



THE UNIVERSITY OF
SYDNEY

 NHMRC
Clinical Trials Centre

Thank you to all current and past staff and collaborators who have contributed to the success and achievements of the CTC and its partners over the past 30 years.

Celebrating
30
years

Of Improving
Global Health
Outcomes

Contents

Introduction 5

30 years of improving global health outcomes 6-7

Our global partner organisations 8-9

Timeline - our 30 year journey 10-11

1988-98: First national trial centre in Australia 12-13

1998-2008: Advancing trials and research 18-19

2008-2018: Responding to changing health needs 24-25

2018 highlights 30-31

Examples of breakthrough research 32-33

Research leaders 34-35

Long serving staff 36-37

Our key collaborators 38-41

The Fun Times 42-47

Introduction



John Simes
Director

When we set up the Clinical Trials Centre, we had no idea how large it would become and how much of an impact our research would have on global health outcomes. It has been a humbling experience. In the last 30 years, the trials we have undertaken with our collaborators have made real differences to patients' lives worldwide. Findings have helped to reduce mortality and illness and improve the quality of life among those with or at risk of cancer, cardiovascular disease and diabetes, as well as help improve the care of premature babies. Sometimes the gains have been by learning that a treatment is not effective. They are the quiet wins that may save patients stress and time from unnecessary therapy, not to mention potential resource savings for the healthcare sector.

With 30 strong years under our belt we are looking ahead to the next 30 years, which will see many challenges and opportunities in the clinical trials environment. Australians are living longer and health conditions are improving. Future clinical trials will need to target new questions that have meaningful impact on patients and healthcare budgets. This will include large international trials assessing moderate but important

health gains, trials that make the best use of digital technology, studies that link trials to patient molecular profiles to provide precision medicine, optimising health care decisions for individuals, and better integration between our work and the healthcare system so more clinicians and patients can benefit quickly from our efforts. We have teams working on each of these challenges, while we continue to evaluate the latest potential advancements in healthcare.

I am proud to say that after 30 years we are continuing to make important progress with the same mission: to improve clinical practice and patients' lives. Clinical trials inform best practice, and best practice results in better health outcomes. While the clinical trial environment in 30 years may be much different than today, our goals and the potential benefits from research will be much the same.

30 years of
improving
global health
outcomes



200
Current
staff



\$409m
Total funding
received



4,000
Peer reviewed
publications



+16,000
Trials registered
in Australia and
New Zealand



+1,000
Students graduated
(including postgraduate,
masters and PhDs)



+80,000
Number of study
participants



+1,000
National &
international
collaborators



+200
Trials
conducted



Our global partner organisations

Europe

Cancer Trials Ireland
Cholesterol Treatment Trialists' Collaboration (CTTC)
Dutch Gynaecologic Oncology Group (DGOG)
European Organisation for Research and Treatment of Cancer (EORTC)
European Study Group for Pancreatic Cancer (ESPAC)
Groupe Coopérateur Multidisciplinaire en Oncologie (GERCOR)
International Breast Cancer Study Group (IBCSG)
Imperial College London
Medical Research Council (MRC)
National Perinatal Epidemiology Unit (NPEU), University of Oxford
National Surgical Adjuvant Breast and Bowel Project (NSABP)
Oxford Clinical Trials Office, Oxford University (OCTO)
Pan-European Trials in Alimentary Tract Cancer (PETACC)
Primary Coronary Angioplasty versus Thrombolysis (PCAT)
Scottish Gynaecologic Cancer Trials Group (SGCTG)
University of Oslo

Asia

Aga Khan University
Chinese University of Hong Kong
National Cancer Centre Singapore
Shanghai Diabetes Cohort Study Group
University of Hong Kong

Australia and New Zealand region

Australasian Gastro-Intestinal Trials Group (AGITG)
Australasian Lung Cancer Trials Group (ALTG)
Australasian Society of Thrombosis and Haemostasis (ASTH)
Australia New Zealand Gynaecological Oncology Group (ANZGOG)
Australian and New Zealand Urogenital and Prostate Clinical Trials Group (ANZUP)
Australian New Zealand Clinical Trials Registry (ANZCTR)
Biostatistics Collaboration of Australia (BCA)
Breast Cancer Trials Group (BCTG)
Centre for Biostatistics and Clinical Trials (BaCT)
Cooperative Trials Group for Neuro-Oncology (COGNO)
Early Prevention of Obesity in Children (EPOCH) collaboration
Heart Foundation
Long-term Intervention with Pravastatin in Ischaemic Disease study group (LIPID)
Medical Services Advisory Committee (Department of Health and Ageing)
NSW Cooperative Oncology Group (NSWOG)
Peter MacCallum Cancer Centre
Primary Care Cancer Trials Group (PC4)
Psycho-Oncology Cooperative Research Group (POCOG)
Royal Australasian College of Surgeons (RACS)
Sydney Catalyst
The Menzies School of Health Research (Charles Darwin University)
Trans-Tasman Radiation Oncology Group (TROG)

Global

Cancer Clinical Trials Unit Scotland (CACTUS)
Cochrane Collaboration
Fenofibrate and Event-Lowering in Diabetes study group (FIELD)
International Breast Cancer Study Group (IBCSG)
International Neonatal Immunotherapy Study group (INIS)
Meta-analysis collaboration (AMICABLE)
Meta-Analysis of Preterm Patients on Inhaled Nitric Oxide collaboration (MAPPiNO)
Neonatal Oxygenation Prospective Meta-analysis (NeOProM) collaboration
Perinatal Antiplatelet Review of International Studies (PARIS) collaboration
Prenatal repeat corticosteroid international individual-patient-data study group (PRECISE)
Prevention of Ventilator Induced Lung Injury collaborative study group (PreVILIG)
Prospective Pravastatin Pooling project (PPP)
Virtual Coordinating Center for Global Collaborative Cardiovascular Research (VIGOUR) group

Americas

Cochrane Prospective Meta-Analysis Methods Group
Eastern Cooperative Oncology Group (ECOG)
Gynecologic Cancer Intergroup (GCIg)
Gynecologic Oncology Group (GOG)
Canadian Cancer Trials Group (CCTG)
National Surgical Adjuvant Breast and Bowel Project (NSABP)
Organizacion de Investigaciones Clinicas SA (ECLA)
Radiation Therapy Oncology Group (RTOG)
Star Child Health
Thrombolysis In Myocardial Infraction (TIMI) Study Group

Our 30 year journey 1988-2018

THE CTC WAS BORN OUT OF A NEED TO PROVIDE EVIDENCE TO HELP CLINICIANS PROVIDE THE BEST CARE AND IMPROVE THE LIVES OF PATIENTS. OVER THE PAST 30 YEARS WE HAVE LIVED UP TO THIS MISSION, IN AUSTRALIA AND AROUND THE WORLD.

1988



1998



2000

2003

2005

2008



2012

2016

2018



\$250K

INITIAL FUNDING
THE CTC BEGINS WITH TWO STAFF, JOHN AND HIS ASSISTANT.

A BIG YEAR
IN THE FIRST YEAR THE CTC RECRUITS 2,000 PATIENTS FOR TRIALS.

+40,000

HEART ATTACKS
CTC AND COLLABORATORS INVESTIGATE THE BEST LIFE-SAVING TREATMENTS FOR PATIENTS EXPERIENCING A HEART ATTACK WITH OVER 40,000 TRIAL PARTICIPANTS.

ANZ
BY 1991, THE CTC IS RUNNING 15 MULTICENTRE TRIALS IN AUSTRALIA AND NEW ZEALAND INVOLVING 600 INVESTIGATORS.

9,000

LIPID
COMPLETED IN 1997, THE LIPID TRIAL IS THE BIGGEST CHOLESTEROL-LOWERING STUDY IN THE WORLD, WITH OVER 9,000 PATIENTS.

IMPROVING DESIGN
THE CTC ADDS EXPERTISE IN RESEARCH ON THE DESIGN, CONDUCT, MANAGEMENT AND ANALYSIS OF CLINICAL TRIALS.

10,000

FIELD STUDY
10,000 PATIENTS FROM AUSTRALIA AND NEW ZEALAND PARTICIPATE IN A STUDY THAT FINDS A DRUG CAN HELP DIABETES SUFFERERS REDUCE DISABILITY RISKS.

CANCER COVERED
CTC AND ITS COLLABORATORS CONDUCT 30 TRIALS ON SOME OF THE MOST COMMON CANCERS.

664

INTERNATIONAL SYMPOSIUM
CTC HOSTS THE FIRST INTERNATIONAL CLINICAL TRIALS SYMPOSIUM IN SYDNEY, WITH 664 ATTENDING.

BREAST CANCER
AN AUSTRALIAN FIRST, THE SNAC TRIAL DISCOVERS WOMEN WITH BREAST CANCER SHOULD CHOOSE BIOPSY-BASED SURGICAL MANAGEMENT FOR BETTER QUALITY OF LIFE.

\$1.5M

NATIONAL REGISTRY
CTC HELPS ESTABLISH A NATIONAL REGISTRY FOR TRIALS WITH \$1.5M IN FUNDING FROM THE NHMRC.

MEDICARE
MEMBERS OF CTC REVIEW EXISTING LITERATURE AROUND DIAGNOSTIC TESTS FOR THE GOVERNMENT SETTING GUIDELINES FOR MEDICARE FUNDING.

COGNO
IN 2007, THE COOPERATIVE TRIALS GROUP FOR NEURO-ONCOLOGY IS SET UP AND HOUSED AT THE CTC.

75%

CANCER
WORK WITH SEVEN COLLABORATOR GROUPS SEES CTC RESEARCH COVER 75% OF CANCER DISEASE IN AUSTRALIA.

SYDNEY CATALYST
THE CTC HELPS ESTABLISH A RESEARCH CENTRE INVOLVING RESEARCHERS AND CLINICIANS FROM ACROSS NSW THAT AIMS TO RAPIDLY TRANSLATE DISCOVERIES INTO PRACTICE.

27,000

CARDIOVASCULAR
TO HELP EASE THE BURDEN OF CARDIOVASCULAR DISEASE, THE CTC HELPS UNDERTAKE NINE TRIALS INVOLVING 27,000 PATIENTS.

PREMATURE BABIES
HIGH OXYGENATION LEVELS ARE FOUND TO INCREASE CHANCE OF SURVIVAL IN PREMATURE BABIES, ACCORDING TO A CTC-LED STUDY (BOOST II).

1,000

GENETICS
IN PARTNERSHIP WITH THE GARVAN INSTITUTE, THE CTC INVESTIGATES ASSIGNING 1,000 PATIENTS TO TREATMENTS BASED ON THEIR GENES INSTEAD OF THEIR SYMPTOMS (MOST TRIAL).

RECTAL CANCER
A CTC AND AGITG STUDY (A LA CART) SUGGESTS OPEN SURGERY MAY BE BETTER FOR PATIENTS WITH RECTAL CANCER.

SKIN CANCER
IN PARTNERSHIP WITH THE MELANOMA INSTITUTE, THE CTC SHOWS SURVEILLANCE CLINICS WOULD HELP CUT COSTS AND IMPROVE OUTCOMES FOR AT-RISK SKIN CANCER PATIENTS.

60sec

UMBILICAL CORD
A CTC TRIAL THAT SHOWS CLAMPING THE UMBILICAL CORD 60 SECONDS LATER CAN IMPROVE SURVIVAL RATES AMONG PREMATURE BABIES WINS THE ACTA TRIAL OF THE YEAR AWARD.

CANNABIS
CAN MEDICINAL CANNABIS HELP CHEMO USERS WITH NAUSEA? CTC COMPLETES THE FIRST STAGE OF THE CANNABISCTC TRIAL.

First national trial centre in Australia 1988-1998

During the mid 1980s, the medical community was concerned about the lack of independent clinical trials in Australia. Clinical trials were needed to provide Australian medical practitioners with sound and relevant local information as a basis for clinical decisions. Trials also help medical practitioners gain first hand experience of new treatments, and they assist researchers in exploring new treatments for disease.

CTC's objectives in 1988:

- Coordinate large multicentre clinical trials across Australia
- Consult to smaller trials on design and analysis
- Provide an educational resource to help clinical investigators run their own trials
- Assist practitioners evaluate trial results for clinical decision making
- Initiate academic courses
- Develop and promote research in clinical trials methodology and research
- Focus on cancer and cardiovascular trials

After one year

The CTC has 17 staff including biostatisticians, computer systems experts, trial coordinators, research fellows and a deputy director. The CTC is conducting and collaborating large trials in cardiovascular disease and cancer, including LIPID and acute coronary treatments, with over 2,000 patients recruited. Funding providers include the National Heart Foundation, ANZ Breast Cancer Trials Group, Boehringer Ingelheim and Pharmatalia.

'It is important for Australia to conduct its own multi-centre trials rather than relying only on the results from overseas studies because the conditions in which therapies are given, and the diseases, are not always identical.' John Simes.

500 INVESTIGATORS FROM 90 HOSPITALS

17 STAFF



2,000 PATIENTS RECRUITED

8 TRIAL PROJECTS

\$400,000 FUNDING (FROM NHMRC)



1988 newspaper front cover

First home, the Edward Building, University of Sydney



1991

During the first three years, the CTC undertakes the coordination and data management of 15 multicentre cardiovascular and cancer trials, involving 600 investigators and 12,000 patients. The studies have the power to detect differences in mortality and morbidity for relatively common diseases like heart attacks and breast cancer.

Aus/NZ Links

- Australian and New Zealand Breast Cancer Trials Group (ANZ BCTG)
- The ANZ Germ Cell Trials Group (ANZGCTC)
- Australasian Gastro Intestinal Trials Group (AGITG)

International Links

- European Organisation For Research and Treatment Of Cancer
- The Medical Research Council (UK)
- Eastern Cooperative Oncology Group (US)

Education

To promote clinical trials research, the CTC begins running two short courses for data managers. During 1991, it also holds its first course in clinical trials for clinicians, a two day course. CTC staff are also involved in postgraduate and academic teaching in clinical trials, clinical epidemiology and biostatistics, as they are today.

Randomisation service for external researchers

In 1991, CTC becomes the statistical and randomisation centre for the Australian and New Zealand Breast Cancer Trials Group (ANZ BCTG). It randomly allocates treatments to screened patients. Two years later, the CTC pioneers dynamic balanced randomisation. And in 1998, CTC establishes a central randomisation service where clinicians can telephone one number in the randomisation centre to register patients for any external trial.

CTC helps form the Australasian Gastro-Intestinal Trials Group in 1991

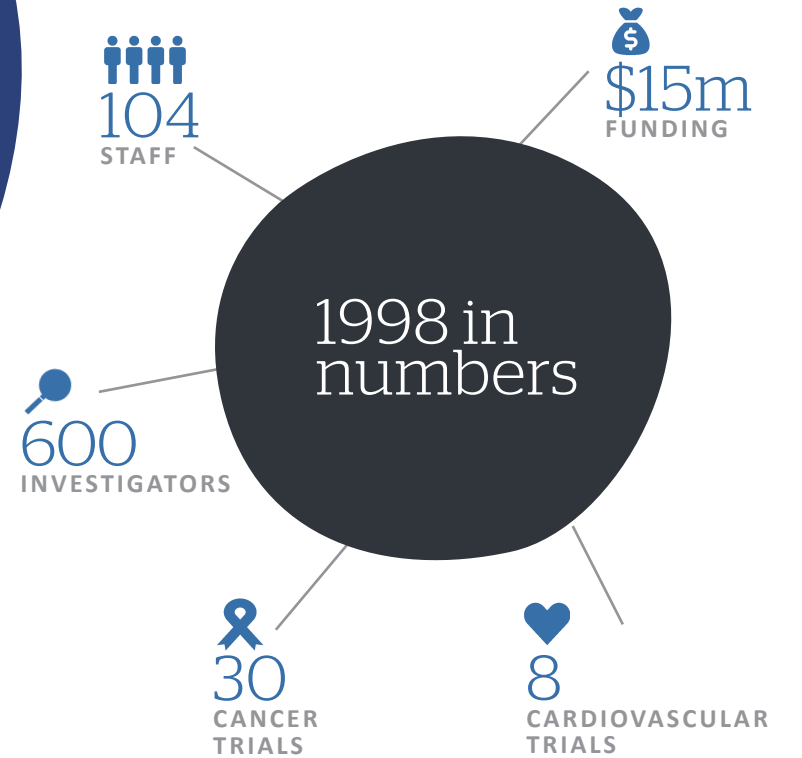


CTC moves into the Mallet Street building, University of Sydney, in 1996.

1988-1998

Treating heart attack patients

In the first 10 years, the CTC and collaborators run a number of trials around how best to treat patients experiencing acute coronary syndrome (a heart attack). Treatments such as opening coronary arteries by inserting a catheter and thrombolytic therapy are investigated with the end aim of saving lives. Over 100,000 patients participate in the GUSTO, PARAGON, SYMPHONY and HERO trials. This valuable work leads to the creation of the VIGOUR group in 1999.



Setting the standard with Cochrane

The CTC and the National Breast Cancer Centre join forces in 1996 to create the Cochrane Breast Cancer Group, the first Cochrane entity in the Southern Hemisphere. Cochrane is a global charity that gathers the best evidence from research to help healthcare workers in 130 countries make informed treatment decisions. Hosted by the CTC, the Cochrane Breast Cancer Group undertakes systematic reviews of all healthcare interventions in breast cancer.

- The CTC becomes the founder and host of the Cochrane Prospective Meta-analysis Methods Group in 1998

Improving trial design

During this period of expansion, the CTC quickly branches out into research on the design, conduct, management and analysis of clinical trials (trials methodology). The CTC also develops its role in advising and consulting on clinical trials research.

World's largest cholesterol-lowering study completed (LIPID)

The LIPID trial (Long term Intervention with Pravastatin in Ischaemic Disease) is completed in 1997 and results are published in *The New England Journal of Medicine* in 1998. This is the biggest cholesterol-lowering study to be completed in the world and the largest randomised trial undertaken in Australia and New Zealand at the time. The trial investigates the effect of lowering cholesterol levels over six years in 9,014 patients with coronary heart disease. The study confirms that pravastatin can help patients with a history of coronary heart disease to avoid another potentially fatal event.

COMPELLING OUTCOMES FROM LIPID

- Major impact on health and on treatment guidelines in Australia and elsewhere
- Continues to this day to prevent premature deaths in Australia and worldwide
- Cost effectiveness analyses shows the treatment and the trial are both economically beneficial
- Long term follow up demonstrates the therapy is safe



Advancing trials and research 1998-2008

The number and breadth of trials at CTC increases, including important initiatives in cancer and neonatal research, improving trial design and outcomes (trials methodology) and reviewing existing data to undertake cost effective and valuable trials.

Educating doctors on cancer treatment options

In this period, over 30 trials are conducted on some of the most common cancers, including breast cancer, gastrointestinal cancer, germ cell cancer and melanoma. Some of the trials assess new chemotherapy drugs while others compare existing treatments to determine which is best for the patient. These trials provide Australian medical practitioners with important information about cancer treatments and the success of tested therapies.

Regular seminars are hosted by the CTC for researchers and clinicians.



Quality of life studies are central to CTC's trials. CTC-led studies assess the tradeoffs of survival versus quality of life, as well as how quality of life is defined in relation to health.

2000
Australia New Zealand
Gynaecological Oncology
Group established




World class diabetes trial launched (FIELD)

The Fenofibrate Intervention and Event Lowering in Diabetes (FIELD) study is the world's largest study into the prevention of heart disease and stroke in patients with diabetes at the time.

- From 1997 to 2007, over 10,000 patients from Australia, New Zealand and Finland take part
- CTC's Tony Keech chairs the global study
- Fenofibrate is found to reduce the risk of amputation, threatened vision and heart attacks in patients with Type 2 diabetes
- Fenofibrate is approved by the Therapeutic Goods Administration (Australia) and in the EU and US
- The main results of the FIELD study are presented and published in *The Lancet* in 2005.

Founding member of international heart disease group (VIGOUR)

As a founding member of the international VIGOUR group (The Virtual Coordinating Center for Global Collaborative Cardiovascular Research), the CTC continues investigating novel treatments and care for patients with heart disease and issues relating to the control of heart disease in 1999. The group studies a range of interventions in patients with acute coronary syndromes and issues, such as pathophysiology, medical economics, quality of life, delivery of health care, and design of clinical trials.

VIGOUR COLLABORATORS

Latin American Coordinating Centre, Argentina
NHMRC Clinical Trials Centre, Australia
Flinders Clinical Trial Pharmacy, Australia
Leuven Coordinating Centre, Belgium
Canadian Coordinating Centre, Canada
Green Lane Hospital, New Zealand
Nottingham Clinical Trial Data Centre, UK
Duke Clinical Research Institute, US
Cleveland Clinic Foundation, US

International Clinical Trials Symposium

The CTC hosts the inaugural International Clinical Trials Symposium in September 1999 at the Sydney Hilton Hotel. The symposium provides a forum for clinical investigators, biostatisticians, and other healthcare researchers to share the latest developments in research and new ideas for future collaborations.

The 1999 Symposium is such a success, the CTC hosts it again in 2002 and 2007. The Australian Clinical Trials Alliance, which the CTC helps establish, takes over hosting in 2015. Tony Keech convenes ACTA's 2015 symposium and will convene the 2019 International Symposium.



1999 SYMPOSIUM

Location: Sydney Hilton Hotel
Attendees: 664
Highlights: CTC chaired or co-chaired nine of the 20 sessions and presented 15 papers



2002 SYMPOSIUM

Location: Sydney Convention and Exhibition Centre, Darling Harbour
Attendees: over 700
Highlights: keynote speakers from the Cochrane Centre, Harvard (US), The Lancet (UK), Bristol Myers Squibb, The Food and Drug Administration (US)



2007 SYMPOSIUM

Location: Sydney Convention and Exhibition Centre, Darling Harbour
Attendees: over 700
Highlights: Launch of CTC's book *Interpreting and Reporting Clinical Trials*, keynote speakers from the University of Oxford, Duke University (US), The Lancet (UK)



Preventing disability and death in newborns (INIS Trial)

CTC's first neonatal trials begin in 2001 with the INIS (International Neonatal Immunotherapy Study) trial. INIS examines whether immunoglobulin, an expensive treatment used by clinicians at the time, helps infants fight off infection. A study of nearly 3,500 infants from nine countries proves immunoglobulin to be ineffective in preventing newborn death and disability. The study saves patients and the healthcare system significant costs and time. INIS is conducted by the National Perinatal Epidemiology Unit (UK) in collaboration with the CTC.



Oncology team, 2004

Shedding light on breast cancer surgery (SNAC trial)

Should women with early-stage breast cancer choose to have their axillary lymph nodes surgically removed? The CTC's SNAC trial (sentinel node biopsy versus axillary clearance) looks to answer this question in collaboration with the Royal Australasian College of Surgeons. An Australian first, SNAC is the fastest recruiting cancer trial in Australia. It finds women with breast cancer should opt for minimally invasive sentinel node biopsy management instead of routine axillary clearance surgery. The newer treatment results in better quality of life (less lymphoedema) for patients and has now become the standard of care.

Lung cancer on the radar

In 2004, The Australasian Lung Cancer Trials Group (ALTG) is formed to support lung cancer trials. The CTC is its central coordinating centre.



CTC establishes Biostatistics Collaboration of Australia

The Collaboration (BCA) is established in 2000 in response to a shortage of biostatistical expertise in Australia. Funding is provided by the Department of Health and Aged Care and the BCA is set up at CTC. Members include leading biostatisticians from the University of Melbourne, Monash University, the University of Queensland, the University of Sydney, Australian National University, Macquarie University and Adelaide University. In 2007, 224 students are enrolled in biostatistics programs Australia wide.

Erica Jobling, BCA





ANZCTR team, 2007

CTC pivotal in establishing national trials registry

In 2005, the CTC helps establish the Australian Clinical Trials Registry with five-year funding of \$1.5 million from the NHMRC. The registry, based at the CTC, is an online register of all clinical trials being conducted in Australia. The registry grows to include New Zealand and become ANZCTR, giving research an audience and informing its future.

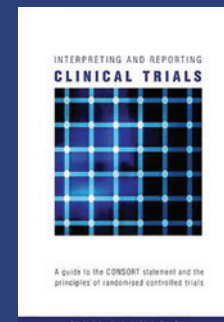
Statin drug proven to reduce heart attack and stroke risks

Analyses of existing trials find statin drugs lower cholesterol to reduce the risk of cardiovascular disease. The Cholesterol Treatment Trialists' Collaboration analyse data from 14 trials comprising 90,056 patients. CTC is the coordinator of this meta-analysis together with the University of Oxford's Clinical Trial Service Unit and Epidemiological Studies Unit (UK).

Other landmarks

- A CTC report on discussing dying with patients (*Communicating prognosis and issues surrounding the end of life*) is published and becomes the basis for doctor-patient guidelines in Australia
- Radiotherapy after a mastectomy is found by CTC and partners to improve survival of patients with breast cancer by 5 to 10 years
- Lancet publishes a CTC review of data from 38 trials involving 38,000 women (meta-analysis) showing that using aspirin reduces the risk of pregnant women experiencing pre-eclampsia by 10%
- A CTC neonatal study shows unrestricted oxygen therapy for premature infants can result in potential harm without clear benefits. The practice is abandoned by clinicians.

CTC moves into the Medical Foundation Building in 2007



Prof Tony Keech and Prof Val Gebski co-author *Interpreting and Reporting Clinical Trials* in 2007



Australian and New Zealand Urogenital and Prostate Cancer Trials Group is formed in 2008 through a merger of APUG and ANZGCTG.

Setting guidelines for Medicare

CTC reviews literature and clinical expertise around health technologies, diagnostic tests and procedures for the Australian Government's Medical Services Advisory Committee. The CTC's strategy for evaluating diagnostic tests becomes the basis for guidelines used by the MSAC on Medicare funding.

New brain tumour collaboration established

The Cooperative trials Group for Neuro-Oncology (COGNO) is set up and housed at CTC in 2007. Its main aim is to conduct investigator-initiated and collaborative group trials addressing important clinical questions in patients with brain tumours.



Systematic Reviews group, 2008



COGNO team, 2010



Responding to changing health needs 2008-2018

Twenty years on and the CTC is at the forefront of research on new treatments and determining the best methods for administering existing treatments. Work with seven collaborator groups in oncology means CTC research covers around 75% of the cancer disease burden in Australia.

CTC 20 year symposium

Leaders from government, industry, research and the community come together to celebrate CTC's 20th anniversary in 2008, and to address the future challenges in clinical trials.



Kate Wilson, John Zalcborg (Chair), and Russell Conley (CEO) of AGITG

'Although local patients may be scarce, Australia has the opinion leaders, the intellectual resources, and the ability to design and analyse studies and undertake biological substudies at the highest global standard.' John Simes

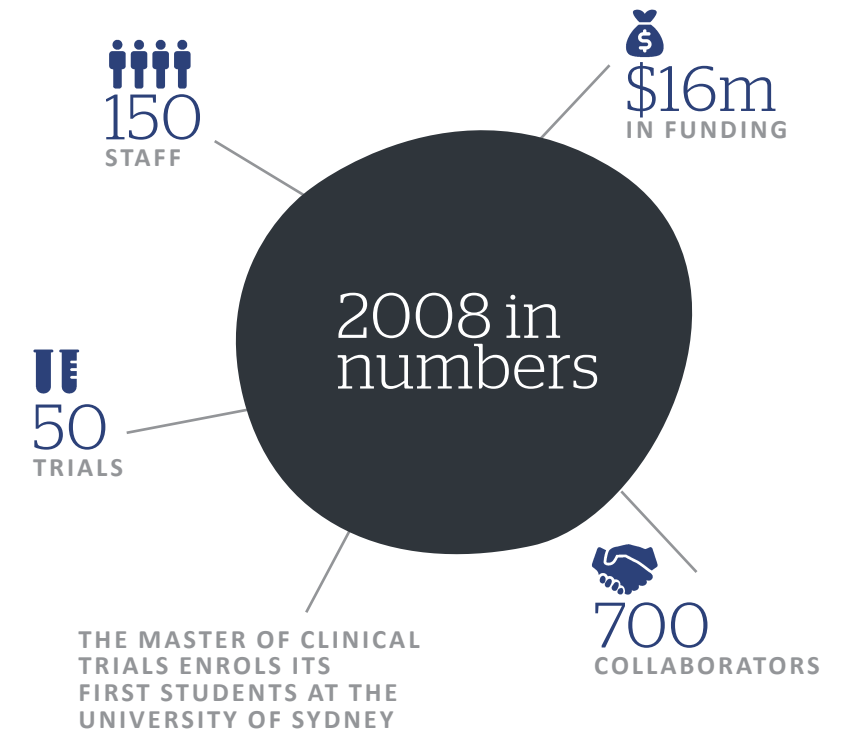
Personal treatment for colorectal cancer (CO.17 trial)

In partnership with the Australian Gastrointestinal Cancer Group (AGITG) and the Canadian Cancer Trials Group, the CTC helps discover that colorectal cancer tumours respond well to biotherapy (cetuximab) provided the patient does not have a KRAS mutation in their genes. Because of these findings, international guidelines go on to recommend patients be genetically tested before tumours are treated, saving many patients from unnecessary treatment, and saving the healthcare sector millions worldwide.



Rachael Morton and Anh Tran of Health Economics

2013 Sydney Catalyst Symposium



Making sure trials impact the real world

In 2010, the CTC formally establishes a Translational Research team and a Health Economics team. Two years later, the CTC plays a pivotal role in getting funding to help establish Sydney Catalyst.

- Translational Research: makes medical research findings usable and applicable to patients with minimum delay
- Health Economics: performs economic evaluations of CTC trials and assessments for government
- Sydney Catalyst: a translational research centre that brings together clinicians and researchers from across NSW to rapidly translate scientific discoveries into clinical policy and practice to improve patient outcomes.



Aspirin prevents deep vein thrombosis (ASPIRE)

In a study completed in 2012 (ASPIRE) involving over 800 patients, the CTC shows that low-dose aspirin can help patients, who have already suffered blood clots in their lungs or legs, reduce the risk of further clots. This simple, inexpensive treatment helps thousands of patients who are not suitable for more cumbersome and expensive anticoagulant treatments. Results from the INSPIRE trial (a combination of ASPIRE and the Italian WARFASA study) achieve worldwide media attention.

NEW TRIALS ALLIANCE

CTC plays a lead role in the establishment of the Australian Clinical Trials Alliance in 2013 to advance trials research and make clinical research a more integral part of healthcare.

ACTA features:

- 6 institutes
- 8 hospitals
- 400 people



Best oxygen levels for infant survival (BOOST II)

Oxygen has been common therapy for preterm infants for 60 years, but doctors and nurses do not know the best levels for babies. In the prize-winning BOOST II trial, the CTC examines oxygen levels in 1,000 infants born prematurely in Australia and New Zealand. It finds preterm infants up to 28 weeks gestational age have a better chance of survival with higher oxygenation levels.

Fighting heart disease and winning

Cardiovascular disease is the underlying cause of more than one in five deaths in Australia. To improve treatment and prevent death, the CTC has undertaken nine cardiovascular trials in Australia and randomised nearly 27,000 patients.

CTC's cancer trials teams move to the Chris O'Brien Lifehouse building across the road from the Royal Prince Alfred Hospital



Impacting surgery and government policy

- In one of the largest trials of complex surgery ever conducted, the CTC and AGITG publish an article in the 2017 *American Society of Clinical Oncology annual review* that shows open surgery may be better than keyhole surgery for certain patients with rectal cancer (A La CaRT trial)
- CTC completes a major review of the evidence on the value of fluoride in water supplies in Australia and other reviews of new technologies for the federal government
- In partnership with the Melanoma Institute of Australia, the CTC publishes a study that shows that specialised surveillance clinics would cut costs and improve health outcomes for people at very high risk of skin cancer
- CTC is awarded a \$2.5 million grant from the NHMRC and the Fred Hollows Foundation to improve the health and eye sight of Indigenous people in remote areas.

Using genetic information to treat tumours (MOST)

In partnership with the Garvan Institute of Medical Research, the CTC investigates linking molecular screening to multiple clinical trials for 1,000 patients. This will enable patients to receive treatment strategies according to genetic information. The CTC works with clinical researchers and key government and industry stakeholders to expand the program and offer more patients with limited treatment options a viable alternative.

Reducing cholesterol and cardiovascular risks (FOURIER)

Can lower cholesterol levels reduce the risk of a cardiovascular event? CTC is a lead author on a paper published in the *New England Journal of Medicine* which states that a new drug, evolocumab, reduces the risk of a major cardiovascular event by 15%. These results lead to changes in clinical management and treatment practices and policies globally.

Diabetes staff, 2013



Lucille Sebastian, MOST trial

REMOVAL of diabetes-related risks

Results from the REMOVAL trial are published in *The Lancet Diabetes and Endocrinology*. The REMOVAL trial investigates the effect of adding metformin to insulin to protect adults with Type 1 diabetes against the build-up of fat in arteries (atherosclerosis). Results indicate reduced thickening of the arteries, in association with less decline in kidney function.

CTC recognised for excellence

In 2015 CTC Director Professor John Simes was identified as a research leader in the successful bid by Sydney Health Partners to be recognised by the NHMRC as an Advanced Health Research and Translation Centre (AHRTC). The AHRTC initiative recognises 'leading centres of collaboration that excel in health and medical research, the translation of evidence into excellent patient care, and demonstrate a strong research and translation focus in the education of health professionals, at an international level'.

Andrzej Januszewski, REMOVAL team



2018 highlights

Prolonging millions of lives

Statin drugs continue to achieve the long term lowering of cholesterol (LIPID trial), with 7,000 survivors of the original 9,014 patients being assessed 20 years on. Samples from this groundbreaking trial continue to be analysed in different parts of the world. Millions of patient lives worldwide have been prolonged by the prescribing of statins, thanks to the CTC and its collaborators.

Neonatal win Trial of the Year

An international neonatal trial coordinated by the CTC wins the Australian Clinical Trials Alliance (ACTA) 'Trial of the Year' Award. The Australian Placental Transfusion Study (APTS) shows that thousands of preterm babies can be saved by waiting 60 seconds before clamping the umbilical cord after birth instead of clamping it immediately.

Trial of the Year team with Federal Minister for Health Greg Hunt.



Does Cannabis reduce nausea?

A CTC trial determining whether the use of medicinal cannabis can prevent nausea in people undergoing chemotherapy finishes its first stage. Progress is described in an article published in the *Medical Journal of Australia*. The trial is part of the NSW government's \$21 million commitment to support medicinal cannabis reforms.

Nicole Wong, CannabisCINV trial

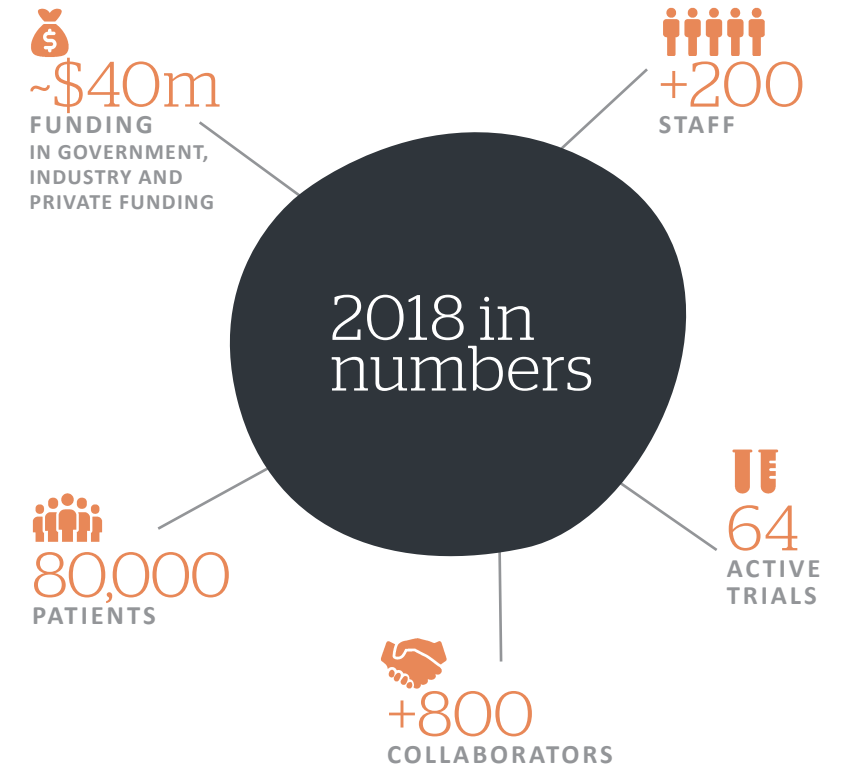


20
STUDENTS ANNUALLY IN MASTERS IN CLINICAL TRIALS RESEARCH

50-60
STUDENTS ANNUALLY IN MASTER IN BIostatISTICS

5
MASTERCLASSES HELD FOR PROFESSIONALS IN AUSTRALIA AND OVERSEAS

Educating the future of trials



Landmark moments

- CTC starts recruiting for the FAME-1 Eye study, which seeks to determine if the drug fenofibrate protects against the progression of established eye disease in patients with Type 1 diabetes
- A study of five existing trials around the right oxygen levels for preterm babies undertaken by CTC and its collaborators is published in the *Journal of the American Medical Association (JAMA)*, showing that rates of death were lower in the higher oxygen target group
- CTC and AGITG open their first recruitment sites in Korea and Taiwan for the INTEGRATE II trial, a study to see if the drug Regorafenib can prolong survival in patients with advanced gastro-oesophageal cancer

- The MOST study, where a patient's genetic information is used to inform the treatment of their tumours, is part of a new \$50 million federal government grant
- Australian New Zealand Clinical Trials Registry publishes *The clinical trials landscape in New Zealand 2006-2015*, the most complete overview of trials in the country. This follows the publishing of *The clinical trials landscape in Australia 2006-2015* in 2017



ANZCTR meeting

Examples of breakthrough research



Heart disease and prolonging life (LIPID)

In one of the world's largest cholesterol-lowering studies, the drug pravastatin successfully lowers cholesterol levels for patients with a history of coronary heart disease, reducing the risk of death by 23% and coronary heart disease by 24%.

'I feel really proud I was involved in the LIPID trial because of the benefits it has given to so many people all around the world.'
Kenneth O'Loughlin,
LIPID trial participant



Treating heart attacks

Evidence that opening blocked coronary arteries (balloon treatment or clot-buster drugs) during a heart attack improves survival and quality of life is confirmed during the GUSTO group of trials.



Preventing diabetes-related disease (FIELD)

The drug fenofibrate is found to reduce eye disease, amputation, kidney damage and heart attacks in adults with Type 2 diabetes. Fenofibrate tablets have been approved to treat eye disease in Type 2 diabetes patients in Australia and in fifteen other countries around the world.



More surgery not always the best for breast cancer sufferers (SNAC)

In a world first, women with early stage breast cancer are found to be better off undergoing minimally invasive lymph node biopsy management instead of more extensive surgery, improving the quality of life of sufferers.



Oxygen good for preterm babies (BOOST II)

Oxygen has been used on preterm infants for 60 years. A CTC study and combined analysis of five international trials discovered higher oxygenation levels increased life expectancy among preterm infants up to 28 weeks gestational age.



Using aspirin to prevent deep vein thrombosis (ASPIRE)

For patients who have already suffered blood clots in their lungs or legs, low-dose aspirin is found to significantly reduce the risk of a further clot, providing an inexpensive and safe treatment for those not suited to further anticoagulants.



Is biotherapy the best treatment for bowel cancer? (CO.17)

In partnership with AGITG and the Canadian Cancer Trials Group, the CTC discovered that colorectal cancer tumours respond well to targeted therapy provided the patient does not have a KRAS mutation in their genes. International guidelines go on to recommend genetic testing before tumours are treated, saving many patients from unnecessary treatment.



Lowering heart attack and stroke risk (FOURIER)

A new drug, evolocumab, is found by the CTC and its international partners to reduce the cholesterol levels of high risk patients by 59% into a healthy target range, resulting in a 15% reduction in the risk of a major cardiovascular event. Clinical management and treatment practices change as a result.



Cutting the umbilical cord later (APTS)

By delaying the clamping of the umbilical cord by 60 seconds, a CTC study shows reduced risk of perinatal death by one third.

Research leaders



Tony Keech

- 2018 University of Sydney Vice Chancellor's Award for Research
- 2017 Royal Prince Alfred Hospital Foundation Medal for Research Excellence
- Consultant cardiologist at Royal Prince Alfred Hospital



William Tarnow-Mordi

- Professor of Neonatal Medicine
- The lead investigator on the 2018 Trial of the Year Award winner, the APTS trial
- Leader behind BOOST II and NEOPROM trials determining the best oxygen levels for babies



Val Gebski

- Professor of Biostatistics and Research Methodology Medicine and Head of Biostatistics and Research methodology at the CTC
- Statistical examiner for the Royal Australian and New Zealand College of Radiologists



Rachael Morton

- Associate Professor and Director of Health Economics at the CTC
- President of the Health Services Research Association of Australia and New Zealand (HSRAANZ)



Lisa Askie

- Professorial Research Fellow Medicine at the CTC and Director of Integrating Evidence (Systematic Review and Health Technology Assessment)
- Developed world first test evaluation methods that are used in guidelines and clinical groups worldwide



Mustafa Khasraw

- Principal Research Fellow and Clinical Lead at the CTC
- Medical Oncologist at Royal North Shore Hospital, Sydney and The Northern Cancer Institute
- Fellow of the Royal College of Physicians (UK) and the Royal Australasian College of Physicians



Anand Hardikar

- Associate Professor and Australian Future Fellow (ARC) at the CTC
- Visiting Professor at Roskilde University Copenhagen and University of Copenhagen, and member of the Danish Diabetes Academy
- Editor of *Pancreatic Islet Biology*



John Simes

- NSW Premier's Outstanding Cancer Researcher of the Year Award, 2016
- Alan Coates Award for Excellence in Clinical Trials Research, 2016
- Practising medical oncologist in neuro-oncology at Royal Prince Alfred Hospital and the Chris O'Brien Lifehouse



Martin Stockler

- Professor of Cancer Medicine and Clinical Epidemiology
- Consultant medical oncologist at the Concord Repatriation General Hospital and Chris O'Brien Lifehouse
- Oncology Co-Director at the CTC and on the scientific advisory committees of ANZUP, ALTG and ANZGOG



Alicia Jenkins

- Professor and specialist in Endocrinology
- Chief Editor of *Lipoproteins in Diabetes* book and co-author of *Reshaping Teaching in Higher Education* book
- Leading investigator in CTC studies relating to Type 1 Diabetes



Wendy Hague

- Director of CTC's Clinical Trials Program for past 18 years
- PhD in clinical trials management
- Current consultant to CTC



Burcu Vachan

- Current Clinical Trials Program Manager at CTC
- Worked for 10 years as CTC's Oncology Program Manager
- Completed a Masters in Public Health in 2002 and a Diploma of Management through Stanford University in 2011



Ian Marschner

- Professor of Biostatistics at the NHMRC CTC with over 20 years of experience in biostatistics
- Worked on large scale clinical trials in a range of disease areas, particularly cardiovascular medicine



Chee Lee

- Associate Professor in Oncology
- Staff specialist in medical oncology at Sutherland Hospital
- Visiting medical oncologist at St George Private Hospital



Katrin Sjoquist

- Senior Research Fellow and Clinical Lead at CTC
- Practising medical oncologist and staff specialist at St George and Sutherland hospitals
- Group coordinator for AGITG trials

Long serving staff

30 years

JOHN SIMES
VAL GEBSKI

25 years

TONY KEECH
WENDY HAGUE
ANH TAI NGUYEN

20 years

DINH TRAN
ERICA JOBLING
HELEN PATER
LI PING LI
SAN YIP CHAN

10 years

AGNES HO, ALPANA GHADGE, ANDREW MARTIN, ANN LIVINGSTONE, ASANKA PERERA, BURCU VACHAN, CAITLIN VAN HOLST PELLEKAAN, CARLOS STERLING, CHRIS BROWN, CHRIS (CHRISTINE) AIKEN, COLIN SUTTON, CYNTHIA CARR, ERIC TSOBANIS, HANNAH CAHILL, IAN MARSCHNER, ILKA KOLODZIEJ, JENNY CHOW, KAREN BRACKEN, KAREN WILKINSON, KAREN BYTH WILSON, KATE (CATHERINE) WILSON, KRISTY ROBLED0, LISA BAILEY, LISA ASKIE, LIZ (ELIZABETH) BARNES, LUCILLE SEBASTIAN, MAKI JOSEPH, MARK MACLEAN, MERRYHALL, NICOLE WONG, RACHEL O'CONNELL, REBECCA MISTER, SALLY (SARAH) LORD, SAMARA LEWIS, SARAH CHINCHEN, SESHU ATLURI, SUZANNE EVERETT, XANTHI COSKINAS



Our key collaborators

The CTC works with organisations around the world in collaborations that lead to better health outcomes in Australia and internationally. New collaborations are continually sought and then consolidated in research projects, improving global health outcomes.

| Group | Nature of group | CTC activity |
|--|---|---|
| ONCOLOGY INVESTIGATOR GROUPS | | |
| Australasian Gastro-Intestinal Trials Group (AGITG) | Collaborative group for gastrointestinal cancer trials: Australia, New Zealand International collaborations: Cancer Clinical Trials Unit Scotland (CACTUS), Eastern Cooperative Oncology Group (ECOG), European Organisation for Research and Treatment of Cancer (EORTC), European Study Group for Pancreatic Cancer (ESPAC), Groupe Coopérateur multidisciplinaire en Oncologie (GERCOR), National Cancer Centre, Singapore, National Cancer Institute of Canada Clinical Trials Group (NCIC CTG), National Surgical Adjuvant Breast and Bowel Project (NSABP), Medical Research Council (MRC), Oxford Clinical Trials Office, Oxford University (OCTO), Pan-European Trials in Alimentary Tract Cancer (PETACC) | Coordinating centre and collaborator |
| Australasian Lung Cancer Trials Group (ALTG) | Collaborative group for lung cancer trials: Australia, New Zealand International collaborations: NVALT (Netherlands), NCIC CTG (Canada) | Coordinating centre and collaborator |
| Australia New Zealand Gynaecological Oncology Group (ANZGOG) | Collaborative group for gynaecological cancer trials: Australia, New Zealand International collaborations: Dutch Gynaecologic Oncology Group (DGO), Group d'Investigateurs Nationaux pour l'Etude des Cancers Ovariens (GINECO), Gynecological Cancer Intergroup (GCI), International Gynaecological Cancer Intergroup (IGCI), Gynecologic Oncology Group (GOG), Medical Research Council (MRC), Scottish Gynaecologic Cancer Trials Group (SGCTG) | Coordinating centre and collaborator |
| Australian and New Zealand Urogenital and Prostate Clinical Trials Group (ANZUP) | Collaborative group for cancer of the genitourinary system: Australia, New Zealand. International collaborations: Cancer Research UK (CRUK), European Organisation for Research and Treatment of Cancer (EORTC), Groupe Coopérateur multidisciplinaire en Oncologie (GERCOR), Institute of Cancer Research (ICR), National Cancer Research Institute (NCRI), Swedish & Norwegian Testicular Cancer Project (SWENOTECA), Wales Cancer Trials Unit (WCTU), and CTRI (Ireland) | Coordinating centre and collaborator |
| Australian New Zealand Breast Cancer Trials Group (ANZ BCTG) | Collaborative group for breast cancer trials: Australia, New Zealand International collaborations: International Breast Cancer Study Group (IBCSG), Breast International Group (BIG), International Breast Cancer Intervention Study (IBIS) | Statistical centre for group, including randomisation |
| Cooperative Trials Group for Neuro-Oncology (COGNO) | Collaborative group for brain cancer trials: Australia International collaborations: European Organisation for Research and Treatment of Cancer (EORTC) | Coordinating centre and collaborator |
| RACS-SNAC collaboration | Collaboration with Royal Australasian College of Surgeons on SNAC trials: Australia | Coordinating centre and collaborator |
| Trans-Tasman Radiation Oncology Group (TROG) | Collaborative group: Australia and New Zealand | Collaborator |

| Group | Nature of group | CTC activity |
|--|---|--|
| COLLABORATIONS FOR META-ANALYSIS | | |
| Antenatal Magnesium IPD International Collaboration (AMICABLE) | Meta-analysis collaboration: international | Collaborator |
| Cholesterol Treatment Trialists' Collaboration (CTTC) | Investigators of cholesterol treatment trials: Australia, New Zealand, United Kingdom, United States, Italy | Coordination of meta-analyses in heart disease |
| Cochrane Collaboration Breast Cancer Group | Collaborative group undertaking systematic reviews of trial evidence: international | Editorial base |
| Cochrane Prospective Meta-Analysis Methods Group | Collaborative group undertaking systematic reviews of trial evidence: international | Coordinating centre |
| Cord Clamping and other Measures to Influence Placental Transfusion at Preterm Birth (CCPTP) | Prospective meta-analysis collaboration: international | Collaborator |
| Early Prevention of Obesity in Children (EPOCH) collaboration | Prospective meta-analysis collaboration: international | Data coordination centre |
| INSPIRE (International Trials of Aspirin to Prevent Recurrent Venous Thromboembolism) | Meta-analysis: ASPIRE and WARFASA (Italy) | Data coordination centre |
| Meta-Analysis of Preterm Patients on Inhaled Nitric Oxide (MAPPINO) | Meta-analysis collaboration: international | Data coordination centre |
| Neonatal Oxygenation Prospective Meta-analysis (NeOProm) collaboration | Prospective meta-analysis collaboration: international | Coordinating centre |
| Perinatal Antiplatelet Review of International Studies (PARIS) collaboration | Meta-analysis collaboration: international | Co-coordinating centre |
| Prenatal repeat corticosteroid international individual-patient-data study group: assessing the effects using the best level of evidence (PRECISE) collaboration | Meta-analysis collaboration: international | Collaborator |
| Prevention of Ventilator Induced Lung Injury collaborative study group (PreVILIG) | Meta-analysis collaboration: international | Data coordination centre |
| Star Child Health | Meta-analysis collaboration: international | Member |

| Group | Nature of group | CTC activity |
|--|--|---|
| OTHER COLLABORATIONS | | |
| Australasian Society of Thrombosis and Haemostasis (ASTH) | Professional group undertaking thrombosis trials: Australia, New Zealand | Coordinating centre and collaborator |
| Australian New Zealand Clinical Trials Registry (ANZCTR) | National register of clinical trials: Australia, New Zealand and international | Coordinating centre |
| Biostatistics Collaboration of Australia (BCA) | Universities undertaking postgraduate education in biostatistics: Australia | Coordinating centre |
| GUSTO-VIGOUR Group | Investigating improved treatments for heart attack sufferers | Asia Pacific Data Coordination |
| The FIELD Investigator Group | Evaluating treatments to prevent complications from Type 2 diabetes | Coordinating Centre |
| The LIPID Investigator Group | Evaluating the role of cholesterol lowering to reduce cardiovascular disease | Coordinating Centre |
| ORGANISATIONS | | |
| Australian Clinical Trials Alliance (ACTA) | Advocacy body for investigator-initiated trials groups: Australia | Founding member |
| Clinical Trials Transformation Initiative (CTTI) | Advocacy body for clinical trials: international | Member |
| RNA-based Analysis for Prediction of Islet Death (RAPID) | Collaborative group: Australia | Collaborator |
| Sydney Catalyst | Consortium for translational research in cancer | Collaborator |
| Medical Services Advisory Committee (MSAC) and Department of Health and Ageing | Government: Australia | Assessments of new technologies and other research services |
| Menzies Research Institute and Charles Darwin University | Research institution: Australia | Collaborator |

The fun times

At the CTC, we believe time out is crucial for perspective. Trials can be fun in terms of challenges and rigour, but it is also important to unwind and find that work-life equilibrium. That is why we like to get together and have fun as often as we can.







‘None of this would have been possible without the participation of patients and consumer representatives in studies undertaken by us and our collaborators. Patient participation is vital for us to continue to improve global health outcomes. Thank you.’
Tony Keech
