Heart Abstracts

H1: Designing therapy that targets the L-type calcium channel to reduce cardiovascular morbidity and mortality

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Cardiovascular disease is the world's no. 1 killer responsible for premature death and disability affecting all stages of life. Sudden cardiac death accounts for approximately half of all heart disease related deaths and structural heart disease such as familial hypertrophic cardiomyopathy is the leading cause of death in people under the age of 30. Hypertrophic cardiomyopathy (HCM) is an autosomal dominant genetic heart disease that affects approximately 1:500 of the general population. Pathogenic features include ventricular hypertrophy, myocardial fibrosis, and diastolic dysfunction. At the level of the myocyte there is cytoskeletal disarray, hypercontractility and altered mitochondrial function. Mitochondrial dysfunction is considered to be a key driver in HCM pathology. The recent FDA approved cardiac myosin small molecule inhibitor mavacamten has demonstrated effective improvement in symptoms associated with severe outflow tract obstruction. Calcium channel antagonists are prescribed for the treatment of the symptoms of hypertrophic cardiomyopathy and the prevention of arrhythmias. However, there is no treatment that prevents the hypertrophy. Identifying therapeutic strategies to prevent the development of HCM is a significant clinical need. We previously demonstrated that the L-type Ca^{2+} channel plays a role in the development of HCM facilitated by a structural-functional communication between the channel and mitochondria involving the auxiliary beta subunit. We have designed peptides that interfere with the binding of the auxiliary β_2 subunit to the α_{1C} subunit causing immobilisation of the β_2 subunit and decreasing mitochondrial metabolic activity. The peptides significantly improve contractility and prevent the development of the hypertrophy in murine models of HCM, providing evidence for an effective and safe first in class preventative therapy.

H2: Novel targets to treat diabetic heart disease

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Diabetes is a significant risk factor for diastolic dysfunction and heart failure with preserved ejection fraction (HFpEF), but limited understanding of the underlying mechanisms has hindered development of specific treatment strategies. Diabetic patients exhibit both elevated circulating and cardiac fructose levels, and fructose-induced cardiomyocyte hypertrophy and lipid accumulation has been demonstrated *in vitro*. Our studies have evaluated the therapeutic potential of targeting cardiac fructose metabolism to treat diastolic dysfunction in diabetes. Using cardiac-targeted gene therapy approaches, and pharmacological interventions, our findings demonstrate a causal role for fructose accumulation in cardiac lipotoxicity and diastolic dysfunction in diabetes. Our recent studies suggest that cardiac fructose metabolism is a potential therapeutic target for the treatment of cardiac functional deficit in diabetes.

H3: A tale of two triggers: Heart failure in families affected by inherited PPA2 deficiency.

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Pyrophosphatase 2 deficiency is caused by biallelic variants in the *PPA2* gene, encoding a mitochondrial-specific pyrophosphatase enzyme (PPA2), which provides orthophosphate (Pi) for ATP generation in the mitochondrial matrix. Cardiomyocytes, nerves, and other tissues rely on pyrophosphatase activity for normal cellular respiration. Affected individuals typically present with cardiac arrhythmias or acute heart failure following two distinct triggers: common viral illnesses in infants and toddlers or exposure to small amounts of alcohol - usually as teenagers. The condition has a considerable mortality rate, and an enhanced inheritance pattern of affected alleles.

Here, using collated patients from over 50 families, pedigree analysis shows a pronounced inheritance rate of pathogenic alleles from carriers, indicating a possible gamete advantage for PPA2 deficiency in sperm and ova. Considering an expected 25% of affected inheritance rates for this recessively inherited disorder, an observed 75% rate remains; even as the number of affected families grow. Clinically, patient presentation is invariably acute, often associated with fatigue, gastrointestinal issues such as vomiting, seizures and collapse. If patients remain healthy until and beyond the age of 3, fatal viral triggers dissipate, and if diagnosed, alcohol avoidance means affected individuals lead normal lives. In response to these observations, we present hypotheses for the apparent non-mendelian inheritance of affected alleles and possibly, more pertinently, how the two distinct trigger mechanisms may affect compensatory cytoplasmic Pi recruitment through mitochondrial membrane channels into the inner mitochondrial matrix, resulting in electron transport chain attenuation, cardiomyocyte death, arrythmia and ultimately heart failure.

H4: Mathematical modelling of the coupling between blood pressure control and breathing

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High blood pressure (hypertension) affects nearly 25% of the population in New Zealand and is the highest risk factor for cardiovascular complications such as stroke and heart failure. Up to 50% of patients on medication to lower blood pressure remain hypertensive and at high risk of a cardiovascular event. This suggests that there are other mechanisms affecting the regulation of blood pressure and motivates our work.

We explored how intra-cranial baroreceptors, which were recently discovered, contribute to blood pressure control, and found previously underappreciated coupling with breathing. To understand the experimental observations, a new mathematical model of blood pressure regulation has been developed. The model couples the circulation[1], lung mechanics and heart rate control[2] with a Boolean respiratory network (where nodes can have only two values "1" or "0")[3]. The Boolean network enables full control over inspiration and expiration times and can generate a variety of breathing patterns. This allows us to explore pathways through which the intracranial and arterial baroreceptors interact. Our integrated model can also simulate the dynamic change of pressures and volumes in the four chambers of the heart, the mesenteric circulation and intracranial compartment. Uniquely, the model successfully reflects experimental findings and can be used to study the contribution of the respiratory system to the development of hypertension.

1. Noreen S, Ben-Tal A, Elstad M, Sweatman WL, Ramchandra R, Paton J. (2022) Mathematical modelling of atrial and ventricular pressure-volume dynamics and their change with heart rate. Mathematical biosciences. 2022;344:108766. doi: https://doi.org/10.1016/j.mbs.2021.108766
2. Ben-Tal A., Shamailov S.S. and Paton J.F.R. (2014), Central regulation of heart rate and the appearance of Respiratory Sinus Arrhythmia: new insights from mathematical modeling, Mathematical Biosciences, 255: 71-82. doi: 10.1016/j.mbs.2014.06.015
3. Ben-Tal A, Wang Y, Leite MCA. (2019), The logic behind neural control of breathing pattern. Scientific Reports. 9(1):9078. doi: 10.1038/s41598-019-45011-7.

H5: Developing an *in vitro* Model for the Discovery of Early Markers of Cardiac Ischaemia

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Each year ~65,000 New Zealanders attend hospitals with chest pain suggestive of myocardial infarction (MI). About 10–15% will be diagnosed with a MI. However, in many of the ~85% of patients in whom an acute MI has been ruled out, there remains uncertainty as to whether their presentation is due to coronary-related cardiac ischaemia. Some of these patients have a higher risk of future MI. We aimed to establish an *in vitro* model using human cardiomyocyte cultures derived from induced pluripotent stem cells (iPSC-cardiomyocytes; Joseph Wu, Stanford Cardiovascular Institute) to discover markers for cardiac ischaemia that could be used to identify patients who would benefit from proactive follow-up testing.
We have developed protocols to model ischaemia in iPSC-cardiomyocytes, testing 0.5% and 1% O_2 over 6, 12, 24, 48 and 72 hours after 7 days equilibration at 6% O_2 (normoxia for the heart). We measured expression of four genes, *SLC2A*, *VEGF2*, *BAX* and *BCL2*, at each timepoint using real-time quantitative PCR (Taqman assays). In this ischemic model, we found higher expression of the hypoxia-response genes *SLC2A* and *VEGF* after 12 hours (4-fold and 2-fold versus baseline, respectively), both peaking at 48 hours (11-fold and 15-fold, respectively), and 3-fold higher expression of the cell death marker *BAX* relative to *BCL2* at 72 hours.

Our data show that iPSC-cardiomyocytes can tolerate culture at 6% O_2 (as opposed to air, 21% O_2), and suggest that exposure to hypoxic conditions for 12 or 48 hours is sufficient to generate robust early and late ischaemic responses without cell death. This model may accelerate the discovery of early biomarkers for cardiac ischaemia to identify patients in whom an acute MI has been ruled out, but who are at higher risk of future cardiac events and would benefit from follow-up testing and preventative treatment.

H6: Prohormone enzyme in Aotearoa heart failure populations

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Plasma natriuretic peptides (NPs), including NT-proBNP and NT-proANP, are key biomarkers of cardiac stress, with NT-proBNP being a leading diagnostic and prognostic marker for heart failure (HF). Many factors, including ethnicity and body mass index (BMI), contribute to circulating concentrations of NPs, raising concerns about their clinical interpretation across diverse populations. We previously observed lower NT-proBNP concentrations in Pacific Peoples compared to New Zealand Europeans. We hypothesised that this difference might reflect variability in the levels of corin – an enzyme that cleaves NP prohormones to produce the biologically active peptides (BNP and ANP) and their inactive amino-terminal counterparts (NT-proBNP and NT-proANP).

To explore this, we examined the relationships between corin and demographic factors. Circulating corin concentrations were measured in 500 NZ patients stratified by ethnicity and BMI (Europeans n=250 [50% BMI>30], Māori n=125 [61% BMI>30], Pacific n=125 [90% BMI>30]). Multiple regression analysis showed that corin concentration was associated with higher BMI, male sex, younger age, and ethnicity, with Pacific participants having the highest median corin levels (1884.0pg/mL [IQR:1195.0]), followed by Māori (1651.0pg/mL [IQR:975.0], $p=0.017$ compared to Pacific) and New Zealand Europeans (1432.5pg/mL [IQR:835.0], $p<0.001$ compared to Pacific). A significant interaction between sex and BMI was also observed, with males exhibiting markedly elevated corin levels at higher BMI. This model accounted for 27.4% of the variation in corin concentration. Finally, we tested whether corin explained NT-proBNP variability. Corin was inversely correlated with NT-proBNP ($r=–0.243$, $p<0.001$), accounting for 5.9% of its variance.

In summary, Pacific participants exhibited higher circulating corin concentrations. However, differences in corin do not appear to be the primary driver of reduced NT-proBNP in Pacific Peoples with HF. The mechanisms underlying lower NT-proBNP levels in Pacific Peoples with HF remain unclear and warrant further investigation.

H7: Investigating the role of the epicardial adipose tissue secretome and obesity in atrial fibrillation

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The risk of developing atrial fibrillation (AF), the most common cardiac arrhythmia worldwide, is increased by obesity. Expansion of the visceral cardiac fat depot, epicardial adipose tissue (EAT), is associated with both AF and obesity. This study aimed to examine acute mechanisms of EAT-induced arrhythmogenesis, focusing on the involvement of acute metabolic stress and chronic obesity.

Using an *in vitro* isolated right atrial trabecula model, human trabeculae (n = 21) were exposed to the 24-hour cultured secretome of human EAT from non-obese (BMI < 30 kg/m^2; n = 6) or obese (BMI > 30 kg/m^2; n = 7) cardiac surgery patients. EAT biopsies were bisected and either left untreated (control) or treated with an acute metabolic stress cocktail of hyperglycaemia, hyperlipidaemia, and hyperinsulinaemia (treatment). Furthermore, EAT secretome samples from non-obese (n = 7) and obese (n = 7) participants underwent proteomic analysis.

Neither control nor treatment secretomes increased the proportion of trabeculae that developed unstimulated, spontaneous contractions (SCs) (control: 6/21 & treatment: 5/21 vs. baseline: 8/21, P = 0.70). Similarly, there was no difference in the SC propensity induced by control secretome from non-obese (2/7) and obese participants (4/14, P = 0.56). The control secretome induced a distinctly negative inotropic (F_{dev}: 2.6 ± 0.7 mN/mm^2 vs. baseline 4.0 ± 0.9 mN/mm^2, P < 0.0001) and lusitropic (-dF/dt$_{max}$: -26.2 ± 6.0 mN/mm^2/s vs. baseline −35.1 ± 7.1 mN/mm^2/s, P = 0.01) effect, however this was unchanged by either the treatment or obesity. We identified for the first time alterations in adipokine expression in the EAT secretome in obesity, in particular increased expression of calcium-binding S100 proteins (S100A, S100A11, and S100B).

This study provides novel mechanistic insight into the acute paracrine relationship between EAT and the atrial myocardium in humans, and how this is informed by acute metabolic stress and chronic obesity.

H8: A maternal obesogenic diet impacts key cardiac structural adaptations during pregnancy and lactation in rats.

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Background/aims: Pregnancy complications are linked to an increased risk of cardiometabolic diseases. The maternal cardiometabolic system undergoes significant adaptations during pregnancy and lactation. Effects of an obesogenic (OB) diet on these maternal adaptations are unknown. The aim of this study was to analyse the effects of an OB diet on cardiac structure in mothers, both pre-pregnancy and post-lactation.
Method: Female Sprague-Dawley rats were fed either control (CON) or OB diet for five-weeks pre-mating, then mated with males on CON diet. Females continued their respective diets throughout pregnancy and lactation (PL). Maternal heart tissues were collected either pre-pregnancy (CON-PP, n=10; OB-PP n=8) or after PL, (CON-PL, n=14; OB-PL n=15). Total body weight (TBW) and heart weights (HW) were recorded. Cardiac morphology was assessed using histology.
Results: Diet increased TBW in OB-PP, CON-PL and OB-PL mothers compared to CON-PP with no difference between OB-PP and OB-PL groups. This is suggestive that PL offsets TBW gain in OB rats, with a significant diet-PL interaction. Raw HW only increased in OB-PL compared to CON-PP mothers. This resulted in a disproportional increase in normalised (to TBW) HW in OB-PL mothers compared to CON-PL. Nuclei density of cardiomyocytes increased in CON-PL compared to CON-PP mothers and reduced in OB-PL compared to CON-PL, with a diet-PL interaction. Left ventricular (LV) internal perimeter increased in CON-PL and OB-PL mothers compared to CON-PP with an overall diet-PL interaction, while LV posterior wall thickness decreased in CON-PL and OB-PL mothers compared to OB-PP, with a significant PL effect. Collagen I and III levels in OB-PP and CON-PL mothers decreased compared to CON-PP while no differences were observed between OB-PP and OB-PL mothers.
Conclusion: There are significant cardiac structural changes due to PL and some parameters are impacted by a maternal obesogenic diet pre-pregnancy and throughout lactation.

H9: Ethnicity and cardiovascular disease influence the relationship between *TXNIP* DNA methylation and type 2 diabetes

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The association between DNA methylation (DNAm) at the *TXNIP* locus and type 2 diabetes (T2D) has been widely reported including in our own Pasifika Heart Study (PHS), a community cohort of Pacific Peoples living in New Zealand. We hypothesised that the association may be different in Pacific Peoples. To test this, we conducted a meta-analysis of reported effect sizes between DNAm at the probe cg19693031 in the *TXNIP* gene and T2D and compared this to whole-blood DNAm (Illumina MethylationEPIC arrays) in participants from the PHS (n=191) and Pacific and European participants from the Multi-Ethnic New Zealand Study of Acute Coronary Syndromes (MENZACS, $n_{Pacific}$=98, $n_{European}$=526), a cohort of patients with acute coronary syndromes.

We identified 16 reported associations between *TXNIP* DNAm and T2D in the literature and meta-analysed these using a random-effects model. The overall pooled difference in *TXNIP* DNAm in those with T2D compared to those without T2D was -3.59% [95% CI -4.28, -2.90, I^2=83.18%]. This was smaller compared to the average difference associated with T2D in PHS (-6.16% [95% CI, -7.77, -4.56]), the MENZACS European participants (-6.64% [95% CI, -7.80, -5.48]) and the MENZACS Pacific participants (-9.60% [-11.62, -7.58]), suggesting the relationship between *TXNIP* DNAm and T2D may be influenced by ethnicity and cardiovascular disease (CVD). Of the 16 studies, 8 (69%) cohorts had majority Europeans participants and 2 (11%) recruited participants upon hospital admission with CVD. Including ethnicity and CVD as moderators in the meta-analysis gave a new pooled estimate of -2.56% [95% CI, -3.11, -2.01, I^2=50.98%]. Non-European ethnicity and CVD had additional effects of -2.28% [95% CI, -3.18, -1.39] and -2.44% [95% CI -3.95, -0.92] respectively.

In summary, we identified a potential additive effect of non-European ethnicity and CVD on T2D and DNAm at *TXNIP*, providing evidence for population and disease specific epigenetic relationships with cardiometabolic traits.

H10: Investigating the Mechanism of Lp(a) Uptake via the PlgRKT Plasminogen Receptor

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Lipoprotein(a)[Lp(a)] is a plasma lipoprotein strongly associated with cardiovascular diseases. It comprises a low-density-lipoprotein (LDL)-like particle linked to apolipoprotein(a)[apo(a)], which shares significant homology with plasminogen. While multiple hepatic receptors have been implicated in Lp(a) clearance, PlgRKT (plasminogen receptor with C-terminal lysine) has emerged as a strong candidate receptor due to its known role in plasminogen binding and in promoting Lp(a) uptake. This study aimed to investigate whether Lp(a)/apo(a) exploits similar mechanisms as plasminogen for binding to PlgRKT i.e. through binding of the plasminogen kringle IV domain to the PlgRKT C-terminal lysine. To test this, a K147A mutant of PlgRKT was generated. Both wild-type and mutant constructs were overexpressed in HepG2 cells, and uptake of purified apo(a) and Lp(a) was visualized and quantified using confocal microscopy and western blotting. Comparable uptake of both apo(a) and Lp(a) was observed for both constructs, indicating that the PlgRKT C-terminal lysine was not essential for internalization. To explore alternative interaction sites, AlphaFold-Multimer was used to dock various apo(a) kringle IV subtypes to extracellular PlgRKT regions. Docking of apo(a) KIV-10 to PlgRKT yielded two regions with interface Predicted Template Modelling (ipTM) scores of 0.71 and 0.74. Similar values (0.71 and 0.63) were obtained when docking the plasminogen KIV domain on to the same two regions in PlgRKT, supporting a potential shared binding interface. These two PlgRKT regions involved in high-confidence docking were found to be conserved across species. These findings suggest that apo(a) engages PlgRKT through a mechanism that does not solely depend on the C-terminal lysine, indicating alternative binding sites for apo(a) KIV. These results suggests a non-canonical pathways for Lp(a) uptake and identify novel interaction regions within PlgRKT for future mutagenesis studies. Competitive binding assays between plasminogen and Lp(a)/apo(a) are underway to further investigate these interactions and confirm mechanistic divergence in PlgRKT binding.

H11: Mitochondria-derived peptide MOTS-c restores mitochondrial respiration in type 2 diabetic heart

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Type 2 diabetes (T2D) is a global epidemic, and heart failure is the primary cause of premature death among T2D patients. Mitochondrial dysfunction has been linked to decreased contractile performance in diabetic heart, partly due to a disturbance in the mitochondrial capacity to supply adequate metabolic energy to contractile proteins. MOTS-c, a newly discovered mitochondrial-derived peptide, has shown promise as a therapeutic for restoring energy homeostasis and muscle function in metabolic diseases. However, whether MOTS-c therapy improves T2D heart function by increasing mitochondrial bioenergetic function remains unknown. Here we studied the mitochondrial bioenergetic function of heart tissues isolated from a rat model mimicking type 2 diabetes induced by a high-fat diet and low-dose streptozotocin. Treated diabetic group received MOTS-c (15 mg/kg) daily injection for three weeks. We employed high-resolution respirometric and fluorometric techniques to simultaneously assess mitochondrial ATP production and hydrolysis capacity, reactive oxygen species (ROS) production, and oxygen flux in cardiac tissue homogenates. We found that untreated T2D rats had hyperglycemia, poor glucose control, and left ventricular hypertrophy relative to controls. T2D mitochondria showed decreased oxygen flux at the oxidative phosphorylation (OXPHOS) while ROS production, ATP production and hydrolysis rates remained unchanged. Diabetic rats treated with MOTS-c showed decreased fasting glucose levels, improved glucose homeostasis, and decreased degree of cardiac hypertrophy. At the subcellular level, MOTS-c treated mitochondria showed increased OXPHOS respiration and ROS levels and decreased ATP hydrolysis rate during anoxic conditions. These findings demonstrate beneficial effects of MOTS-c treatment on glucose homeostasis and suggest a useful therapeutic option for diabetic-related cardiomyopathy and mitochondrial dysfunction.

H12: Imaging the movement of gold labelled monocytes into live human atherosclerotic plaques by Spectral Photon Counting CT.

Holmes, D.[1], Moghiseh, M.[2], Healy, J.[2], Atlas, J.[2], Kim, J.[6], Dong, Y.[6], Benson, R.[5], Roake, J.[5], Hock, B.[7], Butler P.[2,4], Cormode, D.[6], Butler, A.[2,3,4], Gieseg, S.[1,2,3,4].

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The growth of atherosclerotic plaques is driven by the recruitment, differentiation, and accumulation of blood monocytes into the artery wall. The rupture of these plaques causes ischemic strokes and myocardial infarction. Here, we track the recruitment of monocytes into human atherosclerotic plaques using Spectral Photon Counting Computed Tomography (SPCCT), a highly sensitive, non-invasive X-ray imaging modality.

Human monocytes isolated from peripheral blood via density gradient centrifugation and plastic adherence were labelled with 0.5mg Au/mL 11-mercaptoundecanoic acid gold nanoparticles (AuNP) for 24 hours. Excised carotid plaques from stroke patients were sliced into 3-4 mm thick sections and incubated with AuNP labelled monocytes in tissue culture media for up to 24 hours at 37ºC. The plaque sections were imaged at 12-hour intervals using a MARS SPCCT scanner. Material identification and quantification (MIQ) images of the carotid plaque sections were generated using proprietary MIQ software at 0.09 mm^3 volumetric pixels (voxels).

AuNP uptake measurements in monocytes from SPCCT were compared to measurements obtained from microwave plasma atomic emission spectroscopy (MPAES). SPCCT provided comparable concentration results, with the advantage of being non-destructive. AuNP uptake in monocytes was 135 pg Au/cell with minimal inflammation as indicated by HPLC analysis of neopterin and 7,8-dihydroneopterin. SPCCT imaging showed that the monocytes rapidly penetrated deep within the live plaque sections. Quantitative analysis showed an estimated average uptake rate of 0.4×10^6 monocytes at 12 hours, increasing to an average of 0.55×10^6 at 24 hours. Heavy calcified regions excluded the monocytes while soft tissue and lipid rich regions accumulated monocytes. The SPCCT imaging of the live tissue demonstrates the dynamic environment of the atherosclerotic plaque and the ease in which monocytes can penetrate deep within the tissue.

H13: *DMPK* 3' untranslated repeat expansion in unexplained sudden cardiac death

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Background: Sudden cardiac death (SCD) in the young is a devastating event for families. Inherited cardiac diseases, including arrhythmogenic disorders and cardiomyopathies, are an important cause of SCD. Identifying the underlying genetic aetiology is critical for patient/family management.
Methods: We present three SCD families in whom panel and exome sequencing failed to provide a genetic diagnosis for up to 20 years. A combination of whole genome sequencing (WGS) and an expanded cardiac panel using Oxford Nanopore (ONT) long reads and Illumina short reads was performed.
Results: Case 01 – a family with three teenage SCDs; Case 02 – an elite athlete with an SCD during exercise; Case 03 - a 6-year-old SCD while playing sports. In all three cases a heterozygous *DMPK* repeat expansion in the 3' untranslated region was identified as the cause of SCD: in Case 01 following WGS in multiple family members, in Case 02 following a Myotonic Dystrophy diagnosis (DM1) in a relative; in Case 03 following cardiac panel ONT sequencing.
Conclusions: *DMPK* repeat expansions are not routinely tested in SCD cases and are potentially missed with exome/panel sequencing. Our findings advocate incorporating *DMPK* testing in genetically unexplained SCDs. It remains uncertain whether the *DMPK* expansion alone is sufficient to guide preventative screening decisions in SCD families and further research is also needed to uncover potential genetic modifiers. The cases also highlight the importance of comprehensive phenotyping and detailed family history (e.g., DM1 diagnosis) in the search for the underlying cause of SCD.

H14: Abdominal Aortic Aneurysm in Women: How can we reduce the inequity?

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Women with an abdominal aortic aneurysm (AAA) in Aotearoa New Zealand experience inequity at every stage of diagnosis and management. This has long been known, and should be addressed. We currently treat women too late in their clinical course, where increased age, comorbidities, larger AAA diameter, preventable ruptures, loss of eligibility for simple EVAR, and clinical 'turn down for surgery' (palliation) rates all add to higher AAA mortality. Currently smoking wāhine Māori have a particularly high disease prevalence. Substantial inequity in mortality persists because we do not know when it's best to offer women surgery to repair their AAA, and because their high cardiovascular risk is poorly managed. AAA growth and rupture rates are increased by smoking. The presence of an AAA indicates very high risk of future cardiovascular events including stroke and myocardial infarction. There is scope for great improvement in cardiovascular risk reduction for people living with a small AAA, and for reconsidering the inclusion of women in proposals for a AAA screening programme. There is an urgent need to identify the optimal size threshold at which to offer elective AAA repair. The International Women's Small Aneurysm Trial is an investigator-initiated, pragmatic, international, comparative effectiveness randomised controlled trial of early elective keyhole AAA repair versus 'current gold standard' care in women with small asymptomatic AAA who are eligible for EVAR, nested within a cohort study, and will recruit at four centres in Aotearoa. This trial will provide the first randomised evidence to guide management of women's AAA, and is strongly supported by patients and vascular surgeons in Aotearoa.[1]

1. Williams T, Benson R, Lyons OT. *Solutions to Reduce Inequity for Women with Abdominal Aortic Aneurysm.* Eur J Vasc Endovasc Surg. 2025 Jan;69(1):166.

H15: Barriers and bridges to translating a new biomarker into clinical practice: The ICare-FASTER story

Pickering, J.W.[1,2], Joyce, L.J.[2,3], on behalf of the ICare-FASTER team.

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Background

In patients with possible myocardial infarction delay to laboratory-based cardiac troponin (cTn) results extends Emergency Department (ED) lengths of stay (LOS). The first high-sensitivity cTn point-of-care (POC) assays are now available with ~8min turnaround time. We implemented hscTn POC into multiple hospitals. The process encountered several scientific and practical barriers that needed bridging.

Methods & barriers

Setting: The establishment of the Siemens VTLi hscTn POC assay in 6 NZ EDs

Barriers:

1. Analytical verification of the assay and secondary verification of devices.
2. Finding a suitable quality control (QC) material that covers the concentration range used clinically.
3. Establishing a threshold concentration below which it is safe to discharge patients.
4. A new information technology pathway to get data from machines into the clinical record in real-time across multiple hospitals
5. Implementing new procedures for nurses.
6. Incorporating a second troponin assay into established diagnostic pathways that does not perform identically.

Results

Bridges:

1. Using the literature and simulations, minimal analytical performance metrics were established.
2. A different QC material than manufacturer recommended and a plasma pool was needed.
3. Working within rules allowing non-consent, 2000 measurements were made to enable threshold to be established.
4. Health NZ established a first national process for centralised handling of biochemical data.
5. Value to nursing staff was proven via value stream mapping, with training provided, building confidence in a new more pro-active role.
6. Issues around discordant results between assays at the Upper Reference Limit was addressed.

Preliminary results in Christchurch were a mean 30min reduction in LOS.

Conclusion

We established a hs-cTnI point-of-care assay in 6 hospitals through a process that required far more resources than anticipated. This can shorten LOS via expedited decision-making. Multiple complex and interacting factors must be carefully established and evaluated before project initiation.

H16: Premature Birth and Long Term Cardiovascular Health for Mother and Baby

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[2]Department of Medicine, University of Otago, Christchurch, NZ,
[3]Department of Psychological Medicine, University of Otago, Christchurch, NZ,

Background:

Premature birth disrupts cardiovascular development exposing an immature cardiovascular system to suboptimal conditions. Prematurity is associated with higher blood pressure and heart failure in adulthood.[1,2] Pregnancy is a cardiovascular stress test and premature birth is associated with heightened maternal risk of cardiovascular disease.[3] Premature birth is not considered in cardiovascular risk screening. Longitudinal cohort studies can offer insights into the impact of premature birth on cardiovascular health.

Methods:

The New Zealand Very Low Birth Weight (VLBW) cohort were born at <1500g in 1986 with adult follow-up at 22,28, 36 years. Cardiovascular health has been compared to a control group: blood pressure, echocardiography, BNP, HbA1c, lipids, anthropometrics, cardiorespiratory exercise testing, DNA methylation, health questionnaire. At the 36-year study, cardiovascular health of the mothers was studied: health questionnaire, blood pressure, lipids, HbA1c and anthropometrics.

Results:

VLBW adults have smaller cardiac size and mass, with differences in function at rest and with exercise. Blood pressure and measures of vascular stiffness are higher in VLBW. Differences in methylation patterns of cardiac signalling pathways were seen. Estimated 5-year cardiovascular was higher in VLBW group. Preliminary analysis of mothers study suggests VLBW mothers have a less favourable cardiovascular risk profile than control mothers.

Conclusion:

Premature birth may be an under recognised marker of cardiovascular risk and provide an opportunity to influence the future heart health of both mother and baby.

1. Crump C, Sundquist J, Sundquist K. *Risk of hypertension into adulthood in persons born prematurely: a national cohort study*. Eur Heart J. 2020;41(16):1542-1550.
2. Crump C, Groves A, Sundquist J, Sundquist K. *Association of Preterm Birth With Long-term Risk of Heart Failure Into Adulthood*. JAMA Pediatr. 2021;175(7):689-697.
3. Wu P, Gulati M, Kwok CS, et al. *Preterm Delivery and Future Risk of Maternal Cardiovascular Disease: A Systematic Review and Meta-Analysis.* J Am Heart Assoc. 2018;7(2):e007809.

H17: Restoring cardiac function by reinstating respiratory heart rate variability in heart failure.

Shanks, J.[1], Pachen, M.[1], Lever, N.[1,2], Paton, J.[1] Ramchandra, R.[1]

[1]Manaaki Manawa – The Centre for Heart Research, Department of Physiology, University of Auckland, New Zealand. [2] Te Whatu Ora Te Toka Tumai Auckland.

Heart failure is characterised by reduced heart rate variability, in particular loss of heart rate modulation with breathing: respiratory heart rate variability (RespHRV). Using a novel cardiac pacemaker (Ceryx Medical), we have shown that reinstating RespHRV in reduced ejection heart failure can improve cardiac output and myocyte structure compared to monotonic pacing. Individuals living with heart failure exhibit life-limiting reduced exercise capacity. We hypothesised that reinstating RSA in heart failure would not only improve cardiac function at rest but would also improve cardiac responses to exercise.

Heart failure was induced in adult sheep by a microembolisation technique. Eight weeks after embolisation, sheep were split into two groups: RespHRV-paced (n = 5-6) and monotonically-paced (n = 5-7). After instrumentation with chronic arterial pressure and cardiac flow probes sheep underwent a one-week baseline recording and were paced daily for two weeks. At baseline and after two weeks of pacing, direct recordings of cardiac output, coronary artery blood flow, and heart rate were recorded in conscious adult sheep during exercise.

RespHRV pacing for two weeks increased cardiac output (P<0.01) with no change in coronary artery blood flow at rest. At baseline, there were no differences in the hemodynamic and cardiac responses to graded exercise between groups. After two weeks of RSA, sheep showed an increase in coronary artery blood flow (pre-pace: 61.4±10.1 ml/min, post-pace: 90.6±11.3 ml/min, n = 5, P <0.01), during exercise and a faster heart rate recovery post-exercise. After two weeks of monotonic pacing, there was no change in cardiac function during exercise compared to baseline.

Reinstalling RespHRV is now undergoing clinical safety and feasibility testing at six sites globally. To date, 12 patients post-CABG surgery have received RespHRV or monotonic pacing (n = 6, each group) by temporary pacing wires. Preliminary results indicate feasibility with no adverse events.

H18: The Ideal Valve for the Treatment of Rheumatic Heart Disease

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Rheumatic heart disease (RHD) is a leading cause of valvular heart disease in children and young adults, and disproportionately affects Māori and Pacific people in New Zealand. Current valve replacement options, are inadequately suited to pediatric patients. Mechanical and bioprosthetic valves are unable to grow, repair, or remodel, often requiring multiple open-heart surgeries over a child's lifetime. We present the progress and limitations of tissue-engineered heart valves (TEHVs) as a promising alternative for young RHD patients, and focus on the key requirements of the “ideal valve”: physiological haemodynamics, durability, growth, non-thrombogenicity, immunocompatibility, and resistance to calcification. We examine the in vitro, in vivo, and in situ tissue engineering approaches, and discuss novel advances in scaffold design and scaffold material. Decellularized matrices, hybrid polymeric scaffolds, and hydrogels have demonstrated significant progress towards achieving key elements of the ideal valve. In addition, in situ engineering strategies offer promising potential for pediatric use due to their endogenous recruitment of cells for remodelling capacity. Strong progress has been made in improving durability, reducing thrombogenicity, and replicating physiological haemodynamics. However, challenges remain in understanding remodelling processes, demonstrating somatic growth, and warding off calcification. Advances in biofabrication technologies, computational modelling, and stem cell biology are hastening progress toward an ideal valve to improve the management of, and outcomes for pediatric RHD - addressing a critical unmet clinical need and reducing the lifetime requirement for reoperation in vulnerable populations.

H19: Enhancing Atrial Fibrillation Treatment with AI and Digital Twin Technologies

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Atrial fibrillation (AF) is the most common long-lasting heart rhythm problem and a leading cause of stroke and heart failure. It places a heavy burden on heart health. Early diagnosis and personalised treatment are vital, but current tools often fall short. Our research aims to improve AF care using artificial intelligence, digital twins, and advanced heart imaging.

We present new results from clinical **late gadolinium-enhanced MRI**, where our AI-based analysis pipeline now supports standardised assessment of both left and right atria. These tools are being applied across multiple centres and support our digital twin modelling.[1-2] These personalised atrial models simulate AF dynamics and help test treatment strategies virtually before clinical intervention. We also report on **ex-vivo analysis** using optical mapping and high-resolution MRI of donor hearts. This dataset allows us to explore how fibrosis, wall thickness, and conduction patterns contribute to AF. For **cardiac CT**, we are developing AI tools to identify structural markers—such as atrial volume, wall thickness, and fat distribution—that may predict AF recurrence after ablation.[3] Early results show strong potential for improving patient selection. Finally, in the **ECG domain**, we are building AI models for arrhythmia classification and beat detection using wearable patch ECGs. These models include explainable outputs and decision confidence to support clinician trust. Together, these efforts are advancing our ability to support early diagnosis, risk prediction, and precision treatment for AF in both clinical and community settings.

1. Kulathilaka et al. Structural determinants of re-entrant drivers in atrial fibrillation: insights from digital twins of 3d micron-resolution imaging of human heart. *The Journal of Physiology*, 2025.
2. Xiong et al. A global benchmark of algorithms for segmenting late gadolinium-enhanced cardiac MRI. *Medical Image Analysis*, 2021.
3. Feng et al. AI-driven segmentation and morphogeometric profiling of epicardial adipose tissue in type 2 diabetes. *Cardiovascular Diabetology*, 2025.

H20: Integration of high-quality cardiovascular disease risk assessment in pathology services to improve health care delivery

Sharman, J.E.[1]

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Cardiovascular disease (CVD) is the leading global cause of death for non-communicable diseases. Significant CVD morbidity can be prevented through interventions targeted at people at high risk of developing CVD. The clinical assessment and management of CVD risk is mostly carried out by general practitioners, in which treatment decisions should be based on CVD risk stratification that is calculated from multiple risk factors. The recommended management strategy for people identified with high CVD risk is treatment with both cholesterol-lowering and antihypertensive therapies. However, this does not routinely occur in general practice where only a low percentage of high-risk patients receive guideline-recommended medications. Effective solutions to address this deficit are needed, and must consider barriers faced by general practitioners (i.e. lack of time, lack of access to risk factor information). An opportunity to assist general practitioners to improve CVD risk management could be achieved by integration of high-quality CVD risk assessment being performed in pathology services during the visit where patients provide a blood sample for cholesterol analysis. A large-scale, cluster, randomised controlled trial was conducted to determine if CVD risk assessment conducted in a pathology service and reported to general practitioners would improve clinical management of people at high CVD risk. A high throughput, semi-automated process of gathering CVD risk information by integrating new technology within existing health systems was tested and shown to improve CVD care. This model is generalisable across health systems internationally where it could improve CVD outcomes and lower health costs.

H21: Identifying the rheological properties of a flexible thrombus

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Modelling thrombosis with numerical simulations remains as a challenging task[1] consisting of multiphysics, multiscale, and complex fluid dynamics with fluid-structure interactions. In this work, we focus on the problem of identifying the rheological properties of developed thrombi within blood vessels, using the dynamics of the interface between blood flow and thrombi.

A viscoelastic porous medium was assumed for the thrombus because of its fibrous network. The fluid-structure interaction between the thrombus and blood flow was modelled in the Eulerian reference frame using the Cahn–Hilliard and Navier–Stokes equations[2]. Two rheological properties of the thrombus, specifically the viscosity and relaxation time, were identified with an inverse model using a twin experiment approach. Synthetic results were first generated with a prescribed viscosity and relaxation time, and then second an optimiser was employed for minimising the difference between the simulated and synthetic thrombus interface. Such a method of parameter identification has previously been used elsewhere, including for describing temperature-dependent lava rheology[3].

We discuss the sensitivity of rheological properties to the thrombus dynamics, and the robustness of the inverse method by adding noisy data to imitate experimental uncertainties. Finally, we compare our results with existing work using physics-informed neural networks[4].

1. Belyaev, A.V. et al. *Modeling thrombosis in silico: Frontiers, challenges, unresolved problems and milestones*. Phys. Life Rev. (2018) **26–27**:57–95.
2. Zheng, X. et al. E. *A three-dimensional phase-field model for multiscale modeling of thrombus biomechanics in blood vessels*. PLoS Comput. Biol. (2020) 16(4): e1007709.
3. Hewett, J.N. et al. *Describing lava rheology using flow dynamics information*. In 22nd Australasian Fluid Mechanics Conference (2020) Brisbane, Australia.
4. Yin, M. et al. *Non-invasive inference of thrombus material properties with physics-informed neural networks*. Comput. Methods Appl. Mech. Engrg.(2021) 375: 113603.

H22: Phosphodiesterase-9 inhibition improves cardiac structure after myocardial infarction in an ovine model.

Scott, N.J.A.[1], Rademaker, M.T.[1], Lewis, L.K.[1], Lee, J.[1], Perston, L.[1], Richards A.M[1], Troughton, R.W.[1], Charles, C.J.[1]

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Although advances in pharmacological and revascularisation therapies following myocardial infarction (MI) have led to improved survival, post-MI adverse left ventricular (LV) remodelling and progression to clinical heart failure remains a significant problem.

The natriuretic peptides (NPs), a family of cardioprotective hormones, inhibit cardiac hypertrophy and fibrosis, and therefore augmentation of the NPs might be beneficial post-MI. Phosphodiesterase-9 (PDE9) is an enzyme that selectively targets degradation of NP-induced cyclic guanosine monophosphate (cGMP), the second messenger molecule that transduces NP-coupled signalling. Inhibition of PDE9 has been shown to enhance NP bioactivity.

We explored for the first time the therapeutic benefit of PDE9 inhibition after experimental MI in a large animal model. Twenty-nine Coopworth ewes underwent permanent ligation of their 2nd diagonal coronary arteries via a left lateral thoracotomy performed under general anaesthesia. Sheep were randomly assigned to receiving a PDE9 inhibitor intravenously twice daily for seven days (100mg PF-04749982, *Pfizer Inc.* New York, USA; n=15) or left untreated (n=14). All sheep underwent serial plasma hormone measurements and echocardiography assessments (pre-MI, and days 7 and 28 post-MI). After 28 days, sheep were euthanised and the hearts excised, weighed and segmented for gross and microscopic examination. Tissues were collected from three regions of LV free wall (remote myocardium, mid-infarct and infarct border zone).

Preliminary results showed no significant difference in end-of-study body weight, heart weight:body weight ratio, cardiac troponin I levels or total size of MI, between the 2 treatment groups. However, compared to untreated controls, sheep treated with the PDE9 inhibitor had significantly greater LV wall thickness at both the mid-infarct (0.706±0.073 cm vs 0.479±0.073 cm, $p<0.001$) and infarct border zone (1.168±0.098 cm vs 0.852±0.078 cm, $p<0.001$), indicating a reduction in adverse LV thinning post-MI.

These preliminary data suggest that augmentation of the NPs via inhibition of PDE9 may beneficially impact post-MI LV remodelling.

H23: Te Ara Poutama: Living Well with Heart Disease – Reimagining Equity in Cardiovascular Health for Māori

Korohina, E.[1], Rolleston, A.[1], Poppe, K.[2], Davis, K.[3], Cheung, M.[4], Devlin, G.[3], Doughty, R.[2]
[1]Manawaora Integrated Health & Research, [2]University of Auckland, [3]Heart Foundation of New Zealand & [4]Cheung Consultancy Limited.

Te Ara Poutama – Living Well with Heart Disease is a Māori-led cardiovascular research programme grounded in the values, aspirations, and knowledge systems of Māori communities in Aotearoa New Zealand. Hosted at Manawaora Integrated Health & Research Centre, the programme was developed in response to persistent inequities in heart health outcomes for Māori, who continue to experience higher rates of cardiovascular disease and systemic barriers to care.

Rather than adapting Indigenous knowledge to fit within existing models, Te Ara Poutama reimagines health research and practice by centring Māori leadership, lived experiences, and mātauranga Māori. A multidisciplinary team—including clinicians, public health experts, scientists, and data specialists—supports this Māori-led kaupapa through collaborative, relational approaches grounded in equity, tino rangatiratanga, and mana motuhake.

A national co-design process was carried out across four regions through a series of wānanga (community-led workshops), shaped by the tikanga of each host community. These gatherings created culturally safe spaces for Māori whānau to share lived experiences of heart disease and to influence the programme's priorities and direction.

In addition to the co-design, two major initiatives sit at the heart of Te Ara Poutama. The Māori Heart Health Survey, which gathered over 1,000 responses, has created one of the largest Māori-specific heart health datasets to date. The Kura Raumati internship programme supports the next generation of Māori heart health researchers by embedding students in kaupapa Māori, community-based research environments.

Te Ara Poutama shows how Indigenous-led, community-driven, multidisciplinary research can re-orient systems, disrupt inequities, and generate solutions that are culturally resonant, structurally informed, and globally relevant.

Acknowledgements: We extend our deep gratitude to the whānau, hapori, and Māori health providers who have guided and supported this rangahau. Nei rā te mihi maioha mō tō koutou tautoko.
Host organisation: Manawaora Integrated Health & Research Centre
Funders: Pūtahi Manawa – Centre of Research Excellence and the NZ Heart Foundation

H24: Equity implementation lessons for heart failure discharge planning in Aotearoa: a qualitative stocktake analysis

Hanchard, S.[1], Ameratunga, S.[1], Selak, V.[1], Harwood, M.[1], Grey, C.[1],

[1]Faculty of Medical and Health Sciences, The University of Auckland, NZ

There is long-standing and growing evidence of disparities in heart failure outcomes experienced by Māori and Pacific peoples in Aotearoa New Zealand (AoNZ). While discharge planning is a crucial phase in the overall care of heart failure, the extent to which service delivery models in AoNZ address inequitable outcomes is unclear. The aims of this study were to gain a picture of discharge planning for heart failure at the interface between hospital-level and community care in AoNZ with a focus on approaches for Māori and Pacific patients.

A stocktake was conducted consisting of semi-structured interviews with heart failure clinicians and a collection of discharge planning documentation. Template analysis (inductive-deductive) was applied to analyse the interview and document data. *A priori* themes were based on consultation of implementation frameworks. [1 2]

Participants consisted of 13 heart failure clinicians (four medical, nine nursing) working in inpatient and outpatient settings across 12 hospitals in 2023-2024. There were 39 documents compiled. Four key themes were identified: Centering the needs of whānau; cultural and clinical expertise of providers; models of care; and the resourcing context of each service.

Several barriers and facilitators were identified to close gaps in discharge planning for heart failure nationally, with more consistent approaches required to ensure Māori and Pacific patient and whānau needs are met during transition into community-level care. This calls for a cohesive national programme for sustainably implemented equity-focused discharge pathways.

1. Gustafson, P., Lambert, M., Bartholomew, K., Ratima, M., Aziz, Y.A., Kremer, L., et al. *Adapting an equity-focused implementation process framework with a focus on ethnic health inequities in the Aotearoa New Zealand context* (2024). International journal for equity in health. 23(1):15.
2. Damschroder, L.J., Reardon, C.M., Widerquist, M.A.O., Lowery, J. *The updated Consolidated Framework for Implementation Research based on user feedback* (2022). Implementation science 17(1):75.

H25: Normalising and Knowledge: How we can improve health equity through inclusive research and practice

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[1]Department of Medicine, University of Otago, Christchurch, NZ,

Rainbow health research, broadly, and transgender health research, specifically, are often separated from other areas of research, creating an dichotomy of 'specialist' interest against 'normal' research. Healthcare engagement is an essential part of addressing CVD and transgender populations are at particular risk of not receiving appropriate healthcare[1]. This is attributable to gaps within healthcare provision, medical education, and health research[1]. While health disparities are significant, there are emerging initiatives to address them.

The Trans Heart Health Project, funded by Pūtahi Manawa – Healthy Hearts Aotearoa, is an community-informed national research effort to understand the state of heart health in transgender populations in Aotearoa. Country-wide community-engagement events were held to explore community concerns on cardiovascular disease, as the leading cause of mortality across all demographics. The project is supported by a Community Advisory Group, other research groups, and advocates. Engagement provided insights into issues within the healthcare system, such as insufficient clinical knowledge, lack of trans-specific cardiovascular risks, as well as systemic factors impacting on 'lifestyle' decisions, such as physical exercise, reflecting wider trans-specific health equity issues.

This talk will outline how socially marginalised identities can be essential to include in health research and medical education, including cardiovascular health. No prior knowledge is needed: an overview of the landscape of transgender health outcomes and transgender health research will be provided. This talk will be relevant to health researchers, providers of medical education or clinical services, and community members.

1. Yee, A., Bentham, R., Byrne, J., Veale, J., Ker, A., Norris, M., Tan, K., Jones, H., Polkinghorne, T., Gonzalez, S., Withey-Rila, C., Wi-Hongi, A., Brown-Acton, P., Parker, G., Clunie, M., Kerekere, E., Fenaughty, J., Treharne, G., & Carroll, R. (2025). *Counting Ourselves: Findings from the 2022 Aotearoa New Zealand Trans and Non-binary Health Survey*. Transgender Health Research Lab, University of Waikato, Hamilton, NZ.

H26: Advancing Health Equity in Gestational Diabetes Care

Ponnampalam, A. P.[1,2], Ormond, S.[2], Haunga, M.[2]

[1] Department of Physiology, [2] Pūtahi Manawa-Healthy Hearts for Aotearoa New Zealand, Centre of Research Excellence, New Zealand.

GDM (Diabetes during pregnancy) is a common complication of pregnancy, with long-term effects on the cardio-metabolic health of both mother and child. The prevalence is disproportionately higher among Indigenous women compared to their European counterparts. While early detection and intervention can prevent/reduce adverse outcomes, significant inequities in GDM management exist between Māori, Pasifika and their counterparts in Aotearoa NZ. Understanding and addressing these health inequities is vital for achieving optimal heart health among marginalised communities.

This study critically evaluated the literature on health inequities in the diagnosis, screening, and follow-up of GDM, focusing on Indigenous populations globally, with a specific emphasis on Māori and Pasifika women in Aotearoa.

Qualitative data highlight Māori and Pasifika women face systemic barriers, including limited access to culturally appropriate care, a lack of trust in the healthcare system, and insufficient support for whānau. Similarly, other indigenous women expressed the desire for culturally tailored care within clinics and through community engagement as well as the presence of socioeconomic barriers influencing health outcomes. Culturally safe, co-designed interventions show promise in overcoming these barriers in addressing these health inequities.

This review underscores the importance of Indigenous-led solutions. Existing disparities reflect structural inequities, including barriers to culturally appropriate healthcare, and the lasting effects of assimilationist policies on Indigenous health systems. They highlight the impact of systemic racism and colonialism on health outcomes for Indigenous peoples. Addressing these issues requires targeted healthcare interventions and a commitment to truth-telling and explicitly implementing the principles of Te Tiriti, with the ultimate aim of decolonisation in health policy.

H27: Unmasking Female-Specific Cardiovascular Risk in Aotearoa

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Cardiovascular disease (CVD) in women is a significant, yet often underestimated, health issue in Aotearoa New Zealand. Historically underrepresented in clinical research, women experience unique, sex-specific risk factors related to pregnancy and reproductive biology that are not captured in current CVD risk screening. This presentation will provide an update from the Pūtahi Manawa-funded research program: Restoring the Balance: Heart health of Wahine, Fafine, Va'ine, Fifine & Women of Aotearoa.

Our research addresses critical gaps in understanding atherosclerotic CVD risk in women. We are analysing associations between menopausal status, sex hormones, and clinical outcomes in a cohort of 800 women following their first acute coronary syndrome. Additionally, we have linked primary care, obstetric, and cardiovascular outcome data for hundreds of thousands of New Zealand women to quantify the impact of pregnancy complications on future CVD.

A key preliminary finding is that younger women (aged <55) with a history of hypertensive disorders of pregnancy face a 68% greater risk of a future cardiovascular event, after accounting for traditional risk factors. Compounding this, we found that pregnancy-related complications are poorly documented in primary care, the primary setting for CVD risk assessment.

Identifying these high-risk women offers a crucial window for low-cost preventative care. Our ongoing work continues to explore how known ethnicity-related inequities in both pregnancy complications and healthcare access further compound this risk. These findings underscore the need to integrate female-specific factors into routine cardiovascular risk assessment to improve health equity and outcomes for all women in Aotearoa.

H28: Fiji Heart Study

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Peoples of Fiji represent approximately 2% of Aotearoa New Zealand's population but account for 20% of heart attacks occurring under the age of 40 - a disproportionate burden that follows a striking pattern of familial inheritance. The two major ethnic groups from Fiji have experienced distinct and prolonged environmental pressures that led to genetic bottlenecks, resulting in altered allele frequencies and long-standing population homogeneity. It is hypothesised that genetic traits once protective in contexts such as famine or introduced infectious diseases may now contribute to increased risk of coronary artery disease (CAD) in environments of nutritional abundance or ecological transition.

The Fiji Heart Study aims to identify monogenic variants associated with premature CAD by collecting detailed family histories and conducting whole genome sequencing (WGS) on 40 unrelated probands with severe early-onset CAD, comparing their genomes to haplotype-resolved WGS data from 200 healthy controls from extant populations. Given this is the first cardiovascular genetics study focused on Peoples of Fiji in Aotearoa, the study prioritised the co-design of a culturally and ethically safe oversight and the development of Na Vunimaqo/Am Pedh, a cultural framework of community-led values to guide governance and decision-making.

Now at the halfway point of the three-year study, this presentation shares progress on community engagement, infrastructure, and recruitment, alongside emerging insights into vascular disease characteristics within the cohort to date. We expect the WGS analyses to indicate the presence of unique variants in known CAD genes, and potentially novel genes or pathways implicated in CAD pathogenesis. These findings have the potential to advance genome-based equity through earlier screening, targeted interventions, and drug development, while also fostering community benefit, health promotion, and capability building to improve cardiovascular outcomes for future generations.

Summary of Abstracts for the Poster Session Template

No.	Title	Presenter	Institutions
P1	'Miniaturizing' Ca^{2+} Imaging for Higher-throughput Screening of RyR2 and RyR2 Variants	Jaxson Murphy-Wint erstein	University of Otago, Dunedin, New Zealand.
P2	Cellular inflammatory status of oxidised low-density lipoprotein on monocytes and atherosclerotic plaque	Martins Obinna Ogugofor	University of Canterbury, Christchurch, New Zealand.
P3	Investigating microRNA therapeutics in a 3D model of the ischaemic heart	Devin Tonkin	University of Otago, Dunedin, New Zealand.
P4	Investigating the effects of CK2 phosphorylation of RyR2 in cardiac arrhythmias	Alycia Kinns	University of Otago, Dunedin, New Zealand.
P5	Obstruction of the cardiac lymphatics alone is sufficient to replicate diastolic dysfunction and exercise intolerance	Dilsha Gimhani	University of Auckland, Auckland, New Zealand.
P6	Phosphorylation of Calsequestrin II alters spontaneous calcium leak	Elena Cruz	University of Otago, Dunedin, New Zealand.
P7	Sex-Specific Mechanisms of CaMKII Nitrosylation in Cardiac Function and Arrhythmia	Lauren Kruger	University of Otago, Dunedin, New Zealand.
P8	The implication of fibrosis in sex-based differences in diabetic cardiomyopathy	Georgia Walsh	University of Otago, Dunedin, New Zealand.
P9	The Sex-Specific Effect of CaMKII S-nitrosylation on Cardiac Ryanodine Receptor Organisation	Lily Burgin Penlington	University of Otago, Dunedin, New Zealand.
P10	Unravelling the Mechanisms of Atrial Arrhythmia	Raihaan Dalwai	University of Otago, Dunedin, New Zealand.
P11	Evaluating the Performance of Polygenic Risk Scores for Atrial Fibrillation in a High-Risk Population	Moizle Ocariza	University of Otago, Christchurch, New Zealand.
P12	Metabolite Sensitivity and Cross-Bridge Kinetics in Diabetic Human Cardiac Muscle: Insights from Experimental and Computational Analysis	Julia Musgrave	Auckland Bioengineering Institute

P13	Quantifying Sex-Based Differences in Apoptosis and Fibrosis in Nitric Oxide Sensitive Hearts	Marnie Hall	University of Otago, Dunedin, New Zealand.
P14	Evaluation of phenytoin-like compounds for anti-arrhythmic potential	Isabel Addison	University of Otago, Dunedin, New Zealand.
P15	Genome Sequencing in Cardiovascular Inherited Diseases – Developing Culturally Appropriate and Accessible Research Documentation	Te Whetu Aarahi Kerekere	University of Otago, Christchurch, New Zealand.
P16	Anti-Arrhythmic Potential of Phenytoin-Derived Compounds: Targeting RyR2-Mediated Calcium Leak	Anna Chang	University of Otago, Dunedin, New Zealand.
P17	Quantification of Sheer stress causing the formation of aggregated low density lipoprotein	Lucas Royds	University of Canterbury, Christchurch, New Zealand.
P18	Comparing the effect of various antidepressants on lipoprotien(a) uptake	Alexandria Rutherford-blyth	University of Otago, Dunedin, New Zealand.
P19	Investigating the Extra-Hepatic Uptake of Lipoprotein(a) and the Effect Of Citalopram Treatment	Cinthana Brabhaharan	University of Otago, Dunedin, New Zealand.
P20	Are genomic structural variants associated with cardiac biomarker concentration in Pacific People?	Simone Cree	University of Otago, Christchurch, New Zealand.
P21	Impact of Parental Obesogenic Diets on Cardiac Health in Adult Rat Offspring	Anna Ponnampalam	University of Auckland, Auckland, New Zealand.
P22	Serotonin-based antidepressants regulate lipoprotein(a) uptake in liver cells and mice	Katie Peppercorn	University of Otago, Dunedin, New Zealand.