team is providing advice regarding implementation and evaluation of the Irish study based on learnings generated from their funded studies.

Policy and practice

Changes to policy and clinical practice

The research has informed national and international guidance on postnatal health. For each of the following examples, though the grant recipient was not funded under the Early Mid-Career Researcher Grant to specifically contribute to the guidelines and resources discussed, the findings and data generated from the research have contributed to the grant recipient's research expertise regarding women's health knowledge and outcomes after hypertensive pregnancy. Their expertise has been sought out to inform the following:

- The implementation of the Pregnancy Passport resource developed by the International Federation of Gynaecology and Obstetrics (FIGO) Pregnancy Passport Working Group. The Pregnancy Passport is intended to provide a resource with which women can record their pregnancy information and cardiometabolic risk indicators to support the identification of risk factors and guidance for improved care (22). The grant recipient is a member of the FIGO Pregnancy Passport Implementation Group, which meets 2-3 times a year to develop and discuss international collaborative work to translate the Passport into practice.
- The development of guidelines on Hypertensive Disorders of Pregnancy by the Society of Obstetric Medicine of Australia and New Zealand (SOMANZ), which are NHMRC-endorsed. For the first time,

[14] The grant recipient was unable to assess which conferences were the most impactful nor provide attendance details.

these guidelines on hypertensive disorders of pregnancy include a chapter on long term health after hypertensive pregnancy. The grant recipient was invited to be on the working group for the development of these guidelines and is a guideline co-author.

- The Royal Australian and New Zealand College of Obstetricians and Gynaecologists are committed to including recommendations for follow up after hypertensive pregnancy into their guidelines on post-natal care. This research has added to the body of research demonstrating the need for follow up after hypertensive pregnancy.

Additionally, research under Aim 2 contributed to the development of a GP-requested HealthPathway for hypertensive pregnancy follow-up, that was then implemented by NSW Health.

New treatments used in clinical care

Treatments are not a direct focus of this research.

Prevention practices

Final data generated is expected to further guide preventative practice for this area. This is because it is expected that the studies will build a strong case for implementing structured postpartum follow-up and lifestyle behaviour change as preventative interventions to reduce CVD risk after hypertensive pregnancy. Specifically, the grant recipient hoped the research might provide evidence to support that Medicare funds an extra post-partum visit for women. However, as noted above, the final data collection is not complete so details on evidence of effectiveness for preventing CVD risk is not finalised, hence this is a hypothesised and not a realised outcome.

It is also hoped that the findings will provide evidence for how management strategies are best implemented. For example, it is hoped that through comparing outcomes for women who received the three management strategies of follow-up and lifestyle and behaviour change, evidence might suggest which management strategies are more effective. Additionally, early findings highlighting mental health impacts that emerge following hypertensive pregnancy suggest support could be strengthened with holistic support including support from a psychologist. Again, as the research is still being completed, findings are not finalised and have not yet contributed to informing prevention practices.

Health and community impact

Potential for improvement in care or outcomes for priority populations and related comorbidities or diseases

One-third of the research population in the cohort study (Aim 1) was ethnically diverse. Though outcomes for this cohort have not yet been measured, it is planned that the data generated will be analysed for any differences in outcomes. This analysis is intended to indicate any differences in risk factors that could then be used to tailor interventions for these groups.

Economic benefits

Impact on funded researchers' career's progression

The OHMR grant was reported to be very important for furthering the grant recipient's career progression, and in particular their progression from Associate Professor to Professor.

This funding was reported to have supported continuity and momentum for the St George Hospital Obstetric Medicine Research Group. This is because the research group had already set up a research cohort in the previous randomised control trial (that Aim 1 followed on from) and gathered data in the previous research that mapped the educational gaps and needs of women and care providers (that Aim 2 followed on from). Receiving the grant meant this data could be built on in further research.

Impact on NSW cardiovascular disease research capacity

The funded research has led to a number of collaborations with other research groups in NSW and interstate. Notable collaborations utilising the cohort data generated by the research include:

- Researchers from Melbourne University working on developing new preventative therapeutics for CVD in women. This project has received NHMRC funding worth $1,129,806.40. This grant was leveraged in part using samples from the research funded under the Early Mid-Career Researcher Grant. Four Chief Investigators from UNSW, and Melbourne University are involved.
- Researchers from University of Tasmania exploring the impact of preeclampsia on cardiovascular phenotypes and risk. This project has received NHMRC funding worth $2,243,507.50. This grant was leveraged using samples from the research funded under the Early Mid-Career Researcher Grant. Seven Chief Investigators from UNSW, and University of Tasmania are involved.

The grant recipient identified that the CVD program has enabled an increased focus on the ultimate outcomes of research, i.e. progression of research by supporting collaboration between researchers at different phases of the research translation pathway (e.g. fundamental scientists and clinician researchers).

Potential for commercialisation of research outputs and revenue forecast

Commercialisation of research outputs was not considered relevant for this project by the recipient.

Economic benefits from improved patient care and reduced burden of disease

Economic benefits from improved patient care were not identified.

Capability building

The funding received was reported to have contributed to building the capability of researchers involved in the project. The grant was, in part, used to fund research midwifery staff at clinical sites, enabling midwifery staff to grow capability in research and to bring clinical research capability into hospitals. Specifically, the grant was used to fund fractional midwifery staff time (0.3 FTE of Project Manager based at St George Hospital, 0.2 FTE midwifery research staff RHW, and a research assistant/PhD candidate who is a midwife at RPA employed at 0.3 FTE).

For one midwifery coordinator, being funded to work on this project meant they were able to grow their capability in project management and progress to a clinical midwifery consultant role.

Several undergraduate students had also conducted research projects on aspects of the funded research, enabling them to grow their research capability. Similarly, a PHD student conducted 3- to 4-year follow-up interviews with project participants to inform a chapter of their PHD. In the post-doctoral context, one of the project researchers has been able to obtain an academic midwifery role based on the research conducted.

Case Study 6: Code storm: standard care or a rapid early invasive management approach to patients with life-threatening heart rhythm disorders

Project summary

Grant recipient: A/Prof Saurabh Kumar	**Grant type:** Early Mid-Career Researcher Grant; Round 2; Clinical medicine & science
Funding received: $450,000 (July 2020 - June 2024)	**Other CVD grants received by recipient:** None

Key outcomes achieved:

Publication metrics – Two publications have been published from this research, and one is additionally under peer review. There have been no conference presentations.

Economic benefits – Additional grants won leveraging this research have totalled approximately $10 million.

Knowledge advancement – Clear evidence was provided that initial catheter ablation was superior to medical therapy for the management of VT storm.

Policy and clinical practice – The research has contributed to establishing initial catheter ablation as best practice for the management of VT storm. Western Sydney LHD has been established as 24/7 referral centre for VT storm, with improved referral pathways to improve access for patients from other LHDs.

The research problem

Ventricular tachycardia (VT) storm is an arrhythmic emergency that involves three or more episodes of sustained VT within 24 hours or incessant VT (23). Up to 40 per cent of patients with an implanted defibrillator inserted to treat spontaneously occurring VT may experience VT storm.[15] Medical therapy with anti-arrhythmic drugs can cause adverse reactions (24), however, they have been the current standard of care for the initial management of VT storm (23). Catheter ablation is an alternative treatment for VT storm, and significant improvements have been made in catheter ablation in recent years. Despite this, it had not been established how initial catheter ablation compared to medical therapy in terms of patient outcomes.

Research aims

The research sought to establish whether initial catheter ablation was superior to medical therapy for the management of VT storm in terms of patient outcomes. It involved an observational study of patients presenting with VT storm, where patients either received early initial catheter ablation or initial medical therapy.

[15] This statistic was provided by the grant recipient.

Research findings

The research established clearly that initial catheter ablation was superior to medical therapy for the management of VT storm, as those who received it had significantly less hospitalisations and days in hospital, ventricular arrhythmia and VT storm recurrence, composite end point of death, and heart transplants. There were significantly less complications due to the procedure, and no deaths during the procedure for these patients (23).

Until this research was funded, it was not known how initial catheter ablation compared to medical therapy, despite significant improvements in catheter ablation technology.

Outcomes generated

Knowledge advancement

New knowledge generated by the funded project

Through this research, catheter ablation has been tested and established as a first line of treatment in Western Sydney LHD. This includes the establishment of a statewide hotline for referral to Westmead Hospital. This is a model of care prototype that has been tested in Western Sydney LHD with potential for scaling across other LHDs. This is further described below in Policy and Practice and Community impact.

Increased publication reach and quality

There have been two publications; '*Early Catheter Ablation Versus Initial Medical Therapy for Ventricular Tachycardia Storm'* in Circ Arrhythm Electrophysiol which had 12 citations and a FWCI of 1.52, and *'Emergency out-of-hours catheter ablation for ventricular arrhythmia storm: A UK and Australian experience'* in Europace which had 2 citations and a FWCI of 0.44. There is additionally one paper under peer review.

There have been no conference presentations from this research.

Policy and practice

Changes to policy and clinical practice

The research has had significant impact on how VT storm is managed in Western Sydney LHD, where the research was undertaken. It was demonstrated clearly and early in the research that initial catheter ablation was a superior treatment option and was achieving better results for the LHD as patients could be treated at a higher rate with fewer complications. Due to this, catheter ablation is now offered as first line treatment for VT storm in Western Sydney LHD, which has also been established as a 24/7 VT storm referral centre. The grant recipient suggested that catheter ablation as first line treatment is scalable and has the potential to see further uptake across other LHDs. They proposed that Western Sydney LHD's uptake had set the 'framework' for other LHDs to follow.

The research is supporting this uptake by informing both national and international best-practice guidelines for VT storm management. This includes guidelines being developed by the Cardiac Society of ANZ, the European Heart Rhythm Association, and the European Society of Cardiology, which referenced the funded study.

New treatments used in clinical care

The research hasn't developed new treatments, but as discussed above has established catheter ablation as a best practice treatment.

Prevention practices

Prevention practices are not relevant to this research project.

Health and community impact

Potential for improvement in care or outcomes for priority populations and related comorbidities or diseases

The research has contributed to equity of care because it has improved access to catheter ablation to patients in LHDs outside of Western Sydney LHD (and particularly those servicing regional areas) who wouldn't typically have this access. These LHDs typically lack the resources required for catheter ablation and tend to rely on medical therapy. As discussed above, the research program has increased awareness of the effectiveness of catheter ablation amongst these LHDs, and Westmead Hospital in Western Sydney LHD has been established as a 24/7 referral centre for accessing catheter ablation, including the establishment of a statewide hotline for referral.

Increased access to care is evidenced in the numbers of patients assisted. The grant recipient suggested that previously around 20 patients would have received catheter ablation at Western Sydney LHD per year and now that number has risen to 200 per year with referrals from other LHDs. Additionally, the research team has recently submitted a paper for publication showing that streamlined referral has contributed to equitable outcomes across LHDs.

Potential to reduce burden of disease

The grant recipient suggested that catheter ablation reduces burden of disease for patients, as it means access to a treatment that can lead to improved quality of life and less suffering from complications, hospitalisation and health care costs.

Economic benefits

Impact on funded researchers' career's progression

The grant has significantly impacted the grant recipient's career progression. Key impacts identified include international recognition, academic promotion to Associate Professor, and multiple collaborations resulting in grants worth over $10 million. This has meant the recipient has been able to progress their research into further stages, notably, to explore the potential of radiotherapy for VT. Grants leveraged include

- NHMRC Synergy Grant: $5,000,000, 5 years
- NHMRC Clinical Trials and Cohort Studies Grant: $2,173,950, 3 years
- NHMRC: $1,515,422.08
- MRFF Cardiovascular Health Mission: $1,499,286, 3 years
- MRFF Cardiovascular Health Mission: $1,104,168, 3 years

- NSW Health Early to Mid-Career Fellowship: $595,000, 3 years for project support
- NSW Health Early-Mid Career Research Grant: $450,000 3 years
- NHMRC Career Development Fellowship: $431,000, 4 years
- Westmead Hospital Charitable Trust Project Grant: $240,000, 2 years
- Perpetual Ramaciotti Health Investment Grant: $150,000, 1 year
- NSW Heart Foundation Vanguard Grant: $150,000, 2 years
- Sylvia and Charles Viertel Charitable Foundation, Clinical Investigator Project Grant: $85,000, 1 year.

Impact on NSW cardiovascular disease research capacity

The grant has had significant impact on NSW CVD research capacity. The grantee suggested it has compelled the Westmead arrythmia group into the 'next stratosphere', supporting Western Sydney LHD to be an internationally recognised research hub for VT storm.

The grantee suggested that the $10 million in grants (mentioned above) have enabled the equivalent of around 50 years of research.

Potential for commercialisation of research outputs and revenue forecast

Commercialisation of research outputs is not directly relevant to this project.

Economic benefits from improved patient care

Initial catheter ablation results in significantly better ventricular arrhythmia and VT storm-free survival, fewer subsequent cardiac-related hospitalisations, shorter cumulative length of hospitalisation, and fewer iatrogenic complications. Reduced hospitalisations and reduced need for medical care suggests reduced burden of disease and significant health care cost savings.

Subsequent analysis planned by the research team over the next year will look at quality of life and cost effectiveness to establish these potential savings. These results are expected to be published once finalised.

Capability building

Ten PHD students and three master's students were supported to undertake their research through involvement on this project. This included three research assistants (one went on to complete a Master's degree, one to complete a PhD and one who is currently enrolled in a PhD). Two PHD students involved in the research won highly coveted awards from the Cardiac Society.

The funding facilitated the employment of two research assistants (100,000-150,000 each per year) and one clinical trial project manager (150,000 per year).

Case Study 7: Implementing genomic medicine in inherited cardiomyopathies

Project summary

Grant recipient: Professor Diane Fatkin	**Grant type:** Investigator Development Grant; Round 2; Basic science
Funding received: $100,000 (February 2020 - December 2022)	**Other CVD Research Capacity Program grants received by recipient:** Senior Researcher (2020-2023); Senior Researcher (2024-ongoing)

Key outcomes generated:

Publication metrics – One publication has been published from this research with nine citations and field weighted citation impact (FWCI) of 1.01 (Scopus). More papers are expected to be published in the coming year, expected to be high impact papers. Findings have been shared at three conferences.

Economic benefits – Additional funding leveraged (through grants and philanthropy) is worth over $3 million. The grant has led to further funding leveraged to progress the research program and build the recipient's career.

Knowledge advancement – A cardiac magnetic resonance (CMR) based imaging protocol for the assessment of atrial structure and function was developed, with data made available to inform further research, such as in collaboration with Imperial College London to explore how atrial parameters can predict fibrosis in the atrium.

The research problem

The research examined the genetic causes of atrial fibrillation (AF) and cardiomyopathies. AF is a type of arrhythmia which can lead to blood clots and is a leading cause of stroke in Australia (25). Atrial cardiomyopathies, which are changes in the atria that can have a genetic cause, are associated with AF.

Genetic testing is used to identify genetic causes for AF; however, it could be improved. As reported by the recipient at the time of the grant, genetic testing based on the genes known to cause AF could only find genetic causes for a minority of patients. This suggested a need to identify more genetic causes of AF to increase the diagnostic yield. Additionally, more needs to be understood about the causes of AF, including atrial cardiomyopathies. The current method used to assess the structure and function of the atria could be improved to provide a more detailed and accurate assessment of any atrial changes.

Research aims

The research had two aims:

- Aim 1: The first was to identify variants in genes that lead to risk of AF, through conducting familial AF genetic studies. It was hoped that identifying more genetic causes could improve the diagnostic yield, because more genes could be tested for.

- Aim 2: The second aim was to develop a cardiac magnetic resonance (CMR)-based imaging protocol for assessment of atrial structure and function. CMR methods could enable a more accurate assessment of atrial structure and function than current, commonly used methods.

Research findings

Under the first aim, the research identified genetic causes of familial AF. Whole genome sequencing data were obtained from 118 probands[16] with AF. Variants in 319 genes were annotated. From this, 394 rare variants were identified via manual curation using the American College of Medical Genetics and Genomics pathogenicity criteria. 49 variants were assessed, finding six pathogenic/likely-pathogenic variants and eight suspicious variants of unknown significance. Following this, the grant recipient is now working to determine whether these variants segregate with disease in the respective families (funded through philanthropy sources).

Under the second aim, a CMR-based imaging protocol for the assessment of atrial structure and function was developed. Novel aspects include 3D whole heart angiography[17] and aspects that quantify atrial fibrosis[18] and estimate 5D whole heart flow.

Outcomes generated

Knowledge advancement

New knowledge generated by the funded project

A CMR-based imaging protocol for the assessment of atrial structure and function was developed, including novel aspects. This protocol has been applied in further research by the research team to better understand the relationship between atrial cardiomyopathies and AF (not funded under this grant). It has been made available to researchers at St Vincents Hospital who have applied it in two projects with another project planned.

Additionally, though the research under this grant hasn't directly developed new treatments, it has generated data that are being used by other researchers to improve treatments. For example, the CMR data generated are being used nationally and internationally by three groups of researchers. This includes a collaboration with researchers at the Imperial College London to develop patient-specific computational atrial electromechanical models to examine how atrial parameters can predict AF. This research has potential to inform improvements in ablation as a treatment for AF.

Similarly, a collaboration with Melbourne University is utilising the data generated from the familial AF genetic studies to understand how ablation with either single or extensive focus might impact differently on patients with genetic risk for AF.

[16] A proband is someone affected by, or concerned they are at risk of a genetic condition. Usually, they are the first person in a family to bring the concern of a genetic disorder to the attention of healthcare professionals (26).

[17] Angiography is a type of X-ray to check blood vessels (27).

[18] Atrial fibrosis is the accumulation of scar tissue in the atria (heart's upper chambers) (28).

Increased publication reach and quality

One paper has been published from this research, “Atrial cardiomyopathy: current and future imaging methods for assessment of atrial structure and function”, Frontiers in Cardiovascular Medicine, 2023. This has nine citations and FWCI of 1.01 (Scopus). More publications in high impact journals are expected in the coming year.

Additionally, findings have been shared at three conferences, attended by academics, clinicians and health services professionals:

- February 2023 - Development of novel CMR methods for deep phenotyping of cardiomyopathy, St Vincent’s Campus Research Symposium, over 100 attendees
- April 2022 - “TTN-related cardiomyopathy”, International Symposium on Advances in Heart Failure, Cardiomyopathies, and Pericardial Diseases, Fondazione Internazionale Menarini, over 100 attendees
- December 2022 - “Titin-related cardiomyopathy”, Cardiovascular Genetics Clinical Conference, Brigham and Womens' Hospital, Boston, USA, 21-50 attendees.

Policy and practice

Changes to policy and clinical practice

Changes in policy and clinical practice were not considered relevant to this project.

New treatments used in clinical care

The research has not yet contributed to new treatments in clinical care.

Prevention practices

The discovery of new genes should eventually contribute to stronger predictive genetic testing by including a broader set of genes on genetic testing panels. This would mean family members of patients with AF could be tested for a broader set of genes to better establish their risk of developing AF. Currently, these additional genes are not included on testing panels, however, a shortlist of variants have been identified through this research and further research is planned to forward this outcome. The grant recipient suggested that it could take up to 10 years to include new genes on clinical diagnostic genetic testing panels. They suggested experimental studies would need to be conducted to confirm the variants cause disease (which could take two to three years), followed by further studies in patient groups to establish the variant’s prevalence. Only with robust evidence and a substantial number of cases could the variants be justified for regular inclusion in clinical testing panels. The process undertaken under this grant marks the beginning of a long journey towards routine clinical use.

The present focus of Aim 2 (CMR imaging) is to provide a method for obtaining superior information on atrial structure and function to better understand the link between atrial structure, genetic variants, and AF in research studies. Additionally, the grant recipient hoped that future screening for AF could be strengthened by improving the assessment of atrial function through CMR imaging. It is understood that genetic variants do not directly cause AF, and instead give rise to an abnormality in the atrial wall that can lead to AF when triggered through various factors such as virus or lifestyle. Therefore, an important part of screening is being able to identify these abnormalities, which may differ with types of genetic

defects. The current method for assessing atrial function is limited to providing an estimate of atrial diameter. The CMR imaging protocol has contributed a method for obtaining a detailed and accurate assessment of atrial size and function and it is possible that with further research this could be used in clinical practice to contribute to improved screening for AF risk. However, for this to happen, additional research would be needed to understand the types of atrial changes with increased AF risk, and in different patient groups to assess whether the CMR methods are indeed superior to current methods for identifying high-risk patients. Additionally, economic analyses would be needed to establish cost efficacy for the CMR methods.

Health and community impact

Potential for improvement in care or outcomes for priority populations and related comorbidities or diseases

Primarily, the research focuses on people who are at risk of developing AF. Including a broader range of variants and more accurate assessment of the atrial wall should eventually improve genetic testing, screening, and diagnostic yield, and inform targeted interventions. However, these outcomes are not yet realised and will not be a direct result of this grant, as the research is ongoing and remains in the early stages of the research translation pathway.

Aboriginal and Torres Strait Islander communities and obese individuals were identified by the recipient as priority groups that could particularly benefit from the longer-term outcomes of this research due to their higher incidence and risk of AF, often linked to conventional clinical risk factors like hypertension and diabetes.

Economic benefits

Impact on funded researchers' career progression

The grant recipient indicated that funding under this grant had helped them to secure further funding for continued research in this area. They considered the grant vital, given that securing research funding can be challenging, and the Investigator Development Grant had operated similar to seed funding, allowing them to establish a base of research through which they could leverage further grants and grow their research program.

Impact on NSW cardiovascular disease research capacity

The grantee considered the Cardiovascular Research Capacity program to be a 'terrific boost to the CVD research sector and a lifeline for many researchers at all levels'. The research enabled through this grant had led to the researcher's successful application for a Heart Foundation Strategic Grant worth $1 million which led to new partnerships with clinicians and consumers in NSW and interstate, a Medical Research Future Fund (MRFF) grant also worth $1 million, and two CVD Senior Researcher Grants worth $750,000.

A collaboration has also been established using the CMR data. This has attracted philanthropic funding worth $50,000 from the IMPACT Philanthropy Application Program from Perpetual Limited. Further philanthropic funding (through private sources) had also been provided to support the development of technology for genetic testing for AF worth $240,000.

As one aim of the Investigator Development Grant was to help progress research to successfully obtain a NHMRC grant, it should be noted that an application was made for a NHMRC Investigator Grant but was unsuccessful. The grant recipient noted that a further attempt will be made this year.

Potential for commercialisation of research outputs and revenue forecast

Commercialisation was not considered relevant to this research.

Economic benefits from improved patient care and reduced burden of disease

The ultimate goal of the research is to improve health outcomes in families by early detection of individuals at risk and early intervention. The present study is a step in this direction but will not in itself directly result in economic benefits.

Capability building

The grant has supported training in bioinformatics and human genome sequence analysis for two research assistants through employment on this project. Training was funded in part by this grant and also by other grants ($96,804 of this grant paid salaries). Additionally, several PhD students have been involved in the research, including one working directly on the CMR protocol. One PhD student was able to receive a stipend top up under this grant. This was considered notable by the grant recipient as university PhD stipends for students are small and being able to provide an additional top up is helpful in being able to attract a high-quality student to the project. Through this experience, these students have been supported to build their research capability.

Case Study 8: Implementing novel approaches to transform blood pressure control

Project summary

Grant recipient: Dr Aletta Schutte	**Grant type:** Collaborative Grant; Round 3; Public health/ Clinical medicine & science
Funding received: $981,000 (July 2023 - ongoing)	**Other CVD Research Capacity Program grants received by recipient:** None

Key outcomes generated:

Publication metrics – Seven publications have been published with an average FWCI of 2.14[19] and two are under review. The research has been shared at eight conferences.

Economic benefit – Additional funding leveraged through this multidisciplinary research totals over $17 million.

The grant has enabled four multidisciplinary research streams the capacity to come together and establish implementation goals and share knowledge under the National Hypertension Taskforce and its guiding Roadmap.

Policy and practice – Over 40,000 people have been screened for hypertension. The World Health Organisation (WHO) has released a statement on low sodium salt substitutes based on this research. The recommendation has been made that drug labels allow for single pill combination therapy as first-line treatment.

The research problem

One-third of Australian adults have raised blood pressure and it is the leading cause of preventable death, due to heart attacks, stroke, kidney disease or dementia (29). Many Australians are unaware they have hypertension and fewer still control their blood pressure with medication (29). This low control rate compares poorly with other high-income countries (29). In late 2022, the National Hypertension Taskforce was launched which aims to improve hypertension control rates from 32 per cent to at least 70 per cent by 2030. To guide this work, a Roadmap was developed focusing on prevention, detection and effective treatment.

[19] Average FWCI for the seven publications calculated by averaging FWCI as given by Scopus.

Research aims

This project involves four aims which support the work of the National Hypertension Taskforce:

- Aim 1: Test innovative approaches to increase community awareness and diagnosis of hypertension. This Shop-to-Stop Hypertension clinical trial placed screening kiosks at 30 Bunnings stores for customers to test their blood pressure and their knowledge on hypertension and treatment. Participants are then randomly selected to receive a follow-up text reminder to visit their GP for management. Although the project is not completed yet, 42,144 people have undergone blood pressure screening and received health information to follow-up on their increased cardiovascular risk.
- Aim 2: Encourage switching from regular salt to potassium-enriched salt. Initial work has included interviews with government stakeholders and consumers to understand consumer preferences and cost effectiveness for salt substitutes.
- Aim 3: Simplify the approach to hypertension management by GPs in line with international best practice. Initial work has included economic analyses to assess potential for cost savings in managing hypertension in primary care.
- Aim 4: Optimise hypertension monitoring and adherence using digital health tools (29). Initial work has included the registration of a new clinical trial and a systematic review to explore the use of artificial intelligence and machine learning in care for hypertension.

The research is being undertaken by a multidisciplinary research team embedded within the National Hypertension Taskforce, a collaborative cross-sector group working to reducing the burden of high blood pressure in Australia (29,30).

Research findings

As the research is currently being undertaken, findings are not yet finalised. However, some emerging findings have been identified:

- Aim 1 is contributing findings regarding participant knowledge on hypertension and treatment.
- Qualitative data obtained for Aim 2 indicates consumer preferences for salt substitute taste, barriers to uptake, and the most cost-effective way to support uptake.
- Qualitative data obtained for Aim 3 is providing insights into how tools for hypertension management can be designed to be most effective in line with GP preferences.

The grant recipient could not provide emerging findings for Aim 4.

Outcomes generated

Knowledge advancement

New knowledge generated by the funded project

The potential to expand population-based volunteer screening for raised blood pressure using store-based kiosks is currently being explored by the study investigators, Bunnings and SiSU Health (who provided the kiosks). The study has contributed key proof-of-concept data.

Increased publication reach and quality

There have been seven publications to date related to the work undertaken, and two registrations (online notification of work being undertaken) including for a new systematic review on Prospero (an online prospective register of systematic reviews) and a clinical trial registered on the Australian New Zealand Clinical Trials Registry. There are additionally two publications either under review or in development; to be published once the ongoing research for the project work is completed. The research also had significant media attention, including coverage in 9 News and ABC News (31,32).

The research has been shared at the following conferences.[20]

- February 2025 - "Scaling up interventions to reduce diet-related diseases and disparities in Australia", Heart Foundation Researcher Showcase
- November 2024 – "A global strategy to scale-up potassium-enriched salt use", National Hypertension Summit, Sydney, Australia
- September 2024 - "Blood pressure lowering therapy with dual or triple single pill combinations or free combinations in Australia – what does it cost and who pays?", International Society of Hypertension Meeting, Cartagena, Colombia
- September 2024 – "Switching the global salt supply - reducing global sodium intake using potassium-enriched salt", NSW Cardiovascular Research Network (CVRN) Rising Stars Seminar, Sydney, Australia
- September 2024 – "Implementation Considerations for Low Sodium Salt Substitutes – Consumer Buy-In", Low-Sodium Salt Substitute Research Prioritization Webinar on Implementation
- May 2024 – "A global strategy to switch the world's salt supply to potassium-enriched salt", School of Public Health, Harbin Medical University, Harbin, China
- April 2024 – "Developing a strategy to scale-up potassium-enriched salt use to prevent cardiovascular disease", Preventive Health Conference, Darwin
- December 2023 – "The cost of treating hypertension in Australia, 2012–22: an economic analysis", Hypertension Australia meeting, Melbourne, Australia

The top five publications by FWCI are:

Publication	Citations (Scopus)	FWCI (Scopus)
"Potassium-Enriched Salt Substitutes: A Review of Recommendations in Clinical Management Guidelines", Hypertension, 2024	16	4.95
"Switching the World's Salt Supply—Learning from Iodization to Achieve Potassium Enrichment", Advances in Nutrition, 2024	5	4.01

[20] The grant recipient was unable to assess which conferences were the most impactful nor provide attendance details.

"The cost of treating hypertension in Australia, 2012–22: an economic analysis", Medical Journal Australia 2024	2	2.27
"Shop-to-Stop Hypertension: A multicenter cluster-randomized controlled trial protocol to improve screening and text message follow-up of adults with high blood pressure at health kiosks in hardware retail stores", Contemporary Clinical Trials, 2024	2	2.25
"Self-Guided Blood Pressure Screening in the Community: Opportunities, and Challenges", Hypertension, 2024	2	0.64

Policy and practice

Changes to policy and clinical practice

Several developments for policy and clinical practice are identified. Broadly, information across the four aims has been collected and made available to the National Hypertension Taskforce, intended to guide implementation of blood pressure control strategies.

- New Hypertension Guidelines for Australia are currently being developed by Hypertension Australia and the Heart Foundation. Several researchers from the multidisciplinary team working on this research are on the Guideline Committee responsible for developing the guidelines. The grant recipient noted the guidelines are being informed by research conducted under Aim 3 that evidenced potential cost savings when switching to single-pill combination therapy (Pikkemaat et al., J Hypertension 2025, in press) and in treating hypertension in Australia (Atkins et al., Med J Aust. 2024).
- Tools for GPs to guide management of hypertension have been designed under this grant and will be released once the Hypertension Guidelines have been published to ensure their alignment. The aim of these are to provide GPs with a one-page reference to help them identify and manage hypertension.
- Research funded through this grant was provided to the World Health Organisation (WHO) regarding the use of salt substitutes. As a result, the WHO has released a statement on low sodium salt substitutes. This is significant as previously the WHO recommendations were limited to lowering salt intake, rather than suggesting switching to salt substitutes.
- Several position statements have been or will soon be published by the Taskforce based on research undertaken. This includes a position statement on blood pressure monitoring in clinical practice, and a position statement on salt substitutes. These position statements should offer guidance for clinical practice.

New treatments used in clinical care

Based on data shared from work undertaken for Aim 3, the Pharmaceutical Benefits Advisory Committee has recommended to government that drug labels allow for the prescription of single pill combination therapy (two drugs combined in one pill) as first-line treatment. This should bring Australia in line with all international guidelines which identify the single pill combination as the ideal treatment for hypertension. If this is implemented, it should enable more simple and effective treatment.

Prevention practices

The Shop-to-Stop Hypertension study in Bunnings (Aim 1) is supporting prevention practice by helping to identify people with hypertension. It is also providing learnings for strengthening prevention practice. Over 40,000 people have been screened for hypertension through this study, meaning they have been provided information regarding their blood pressure and risk for related disease. This meant participants avoided the cost of a traditional GP visit as they were provided a screening, which included a free detailed health report. However, the grant recipient was not able to provide a dollar amount for this avoided cost. Additionally, data has been collected on preferences for follow-up methods to prompt engagement with GPs to start management. It is hoped that the dissemination of the findings of this study, once available, will help inform future prevention practices.

Improving acceptability of salt substitutes is intended to strengthen prevention. Minimising sodium intake through salt substitution is a preventative measure against hypertension and related disease, as salt is a known contributor to these diseases. The research is collecting data on barriers and enablers to implementing salt substitution, including community preferences, to inform strategies that support public uptake.

Under Aim 4, digital tools are being developed to help patients adhere to blood pressure treatment, including monitoring blood pressure and taking medication (as preventative measures against related disease). A trial is underway to evaluate whether the tools improve blood pressure outcomes. If blood pressure management can be improved, this would contribute to the prevention of diseases related to hypertension.

Health and community impact

Potential for improvement in care or outcomes for priority populations and related comorbidities or diseases

Broadly, the research is targeted to all Australians, to improve nationwide blood pressure control rates. The intention of the project is to lay the foundations for what works in improving hypertension awareness and management, so that further research can then target specific groups. There is evidence this is already happening: a screening has been set up for CALD communities in Sydney using the learnings generated under this grant.

The Shop-to-Stop Hypertension trial also included stores located in rural communities. These communities have had improved access to screening, and associated data will be included in findings regarding their screening preferences and hypertension knowledge.

Generally, older people experiencing diseases of ageing and individuals from CALD or Aboriginal communities should benefit from outcomes generated as these groups are more likely than the general population to experience hypertension. However, they are not a specifically identified population for this research due to the extensive prevalence of hypertension in the general population.

The grant recipient noted that improvements in care are expected to be supported in future, as the research contributes preventative strategies to improve hypertension, lowering risk for hypertension-related disease (e.g. heart attacks, stroke, kidney disease and dementia).

Economic benefits

Impact on funded researchers' career's progression

The grant recipient reported the grant contributed to their continued employment in cardiovascular research and in progressing in their research career stage. They highlighted that the grant had been significant in allowing the Taskforce to establish research goals and come together to act on these goals. While all four aims of the research are also supported by other grants and funding sources,[21] this grant had allowed them to focus on linkages between researchers and the four aims and facilitate a multidisciplinary approach. As a result of the momentum and recognition enabled through this grant, the recipient has been invited to the steering committees of international drug companies developing new drugs for hypertension and had been promoted to global cardiovascular lead for the George Institute's global CVD program. They were also invited to be on the advisory board for SiSU Health, to explore possibility for screening kiosks to be expanded into other stores (discussed further below).

Impact on NSW cardiovascular disease research capacity

The research has leveraged additional funding through seven grants, including those led by other researchers on the multidisciplinary team:

- NHMRC Synergy, $5,000,000
- NHMRC Investigator, $3,920,000
- NHMRC Investigator, $3,014,025
- NHMRC Investigator, $2,920,000
- Medical Research Future Fund Cardiovascular Health Mission, $2,460,000
- NSW Health, $449,902
- Heart Foundation Catalyst Grant, $100,000.

Of particular note, the grant was considered highly impactful as it provided the traction needed for the four research streams to pull together their existing work into a cohesive project with the capacity to pursue actionable aims and support the work of the National Taskforce.

[21] The grant recipient was not able to comment on the proportion of the streams funded by the Collaborative Grant compared to other funding streams.

Potential for commercialisation of research outputs and revenue forecast

30 kiosks were established in the study. Wesfarmers, who own both Bunnings and SiSU Health, is exploring potential for further expansion to all 513 Bunnings stores across Australia, though it is not yet clear whether this will be possible. It was noted that the purpose of this research was to gather data around detection of hypertension with the kiosks being an appropriate way to do this rather than seeking to commercialise the kiosks, and the grant recipient could not comment on possible revenue generated from expansion.

Economic benefits from improved patient care and reduced burden of disease

An economic analysis was undertaken by the research team for hypertension management in Australia. It found estimated total expenditure for the diagnosis and treatment of hypertension in Australia was $1.2 billion, with 40 per cent of cost borne by patients (33). Related economic analysis suggests the research being pursued under the grant has potential to lower these costs, with analysis on the cost effectiveness of single pill combination therapy demonstrating that single pill combination therapy would be cost effective for government and patients. Findings showed that for patients, single pill combinations always cost less than free drug combinations, with the greatest savings for general patients before reaching safety net (averaging 30 per cent). For government, the average cost of single pill combinations is less than free-drug combinations, for Concession Card holders both before (averaging 11 per cent) and after reaching the safety net (averaging 26 per cent), and in general patients after the safety net (averaging 11 per cent).

Additionally, cost modelling studies have been done for salt substitutes. The Salt Substitute and Stroke Study, led by the Aim 2 research team (and conducted before the grant) was a cluster-randomised trial assessing the difference in CVD outcomes between salt substitute and regular salt (34). Additional secondary analysis was undertaken on the data from this trail, including cost effectiveness analyses. This secondary analysis showed that salt substitutes have a 95.0 per cent probability of being cost saving and a >99.9 per cent probability of being cost-effective.

Capability building

The project has contributed to building the capability of numerous researchers involved. Particularly, 11 fellows have been directly involved in the project and collectively have been able to lead and publish papers, lead aspects of the research, gain promotions, and apply for and receive additional grants based on this experience.

As the grant recipient notes, “one of the biggest challenges in research is to make sure that these good fellows that we do have stay in research. And competitiveness of grants, especially to support their salaries are ridiculous. So the gaps that these sort of grants fill to make sure they can continue to engage and have a security to do their work in a very supported way is extremely important.”

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