CADENCE

Cardiovascular Disease National Collaborative Enterprise

NMRC Awards Ceremony and Research Symposium 2024

Singapore, Friday 24th May 2024

Prof Derek Hausenloy

National Clinical Translational Programs (NCTPs) - Consortium for Clinical Research and Innovation Singapore (CRIS)

__NCTPs__ were established to drive clinical application and commercialisation by combining basic research, clinical and translational strengths across Singapore and institutions in a __synergistic__ and __integrated__ manner.

Objectives of NCTPs

1. To develop robust **national programmes** with upfront agreement between multi-institutional parties on how resources and outputs will be brought together, shared and enhanced as critical enablers for Singapore to be **globally competitive** in research and translation;
2. To work through **multi-institutional pain-points** constraining ecosystem level research and translation, and put in place national level frameworks and upfront agreements to address them;
3. To identify strategic **use cases** that contribute to the development of peaks of research excellence in identified clinical domain areas of priority and support **value-based healthcare** and **cost-effective care delivery**; and
4. To focus on translating the programme's research into **preventive health** and **public health outcomes**.

Spearheading and developing core capabilities, infrastructure and scientific leadership for clinical research in Singapore

To become a global leader in the translation of cardiovascular research for better health and economic outcomes

Drive impactful health and economic outcomes for Singapore by catalysing innovation and enterprise endeavours

Cohesive and focused national-level cancer research and translational programme for value based treatment of cancers

Provide quality manufacturing of cellular-based therapeutics and develop cell therapy services to industry and patients

Coordinate a whole-of-government effort to implement Singapore's National Precision Medicine programme

CADENCE OVERVIEW

National Clinical Translational Programme (NCTP) established in Feb 2023 focused on CV diseases

Platform 1

NATIONAL DATA, IMAGING & TISSUE REPOSITORY

Integrate data & samples to empower discovery and validation for academia & industry

Platform 2

NATIONAL CV CLINCIAL TRIALS NETWORK

Streamline the design, implementation & conduct of multi-site clinical trials

Platform 3

AI & DIGITAL HUMAN HEALTH & POTENTIAL

AI-enabled Digital Health Platform for primary prevention of CVD

BIDU

BUSINESS INTELLIGENCE & DEVELOPMENT

Research community outreach & Industry engagement

CADENCE
Cardiovascular Disease National Collaborative Enterprise

VISION - A national-level cardiovascular research programme that synergises basic, translational and clinical research strengths across Singapore for better health and economic outcomes.

MISSION - To drive cardiovascular research forward through collaboration and innovative approaches, aiming to improve patient outcomes globally

CADENCE TEAM

Prof Derek Hausenloy
Executive Director

A/Prof Mark Chan
Co-Director

Prof Mark Richards
International Advisor

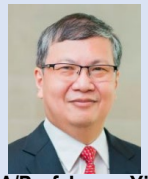
Strategic Planning & Development Unit (SPDU)

Dr Tan Sock Hwee
Assistant Director

Ms Nway Nway
Assistant Manager

Platform 1 DATA, IMAGING & TISSUE REPOSITORY

A/Prof Yeo Khung Keong
Lead



A/Prof James Yip
Co-Lead

A/Prof Sebastian Maurer-Stroh
Co-Lead

Dr. Ho Hee Hwa
Co-Lead

Use Case 1
Clinical and cost-effectiveness of treatments for heart failure

Prof Nicolas Graves
Lead

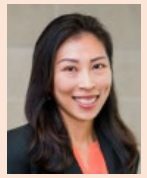
Dr Loh Seet Yoong
Co-Lead

A/Prof David Sim
Co-Lead

Dr Raymond Wong
Co-Lead

Ms Danielle Tan
Project Manager

Platform 2 EARLY PHASE MECHANISTIC CLINICAL TRIALS



Dr Lim Shir Lynn
Lead

A/Prof David Sim
Co-Lead

Dr Cliff Li
Co-Lead

Use Case 2
AI-enabled Imaging Solution to Detect Cancer Therapy-Related Cardiac Dysfunction (CTRCD)

Dr Sia Ching Hui
Lead

Dr Jasper Trompe
Co-Lead

Dr Huang Weiting
Co-Lead

Dr Tong Jieli
Co-Lead

Ms Sik Yin Tan
Project Manager

Platform 3 ARTIFICIAL INTELLIGENCE, DIGITAL HEALTH & HUMAN POTENTIAL

A/Prof Andy Ho
Joint-Lead

A/Prof Andy Khong
Joint-Lead

A/Prof Doreen Tan
Co-Lead

Use Case 3
Digital-enabled Solution for Primary Prevention of CVD in hyperchol patients

A/Prof Doreen Tan
Lead

Dr Chua Ying Xian
Co-Lead

Dr Lim Ziliang
Co-Lead

Dr Iva Bojic
Project Manager

Business Intelligence & Development Unit (BIDU)

Dr Sit Soon Tuck
Lead

Janet Ng
Manager

P1 NATIONAL DATA, IMAGING & TISSUE REPOSITORY

A/Prof Yeo Khung Keong
Lead

A/Prof James Yip
Co-Lead

Dr. Ho Hee Hwa
Co-Lead

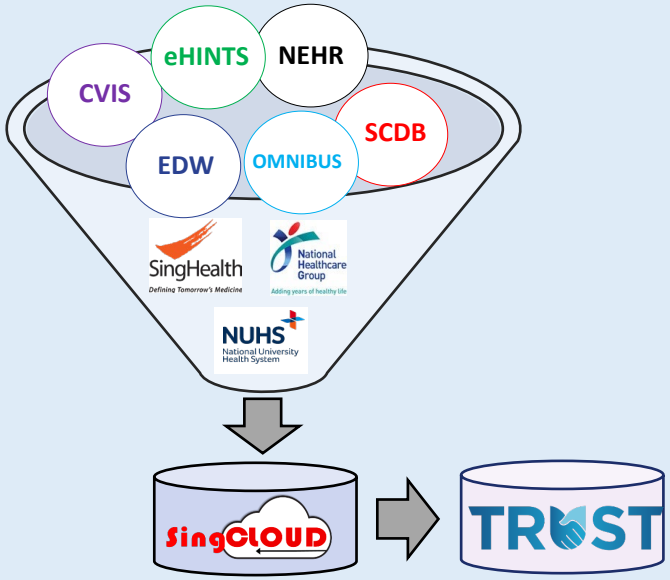
A/Prof Sebastian Maurer-Stroh
Co-Lead

National CVD Patient Registry

Established **SingCLOUD 2.0** as a National CV patient data registry.

Linked SingCLOUD 2.0 to **MOH TRUST.**

Plan for **SingCLOUD 3.0** with near real-time updates for registry-based RCTs.



National CV Data/Imaging Repos

Established National CV data, imaging and tissue directory on **A*STAR BIOMED DAR**.

Hosting clinical data/CT/echo images from **SingHEART** healthy cohort investigating the genetic, metabolic and molecular factors associated with the development of CVD.

Will host clinical/digital data/echo images from CADENCE **Use Cases 2 and 3.**

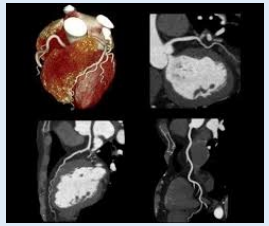
Developing a **National Master Collaboration Framework** to facilitate sharing of patient data, CV images and tissue with Academics and Industry.

National CV Directory

Established a **National CV Directory** of pre-clinical and clinical capabilities to support target discovery and validation and clinical studies

To be hosted on new **Singapore's National Clinical Trials Portal** (CTSG) from July 2024.

CV Biospecimens



CV Images

Clinical Data

USE CASE 1

Clinical and Cost-Effectiveness of Treatments for Patients with Heart Failure

Prof Nicolas Graves
Lead

Dr Loh Seet Yoong
Co-Lead

A/Prof David Sim
Co-Lead

Dr Raymond Wong
Co-Lead

New CVD Health Services Research (HSR) unit

CADENCE has set up a new **CVD HSR unit** and have recruited two health economists from Australia, A/Prof Sanjeewa Kularatna and Dr Sameera Senanayake, one research associate and two PhD students.

The new CVS HSR unit is supporting CADENCE **Use Cases 1-3** and is providing support to other researchers.

Working with and **SCRI Health Economics and Outcomes Research** (HEOR) and **Dr Kelvin Bryan Tan** (Chief Health Economist Office at the MOH).

Clinical and Cost Effectiveness of HF Therapies

To evaluate the clinical and cost-effectiveness of different pharmacological treatment regimens for heart failure.

1. Health services costs of heart failure in Singapore
2. Trends and determinants of drug prescription patterns in Singaporean patients HF.
3. Estimating the effectiveness measures needed for the economic evaluation: triple therapy vs quadruple therapy; and
4. Economic evaluation.

Future plan to establish national heart failure drug treatment protocols and provide guidance to **Agency for Care Effectiveness (ACE)** on heart failure therapies.

AI4HC

Novartis Foundation
Swiss foundation

AI4HealthyCities in Singapore

20% of our health is shaped by the healthcare we access

80% are driven by the conditions in which we are born, grow up and age

SingHealth
Defining Tomorrow's Medicine

A/Prof Yeo Khung Keong

SingHealth
Defining Tomorrow's Medicine

A/Prof Low Lian Leng

NUHS
National University Health System

A/Prof Lim Zheng Jye

DukeNUS
Medical School

Prof Marcus Ong

AI4HC Singapore

Global initiative to identify the key **socioeconomic determinants** of CV health and design an intervention to address the health inequality.

Phase 1 – Determine the key socioecon and behavioural determinants of CV health.
Phase 2 - Design and pilot the intervention in the Queenstown and Bedok/Marine Parade Health Districts and upscale as part of Healthier SG

Healthier SG

AI4HC Singapore

Two **CADENCE-AI4HC workshops**, and presentations at Novartis Foundation Board meeting, and participated in AI4HC global expert panel meetings.

USE CASE

PREPARE

COVID-19 and CV outcomes

Prof David Lye

Prof Kevin Tan

A/Prof Yeo Khung Keong

Dr Chia Yew Woon

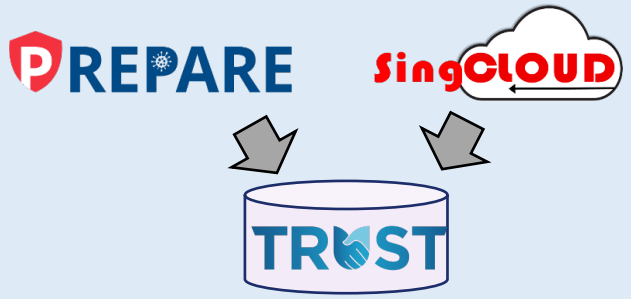
COVID-19 and CV Outcomes

To investigate the interaction between COVID-19 and CV outcomes

1. Analysis of the COVID outcomes, vaccine effectiveness of Post-AMI, Heart Failure patients.

2. Analysis of AMI + HF outcomes during COVID.

3. Impact of Long COVID on CV outcomes.



NATIONAL CV CLINICAL TRIALS NETWORK

P2

Dr Lim Shir Lynn
Lead

A/Prof David Sim
Co-Lead

Dr Cliff Li
Co-Lead

National CV network

Integrated clinical trials units at NUHCS, NHCS, and TTSH into a **National CV Clinical Trials Network** to facilitate the set-up and execution of new multi-site early phase mechanistic **IIT** and **IST** studies.

Future plan to expand the National Network to the other 4 major hospitals (**KTPH, NTFGH, CGH, and SKH**) and polyclinics.

Speeding up trial set-up

Simplified and harmonised the costing process across NUHCS, NHCS and TTSH for undertaking multi-site IITs and ISTs.

CADENCE is currently supporting 3 to 4 CRCs in each of **NHCS, NUHCS and TTSH** as well as 2 CRCs in **NUP** and 1 CRC in **NHGP**.

Expanding CRC coverage to **KTPH, NTFGH, CGH, and SKH.**

Synergising with SCRI

Collaborating with **SCRI** and MOHH Legal to develop a **National Clinical Trials Agreement** to streamline the set-up of multi-site **IITs**.

Use the new **National Clinical Trials Framework Agreement** for **ISTs** developed by SCRI and SAPI.

Collaborating with **SCRI** on a national project to harmonize budgets within clusters to improve the costing process for IITs and ISTs.

SINGAPORE CLINICAL RESEARCH INSTITUTE

USE CASE 2

AI-enabled Imaging Solution to Detect Cancer Therapy-Related Cardiac Dysfunction

Dr Sia Ching Hui
Lead

Dr Jasper Trompe
Co-Lead

Dr Huang Weiting
Co-*Lead*

Dr Tong Jieli
Co-*Lead*

AI-enabled echo solution

Investigate AI-enabled echo imaging solution for detecting cancer-therapy related cardiac dysfunction.

AI used to train CRCs to undertake echo scan and analyse echo scan.

Potential to **decrease** echo waiting times and empower chemotherapy nurses to perform AI-echo screening at cancer centres.

US2.AI

Clinical study

Multi-site clinical study of 300 breast cancer and lymphoma patients (recruited NHCS, NUHCS and TTSH).

Aims of study

1. Demonstrate **accuracy** of AI-echo compared to standard cart-based echo.
2. Investigate whether performing more frequent AI-echo scans can allow **earlier detection** of CTRCD.
3. Show that AI-echo is **cost effective** (Use Case 1 HSR unit).

UNRAVEL

PRECISE
Precision Health Research Singapore

UNdeRstAnding novel Variants in acutE myocardiaL infarction in young adults: UNRAVEL

Dr Nicholas Chew

NUHS National University Health System

Dr Jonathan Yap

SingHealth
Defining Tomorrow's Medicine

Dr Deborah Lee

National Healthcare Group
Adding years of healthy life

New gene variants for AMI

To discover novel gene variants associated with increased risk of AMI in Southeast Asian patients

Aim to recruit and whole genome sequence 5000 relatively young AMI patients and compare to 5000 heathy controls from SG100K.

Identification of new gene variants predisposing to AMI may result in the development of novel treatments to improve outcomes.

SG100K

MUSIC-HFrEF

Modulation of SERCA2a of Intra-myocytic Calcium trafficking in Heart Failure with Reduced Ejection Fraction (MUSIC-HFrEF)

A/Prof David Sim

A/Prof Lin Wei Qin

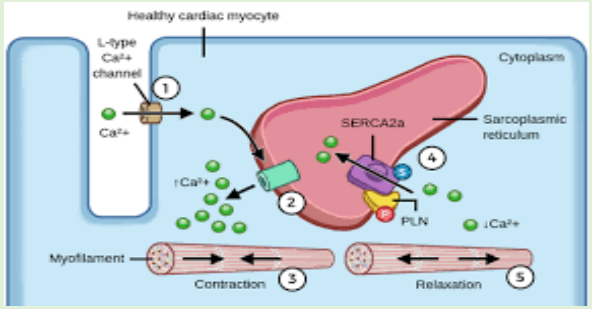
A/Prof Violet Hoon

Gene therapy for heart failure

To investigate whether a novel SERCA gene therapy can improving cardiac function in patients with heart failure.

First Asian gene therapy trial for heart failure that will help put the infrastructure in place for Singapore to undertake future cell and gene therapy trials.

Singapore is the only site outside USA recruiting for this study.



MOU signed

Collaboration with Boston SME, **Sardocor** (**MOU signed**).

P3 AI & DIGITAL HUMAN HEALTH & POTENTIAL

A/Prof Andy Ho
Joint-Lead

A/Prof Andy Khong
Joint-Lead

A/Prof Doreen Tan
Co-Lead

Primary prevention of CVD

To establish a Digital Health CVD Platform for delivering lifestyle and pharmacological behavioural interventions to address modifiable CVD risk factors for the primary prevention of CVD.

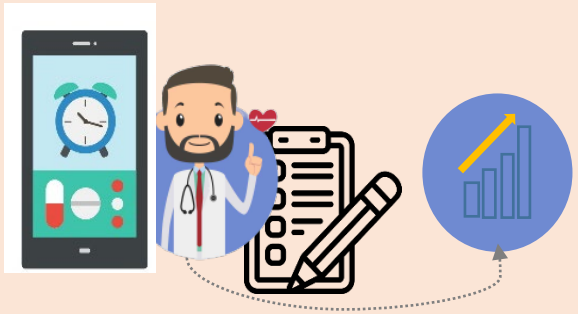
Develop a **human-coach AI digitial app** for improving medication adherence in patients with hyperlipidaemia.

dpha
digital personal health assistant
A project by CADENCE

The app can be adapted to improve medication adherence in other conditions (diabetes, hypertension) and to address other CV risk factors (obesity and sedentary behaviour).

Digital Health CVD platform

- Carefully curated localized educational content, comprising bite-sized animations and videos.
- A live coaching feature that facilitates communication between health coaches and patients.
- Learning analytics to provide personalized insights and recommendations.
- AI capabilities, such as Natural Language Processing (NLP) to analyze user behaviors like engagement with educational content or adherence to health goals. This analysis enhances understanding of user needs and allows for optimization of app features accordingly.



P3

AI & DIGITAL HUMAN HEALTH & POTENTIAL

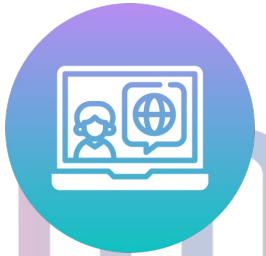
1 real-time user analytics presented to health coaches

2 smart goal setting

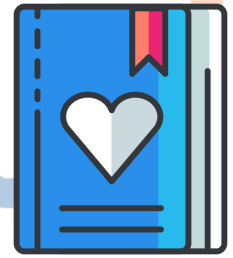
3 motivational interviewing

4 weekly text-based smart goal review

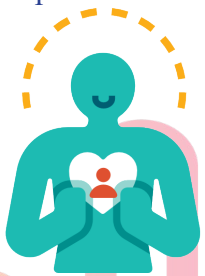
5 monthly live virtual health coaching intervention and goal renewal



6 health gratitude reflective journal



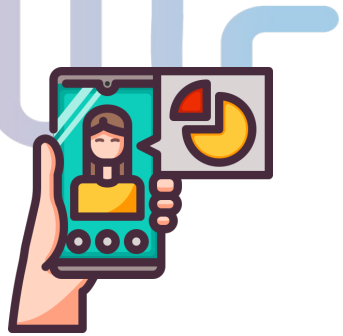
7 mindful self-care practices



8 precise health coaching and psychosocial intervention

9 health coach support is augmented by 24/7 access to intelligent chatbot using Natural Language Models (NLP)

10 personalized learning supported by learning analytics with AI capabilities



Usage Data Analytics

Human-AI Symbiosis

Natural Language Model

Usage Data Analytics

Human-AI Symbiosis

Natural Language Model

dpha digital personal health assistant
A project by CADENCE

USE CASE 3

Digital-enabled solution for primary prevention of CVD in patients with hyperlipidaemia

NUS National University of Singapore

A/Prof Doreen Tan
Lead

National University Polyclinics

Dr Chua Ying Xian
Co-Lead

National Healthcare Group POLYCLINICS

Dr Lim Ziliang
Co-Lead

Digital-enabled solution

50-60% of patients non-adherent to statin medication.

Multi-site randomized clinical trial of 370 patients with hyperlipidaemia (NUP and NHGP).

Aim of study

Determine whether D-PHA digital app can improve medication adherence of chol-lowering medication and decreased LDL-chol.

d-pha. digital personal health assistant
A project by CADENCE

CADENCE
Cardiovascular Disease National Collaborative Enterprise

SUMMARY AND CONCLUSIONS

- CADENCE has set up **3 Joint Platforms** (data, clinical trials and digital health), a **CV health service research unit**, and a **Business Intelligence Development Unit**.
- Our 3 CADENCE Use Cases focused on evaluating the cost efficacy of HF therapies, AI-and digital enabled imaging technologies are ongoing.
- Several **new Use Cases** in collaboration with non-profit organisations (Novartis Foundation), industry (Us2.ai, Sardocor) and Academic (PRECISE and PREPARE).
- We are working through **multi-institutional pain-points** constraining ecosystem level research and translation (data sharing and set-up of multi-site clinical trials), and are preparing in **national level frameworks and upfront agreements** to address them.
- CADENCE NCTP has allowed us to bring together CV researchers across hospital clusters, A*STAR and universities to integrate and synergise efforts to improve CV health and propel Singapore to be a regional and global leader in CV innovation and research.

CADENCE
Cardiovascular Disease National Collaborative Enterprise

Thank you!

contact@cadence.cris.sg

www.cadence-cvd.sg