

# CELEBRATING *25 years* OF RESEARCH





“Cabrini was a very early adopter  
of research.”

“Cabrini has a strong reputation  
for research.”

“Cabrini has unique clinical  
research potential.”

‘The Wright Review’

Michael Wright, Managing Director of the Miller Network Group



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# IN THE BEGINNING....

Cabrini Clinical Education and Research Foundation (now known as Cabrini Research) was established in 1996. It was then, and still is today, an extremely novel venture. There was only one private hospital research institute in Australia at the time (St Vincent's Institute, Melbourne), and we are still considered a relatively rare entity today. In the early 1990's, Associate Professor Doug Lording AM, Cabrini's Medical Director, started to raise the concept of an institute for research and education at Cabrini. They were seeing a larger portfolio of research projects being undertaken at the hospital, increasing numbers of medical staff who had novel research ideas and the ambition to test them, and a greater demand for clinical placements. His vision was if Cabrini hospital was going to grow and continue to attract the best talent in clinicians, then it had to make a commitment to fostering and encouraging a research culture in the hospital and growing education. He took the concept of a 'research and education institute', a space that would bring everyone together to foster growth, learning and outputs, to the Cabrini Board.

In 1995 the governing board of Cabrini Health, Chaired by Mr Alan Molyneux, approved the establishment of a research and education institute. In July 1996 our history began with the official launch of the Cabrini Clinical Education and Research Foundation by the Honourable Dr Michael Wooldridge, then Minister for Health and Family Services.

The hospital pledged three years of funding to make a success of it. The Cabrini Clinical Education and Research Foundation was responsible for fundraising as well as the core education and research activities. In 1999 a decision was made to separate the fundraising from the education and research activities. Cabrini Foundation went on to become a successful fundraising entity for the whole hospital and the Cabrini Institute was established, cementing its place as a research and education institute. A/Prof Lording spent 42 years of his exceptional medical career at Cabrini, 15 as the medical director. He considers Cabrini Institute as his legacy to the hospital and continues to be an avid supporter of its growth and success.



**1997**  
**Cabrini-Deakin University Chair of Nursing established**

Professor Lerma Ung appointed as Chair  
First of its kind in the private sector



**1997**  
**Cabrini supports clinician led research**

Melbourne Gastrointestinal Investigational Unit (MGIU) established by Associate Professor Henry Debinski and Mr Chip Farmer

**1999**  
**Cabrini Clinical School launched**

Formalisation of the medical student training Cabrini had been supporting for many years

**1999**  
**Cabrini Institute established**  
Cabrini Institute represents Research and Education. Foundation decoupled to become a separate entity

## 1996

**1996**  
**Cabrini Clinical Education and Research Foundation official opening**

Associate Professor Doug Lording AM appointed as Inaugural Director  
Foundation Council established



**1998**  
**Cabrini Monash University Department of Surgery established**

Professor Adrian Polglase appointed as Director  
First of its kind in the Victorian private medical sector, and one of the first in Australia



**1999**  
**Institute Council**  
Official formation



# GOOD STEWARDSHIP – SETTING OURSELVES UP FOR SUCCESS

Good research and education practices and financial performance requires good stewardship. The Cabrini Institute was setup as part of Cabrini hospital but it was overseen by its own Council. Shared commitment was a hallmark of those who were involved from the very beginning. The inaugural Cabrini Institute Council was chaired by A/Prof Lording. The membership brought together a diverse skill set in clinical, research, education, financial and management experience from within Cabrini and well respected external organisations. Their mandate was to oversee and advise on the Institute’s strategies and governance.

The original membership of the Council included Mr Lew Saliba, Director of Finance at Cabrini Hospital, Professor Henry Burger AO, Director of the Prince Henry’s Institute of Medical Research (now the Hudson Institute of Medical Research) and Professor Judith Parker, Professor and Head of the School of Post Graduate Nursing, the University of Melbourne. Mrs Mary Jo Pirola, Manager, Business and Strategic Planning, Department of Treasury and Finance, and Mr Paul Excell, Managing Director of Eastern Aluminium, were also council members, and both in later years led the Council as Chair. Associate Professor John Santamaria, an Intensive Care Physician and ethicist, and later Director of Intensive Care at St Vincent’s Hospital Melbourne, was a member of the Cabrini Hospital Board, the founding secretary of the Council, and longest serving member, from its inception in 1996 until its final meeting in 2020. The Institute was fortunate

to have many skilled and experienced people serve on the Council across its 24 years of activity, and who have undoubtedly helped to ensure its success and set it up for its future. We would like to particularly thank Professor Peter Fuller AM and Professor Lawrence St Leger. The Scientific Advisory Committee was established to advise the Institute about matters of a scientific nature. Joining Prof Parker and Prof Burger on the original committee were Professor Rachele Buchbinder AO, Professor Mark Frydenberg, Professor Sandra Legg AM, A/Prof Lording and Associate Professor Paul O’Brien.

Research requires governance to ensure that the boundaries of good and ethical research are adhered to and that the research is being done in accordance with where the organisation wants to go and follows the mission, values and beliefs. Cabrini Institute established one of the earliest human research ethics committees. The original members of the Cabrini Human Research Ethics Committee (CHREC) were Mr Ben Burke, Ms Margaret Coffey, Reverend Dr Norman Ford SDB, Dr Kay Leeton, Prof Sandra Legg AM, A/Prof Lording, Ms Kerry McGeorge-Hodges, Ms Robin Riley, Mr Glenn Staunton and Associate Professor Stan van Hooft. In 2019, Cabrini Institute made the decision to dissolve its CHREC and utilise the Monash Partners joint ethics platform. The model uses ethics committees of partner organisations, Alfred Health or Monash Health, to enable streamlining of ethics review.

See timeline photo reference page 98

2001



2000

## Monash-Cabrini Department of Clinical Epidemiology established

Professor Rachele Buchbinder AO appointed as Director

2001

## Foundation 49 Men’s Health established

Foundation 49 was originally setup as a men’s health promotion initiative of Cabrini Health through the Cabrini Institute. Foundation 49 Men’s Health is now managed and administered within the Baker Heart and Diabetes Institute



2001

## Cabrini Monash University Department of Medical Oncology established

Professor Gary Richardson OAM appointed as Director



2001

## Let’s Beat Bowel Cancer established

A not-for-profit initiative of Cabrini with a vision to significantly lower deaths related to bowel cancer through public awareness, research and medical advances



# A NEW HOME FOR THE INSTITUTE

Malvern's 154 Wattletree Road has been the home to the Institute since 2013. The purpose-built office was the result of a successful grant from Health Workforce Australia and generous donations by major donors, including Mrs Patricia and Mr Nigel Peck AM. The Institute building was named in their honour, Patricia Peck Education and Research Precinct.

Associate Professor Peter Lowthian, the Institute Executive Director from 2002 to 2014, was instrumental in bringing together the grant and philanthropic funding required. In addition to significant growth and changes in education during his time as executive director, he is incredibly proud of what he, Anne Spence and Geoff Fazakerly achieved in establishing a purpose-built facility, which would bring together research and education under the one roof.



2003

### Australian Rheumatology Association Database (ARAD) established



Co-led by Professor Rachelle Buchbinder AO, ARAD is a national Australian database which collects important health information from individuals with inflammatory arthritis conditions



2006

### Cabrini Monash University Department of Medicine established

Associate Professor Michele Levinson appointed as Director. Cabrini and Monash University made the decision to close the department in early 2017 to focus on increasing leadership in the clinical wards



2003

### Cabrini Family Cancer Clinic established by the Cabrini Monash University Department of Medical Oncology

The clinic provides an assessment of a person's risk of cancer based on their family history and environmental factors. It offers advice regarding management and, where necessary, genetic testing



2003

### Cabrini Monash University Department of Medical Oncology endowed, named the Szalmuk Family Department of Medical Oncology in honour of George Szalmuk and the Szalmuk Family

2006

### Offices for the Cabrini Institute formalised

Team of researchers and education specialists are brought together in the same area of the main hospital for the first time

## 2002

2002

### Associate Professor Peter Lowthian appointed as Executive Director Cabrini Institute



2002

### Inaugural Peter Meese Memorial Lecture

Cancer research scholarships, grants and annual lecture established by Dr Darren Lockie in memory of his partner, Peter Meese



2004

### Chair of Surgery endowed, named the Fröhlich West Chair of Surgery in honour of Mr Joseph and Mrs Helen Fröhlich West

Professor Adrian Polglase appointed as the Fröhlich West Chair of Surgery



# FOSTERING AND GROWING RESEARCH

In the first few years of its operation, Cabrini Institute committed to accelerating research and engaging clinicians. Establishing research departments to create an academic presence for the hospital was a high priority. The Cabrini-Deakin University Chair of Nursing was setup first. Sponsored by Tattersalls, it was led by Professor Lerma Ung. Today, Nursing Research is led by Associate Professor Philip Russo. In 1998 the Cabrini Monash University Department of Surgery was established, the first of its kind in the Victorian private medical sector, and one of the first in Australia, led by Professor Adrian Polglase, and now by Professor Paul McMurrick. Shortly afterwards the Monash-Cabrini Department of Clinical Epidemiology, led by Professor Rachelle Buchbinder AO, and Cabrini Monash University Department of Medical Oncology, led by Professor Gary Richardson OAM, were established. The formation of the Cabrini Monash Department of Medicine followed a few years later, led by Associate Professor Michele Levinson, although this is no longer in operation today.

Their appointments and departments took Cabrini Institute from very little in the way of research to dozens of projects running at any one time. In 2008, the Salmuk Family Psycho-oncology Research Unit was established. Initially led by Dr Sue Burney, Professor David Kissane AC is now leading the research direction of the unit. In 2014 Associate Professor Helena Frawley established the Cabrini Allied Health Research and Education (CAHRE) Centre, now directed by Dr Annemarie Lee. The Institute also enjoys a direct connection with clinical services through a number of affiliated research units in Emergency Medicine, Intensive Care and Palliative Care. During the past 25 years there has been significant research growth, and at the start of 2021 we had more than 350 research projects active. The engagement and research culture within Cabrini today truly embodies what they hoped to achieve 25 years ago. Our world class researchers are dedicated to making the breakthroughs that will change healthcare for the better.



2008

### Szalmuk Family Psycho-oncology Research Unit established, named in honour of the Szalmuk Family

Led by Dr Sue Burney, and later Professor David Kissane AC on his return from Memorial Sloan Kettering, New York Cancer Hospital

2010

### Cabrini Monash Colorectal Neoplasia Database established

Conceived in 2006, the registry captures data on patients with either bowel cancer or benign bowel neoplasia surgically treated at Cabrini Health and other Monash affiliated hospitals



2010

2007

### Specialist Training Program (STP) starts

STP starts at Cabrini and is managed by Cabrini Institute. First private hospital to be funded in the program

2007

### Cabrini Human Research Ethics Committee (CHREC)

CHREC recognises the ethical approval of other human research ethics committees properly constituted under the National Statement on Ethical Conduct in Human Research



2009

### Newly appointed Fröhlich West Chair of Surgery, Cabrini Monash University Department of Surgery

Emeritus Professor Adrian Polglase steps down after an 11-year tenure, and Professor Paul McMurrick appointed

2010

### Cabrini Human Research Ethics Committee (CHREC)

Accredited as part of the National Health and Medical Research Council's Harmonisation of Multicentre Ethical Review – Can accept research projects approved at other sites and performs only a governance review

# A CENTRE FOR CLINICAL TRIAL EXCELLENCE

The oncology clinical trials program has been a large part of the Institute and has grown from small beginnings to the extremely successful trials unit it is today. Institute Executive Director A/Prof Lowthian played a significant role in its development, working with Prof Richardson, who had been appointed as the Director of the new Cabrini Monash Department in Medical Oncology only one year earlier. Growth in clinical trials, in medical oncology, but also key clinical service areas including cardiology and musculoskeletal medicine, are key elements of the Cabrini Health strategy for the next five years. Professor Lee Boyd was A/Prof Lowthian's successor in 2014. One of the key highlights during her five years as Institute Executive Director was the development of the phase 1a trial program at Cabrini, which commenced in 2017. On the back of a successful clinical trials program led by Prof Richardson, Prof Boyd strongly advocated for Cabrini to begin first in-human cancer trials.

She was passionate about being able to offer options to cancer patients who couldn't access therapies any other way, and wanted patients to feel connected and supported by Cabrini for their entire cancer journey. Her parting legacy was a successful grant from the Federal Government to establish phase one of the Cabrini Cancer Institute, which will enable Cabrini to double clinical trials, progress translational research, support cancer patients through wellness and exercise programs, and keep patients at Cabrini connected with their oncologists.

To be a leader in research requires networks and collaborations, partnerships which can help you leverage your own assets. Prof Boyd played an important role in expanding Cabrini's connection with Monash Partners and Cancer Trials Australia, two partnerships that have been integral in advancing our standing as a clinical trials site of excellence, a translational research partner, and our external recognition through accomplishments in research.



**2012**  
**First Institute review undertaken**



**2014**  
**Allied Health Research Program founded at Cabrini Institute**  
 Started by Associate Professor Helena Frawley, and now led by Dr Annemarie Lee



**2014**  
**Professor Lee Boyd appointed as Executive Director Nursing and Cabrini Institute**



**2014**  
**Palliative and Supportive Care Research Unit joins Cabrini Institute**  
 Led by Associate Professor Natasha Michael. The unit became a clinical service research unit aligned with the Institute in 2021.

## 2011

**2011**  
**Monash Partners Academic Health Science Centre established**

Accredited in 2015 by the NHMRC as an Advanced Health Research Translation Centre. Cabrini is a founding member

**2013**  
**Patricia Peck Education and Research Precinct officially opened. Named in honour of Mrs Patricia and Mr Nigel Peck AM**  
 \$7.5 million four storey building was also made possible by funding from Health Workforce Australia, a government initiative



# OUR SUPPORTERS – WE DID THIS TOGETHER

Great research success requires great supporters and Cabrini Institute has been incredibly fortunate to have some extremely dedicated and generous supporters. Every dollar makes an impact in research, providing a possibility to improve healthcare. We have many people to thank across our time. Our physical home at 154 Wattletree Road, the Patricia Peck Education and Research Precinct, is named in honour of Mrs Patricia and Mr Nigel Peck AM, incredibly generous donors of Cabrini and supporters of education and research. Mr Brian and Mrs Lee Johnstone have played an exceedingly generous role, funding the Cabrini Library, housed in the Patricia Peck Education and Research Precinct, and establishing the Auric innovation grant, a substantial yearly grant to support innovative big ideas in healthcare. The Szalmuk family have supported research at Cabrini for many years and given sizeable donations to support research, particularly in cancer. Their substantial donations are recognised with their naming of two departments. The Szalmuk Family Department of Medical Oncology and the Szalmuk Family Psycho-oncology Research Unit have the honour of their name. Colorectal research at Cabrini has flourished due the generosity of Mr Joseph and Mrs Helen Fröhlich West.

Their sizeable donation endowed the Chair in Surgery of the Cabrini Monash University Department of Surgery. The Sambor family have made a considerable impact to research at Cabrini. In recognition of their ongoing support, the yearly Cabrini research grant round names the top grant in honour of their commitment to funding new research. Dr Darren Lockie’s commitment during the past 20 years has meant nurse driven research in oncology and palliative care has thrived. Dr Lockie’s generous donations in memory of his partner, Peter Meese, in recognition of the care they both received, has established a program of cancer research scholarships, grants and the annual Peter Meese Memorial lecture. Cabrini Institute has worked closely with the Cabrini Foundation ever since our joint inception in 1996. We wish to specifically pay thanks to Cabrini Foundation Director Sue Parkes and her team. Together we engage with our donors and ensure their important role in research is recognised.

All donations, of all sizes, make an impact. Without the incredible generosity of our donors we couldn’t do the world leading research that will see tomorrow be better than today.



2016

### Cabrini Research and Education 20 Year Celebration, top research grant named in honour of the Sambor Family

A day time research seminar event and evening dinner celebration was held to celebrate the 20 year milestone for Cabrini Institute

2016

### NHMRC Centre of Research Excellence awarded to Wisser Healthcare

Led by Professor Rachele Buchbinder AO at Cabrini, Wisser Healthcare is a research collaboration that looks at reducing overdiagnosis and overtreatment



2016

2015

### Cabrini Institute partners with Cancer Trials Australia (CTA)

Cabrini joins the member based clinical trial network and site service organisation to grow our oncology trial program and bolster our reputation as a trials site

2015

### The University of Notre Dame undergraduate medical student association started at Cabrini

2015

### Second Institute review undertaken



2016

### Colorectal Organoid Research Program established

Led by Professor Paul McMurrick and team in collaboration with Professor Helen Abud’s Epithelial Regeneration Laboratory at the Monash Biomedicine Discovery Institute, Monash University



# A NEW NAME AND TIME TO CELEBRATE OUR ACHIEVEMENTS

Under the guiding leadership of our past Directors, A/Prof Lording, A/Prof Lowthian, Prof Boyd and now Prof Richardson, we have achieved incredible results in research during the past 25 years. The Cabrini Institute has undergone considerable change in the past 12 months, all while adapting to the new 'Covid norm'. Research and education will be decoupled, with education to take a new home and align with the clinical services. In 2021, we celebrate 25 years and proudly take our new name, Cabrini Research.

Under our new leadership of Prof Richardson we are in an exciting chapter of expanding our successful programs. We have established phase one of the Cabrini Cancer Institute and planning is moving ahead for phase two, which will look to support genomics and tissue banking. Complementing this will be growth in areas aligned with our clinical services including cardiac research, musculoskeletal research, mental health research and medical informatics, and continued successes in our established research programs. The future of research at Cabrini is exciting.

Our ability to move confidently ahead into an exciting new era of research comes off the back of 25 years of successful research outcomes achieved by talented and committed researchers. This book celebrates 25 years of world leading research that has changed policy, guidelines and behaviours, clinical trials that have changed practice and provided opportunities for patients to access new therapies, translational research that will be the future of personalised medicine, databases that will drive research questions, and advances in medical, workforce and technology that will improve how we deliver healthcare and improve patient outcomes. We make positive change every day through research. We hope you enjoy reading about some of our successes in the stories that follow. We hope you will stay connected with us, as we continue to make healthcare breakthroughs now and into the future.



2018

**Professor Rachelle Buchbinder AO named on the Highly Cited Researchers list from Clarivate Analytics (2018, 2019, 2020)**



2018

2018

**Cabrini awarded \$6 million in Federal funding to establish the Cabrini Cancer Institute**

The Federal funding will be invested to grow oncology clinical trials, establish a cancer exercise research program, and launch a cancer exercise and wellness centre at Cabrini

**NHMRC Centre of Research Excellence for the Australia and New Zealand Musculoskeletal (ANZMUSC) Clinical Trial Network launched**

Led by Professor Rachelle Buchbinder AO at Cabrini



## 2017

2017

**First phase 1a (first in human) oncology trial undertaken at Cabrini**



2017

**NHMRC Partnership Centre for Health System Sustainability funded**

Led by Professor Rachelle Buchbinder AO, Cabrini is a system implementation partner



2019

**Cabrini Monash University Department of Nursing Research established**

Associate Professor Philip Russo appointed as Director

2019

**Professor Gary Richardson OAM appointed as acting Group Director Cabrini Institute**



2019

**Cabrini adopts the Monash Partners shared HREC review model**

CHREC disbanded and researchers have the option of review through Alfred Health HREC or Monash Health HREC



**2020**

**“Wright Review” undertaken, the third Institute review**

Led by Michael Wright from which the review takes its name, it provided organisational and functional concepts for how Cabrini Institute should operate and grow in the future

**2021**

**Research and Education activities decoupled**

Informed by the Wright review. Cabrini Research will focus entirely on research for the future, and education activities will be managed through the clinical services



**2021**

**Cabrini Cancer Institute opens**

The Cabrini Cancer Institute was officially opened by the Honorable Greg Hunt MP, Federal Minister for Health and Aged Care on 21st April

**2021**

**2019**

**Auric Innovation grant established by Mr Brian and Mrs Lee Johnstone**

A yearly grant established to support innovative big ideas in healthcare. Brian and Lee’s generous support also funds the Cabrini Library which has the honour of their name



**2021**

**Professor Gary Richardson OAM appointed as Group Director Cabrini Research**

**2021**

**Cabrini Institute rebranded to its new name “Cabrini Research”**



*Prof Rachelle Buchbinder AO photographed as part of the 'Women' Public Art Exhibition 12 March to 14 April 2019, Malvern Victoria. The exhibition portrayed eight prominent and inspiring women who have something to say, and the confidence and wisdom to step forward and say it. Artwork credit Sam Burke and Rebecca Umlauf - Rachelle Buchbinder - First do no harm, 2019.*

**First, do  
no harm**

“THERE IS  
AN URGENT  
NEED TO ADDRESS  
THE PROBLEM OF  
OVERDIAGNOSIS AND  
OVERTREATMENT”

# THE PROBLEM OF TOO MUCH MEDICINE

MONASH-CABRINI DEPARTMENT OF CLINICAL EPIDEMIOLOGY

Overdiagnosis and overtreatment are significant problems not only in Australia, but around the world. They occur when patients receive diagnoses and treatments that are technically correct, but unnecessary, won't benefit them, and might cause harm. It can happen when healthy people are screened for diseases like cancer, and abnormalities are found that would never have caused symptoms or harm in their lifetime. Without the screening they would never have known about it, and they would have lived just as long.

Overdiagnosis can also happen when people with minor symptoms are investigated unnecessarily. A scan might show an abnormality that could be an age-related change, but it is then falsely assumed to be the cause of the problem.

The Australian 'Wiser Healthcare' research collaboration was formed to find out more about the problem of overdiagnosis, how it is caused, and how to reduce it in Australia and around the world. Composed of an expert team of healthcare researchers and clinicians, the formidable collaboration brings together Bond University, Monash University, University of Sydney, University of Wollongong, and other national and international colleagues. They have secured more than \$10 million in funding from the NHMRC, through both its Centres for Research Excellence scheme and its Program Grant scheme to perform this work. Professor Rachelle Buchbinder AO, from the Monash-Cabrini Department of Clinical Epidemiology, is co-leader of the collaboration and is joined by members of her research team including Associate Professor Denise O'Connor, Dr Tomas Rozbroj, Dr Romi Haas and PhD student Caitlin Farmer.

Changing people's beliefs and treatment practices is hard. Screening and early detection of cancer can be lifesaving in many circumstances. There is also a strong

belief that more tests, providing more information, must be better. Yet this fails to consider the potential harms of overdiagnosis, which can cause detrimental psychological effects, including undue anxiety and labelling of people with stigmatising disorders. It may also have negative effects on health behaviours, complications related to follow-up tests, and in worse case scenarios – harms from unnecessary treatment.

Wiser Healthcare is leading an Australian alliance of clinical, consumer, research and public organisations to tackle the problem. Their research is investigating overdiagnosis in the areas of cancer, cardiovascular disease and musculoskeletal disorders, with a particular focus on overdiagnosis caused by imaging, testing biomarkers and genetic tests. The research is multifaceted to meet the complexity of the problem. Some of the steps will include public awareness campaigns, developing tools to better help doctors and patients in the process of shared decision-making, reforming system incentives to reward quality rather than quantity of medical care, curbing expanding disease definitions, and greater scrutiny of testing accuracy.

"The sustainability of the healthcare system is threatened by the waste arising from unnecessary, ineffective or marginally effective healthcare, not to mention how this waste is also harming the environment", Prof Buchbinder said.

"There is an urgent need to address the problem of overdiagnosis and overtreatment. This has also prompted me to write a book together with Professor Ian Harris, an orthopaedic surgeon at the University of NSW, entitled '*Hippocracy – how doctors are betraying their oath*', which uses the Hippocratic Oath to outline the problems of too much medicine (release date 1 October 2021, by NewSouth publishing)."



*A/Prof Denise O'Connor,  
Deputy Director Monash-  
Cabrini Department of Clinical  
Epidemiology.*



*Dr Romi Haas, Postdoctoral  
Research Fellow Monash-  
Cabrini Department of Clinical  
Epidemiology.*



*Dr Tomas Rozbroj, Postdoctoral  
Research Fellow Monash-  
Cabrini Department of Clinical  
Epidemiology.*



*Caitlin Farmer, PhD student  
Monash-Cabrini Department of  
Clinical Epidemiology.*

# THE FUTURE OF PERSONALISED CANCER TREATMENT

CABRINI MONASH UNIVERSITY DEPARTMENT OF SURGERY



Bench to bedside translational research has the greatest chance of success when there is a strong connection and common goals between clinician based teams and academic laboratories focused on discovery research. The collaboration between the Cabrini Monash University Department of Surgery (CMUDS) led by Professor Paul McMurrick and the Monash Biomedicine Discovery Institute's Epithelial Regeneration Laboratory led by Professor Helen Abud is a prime example of how translational research can be accelerated. Together they are leading the Colorectal Cancer Organoid Research Program which focusses on personalising cancer medicine.

Colorectal cancer is the third most commonly diagnosed cancer, and the second leading cause of cancer death in Australia. To reduce colorectal cancer-related deaths, new strategies for the detection and treatment of this disease are required. Given that around 50 per cent of patients present with advanced stage disease, and many will fail conventional treatment options, there is significant need to improve treatment strategies and identify new therapeutic targets. The aim of the Colorectal Cancer Organoid Research Program is to identify new and novel treatments, and to be able

to predict which patients will respond to treatment. Distinguishing between effective and ineffective treatments will ultimately spare patients from unnecessary side effects. The Cabrini-Monash collaboration is working towards making colorectal organoid technology a bench to bedside reality, a personalised medicine approach for colorectal cancer.

Organoids are a cutting-edge technology that allows the growth of miniaturised, three-dimensional versions of a patient's tumour in the laboratory. The organoids are essentially cancer avatars that replicate the features of the patient's own tissue, allowing the characteristics of the tumour to be studied on an individual patient level. Dr Rebekah Engel from the CMUDS, with the expertise of Professor Helen Abud and Dr Thierry Jardé from the Monash Biomedicine Discovery Institute, is playing a key role in driving the laboratory discoveries. One of the projects Dr Engel is working on is the development of a pre-clinical test that can determine the likelihood of a patient responding to treatment before they receive it in the clinic.

*Dr Rebekah Engel, Senior Postdoctoral Research Fellow working in the Monash Biomedicine Discovery Institute's Epithelial Regeneration Laboratory.*



*Dr Rebekah Engel,  
Senior Postdoctoral  
Research Fellow.*

Dr Engel says by comparing the response observed in the organoid culture with the patient response, they are determining how effectively a patient's organoid predicts their clinical outcome.

"Our ultimate aim is to apply this technology to guide treatment strategies in the clinic," said Dr Engel.

"We are now expanding this project. Not only will we be testing organoid responsiveness to the drugs the patients currently receive in the clinic, but we are also embarking on high-throughput screening assays using large panels of compounds in various combinations to identify new treatments".

Understanding which patients with rectal cancer may be able to avoid surgery altogether is also a key aim of the program. Currently the treatment of rectal cancer often involves the combination of chemotherapy and radiation therapy prior to radical surgery to remove a significant length of bowel. However, around a quarter of these patients have no residual tumour remaining at the completion of their chemotherapy and radiation treatment, and could be spared from unnecessary surgery. The team is working with organoids derived from patients with rectal cancer to determine if organoids can be used to predict which patients are likely to have a complete response.



*Prof Paul McMurrick,  
Director Cabrini  
Monash University  
Department of  
Surgery.*

Prof McMurrick says if proven this approach will have significant implications for the medical management of patients with rectal cancer.

"Being able to avoid surgery will be a huge advancement in rectal cancer management. Being able to preserve organ function will significantly improve the quality of life for patients," said Prof McMurrick.

A further technological boost to the organoid program, led by Dr Christine Koulis and Dr Engel, is the development of tissue microarrays containing normal and tumour tissue specimens for each patient with matched organoids. Tissue microarray is a platform which allows the identification of tumour markers or 'biomarkers' that can be utilised for cancer research. Results from this platform will provide important novel prognostic and predictive information that may identify factors that can influence chemotherapy choice, leading to more personalised streamlining of therapy to each individual patient. Tissue microarray technology also has the potential to identify new protein targets that could form the basis of targeted therapies.

Cabrini is uniquely positioned to deliver the organoid program as a high-volume centre for the treatment of colorectal conditions. An extensive bioresource has been established which links paired normal and tumour specimens and their patient-matched organoids to patient data on the Cabrini Monash Colorectal Neoplasia Database. This database was established by Prof McMurrick in 2010 and collects over 350 parameters for each treatment episode including co-morbidities/risk factors, family history/genetics, treatment regimens and long-term oncologic outcomes. Together, CMUDS and Monash Biomedicine Discovery Institute have developed a powerful resource with the potential to change the management of colorectal cancer. The formidable alliance has already resulted in a number of published high impact studies.

"BEING ABLE TO AVOID SURGERY WILL BE A HUGE ADVANCEMENT IN RECTAL CANCER MANAGEMENT. BEING ABLE TO PRESERVE ORGAN FUNCTION WILL SIGNIFICANTLY IMPROVE THE QUALITY OF LIFE FOR PATIENTS"

*Microscope image of tumour organoid labelled with fluorescent dyes to visualize live (Hoescht, blue) versus dead cells (PI, red).*

# CLINICAL TRIAL A GAME CHANGER IN TREATING ADVANCED MELANOMA

CABRINI MONASH UNIVERSITY DEPARTMENT OF MEDICAL ONCOLOGY –  
THE SZALMUK FAMILY DEPARTMENT OF MEDICAL ONCOLOGY



*A/Prof Ben Brady, oncologist  
and Checkmate 066 clinical trial  
Principal Investigator. Photo credit:  
Aaron Francis / Newspix.*

Historically, but really only less than 10 years ago, the median life expectancy for a patient diagnosed with advanced melanoma was only eight to ten months, and they only had a ten per cent chance of surviving five years. This was a difficult reality that many Australians faced, as melanoma is the third most commonly diagnosed cancer in Australia. We also hold the unfortunate title of having the highest age-standardised melanoma incidence rate in the world.

In 2013, Ian was faced with this grim reality, diagnosed with stage four advanced metastatic melanoma. His oncologist at the time suggested he may only have three to six months to live. The standard of care chemotherapy treatment had a less than 15 per cent chance of success, and metastatic disease usually didn't respond well.

However, luck was on Ian's side. A new clinical trial, Checkmate 066, had just opened at Cabrini. Ian was eligible, meaning he had a chance of accessing a new experimental drug, Nivolumab, one of many immunotherapies that would go on to be a huge game changer in oncology.

Ian clearly recalls his first meeting with his Cabrini oncologist, Associate Professor Ben Brady.

"Ben spent about an hour and a half talking with me about the trial," Ian said.

"Everyone thought this would be my best hope, as Nivolumab was showing great promise in early trials. I remember my wife saying to me that I might get a couple of extra years to live. I would have crawled over broken glass to get on the trial and receive Nivolumab," Ian said.

The Checkmate 066 trial looked at whether Nivolumab, a new immunotherapy, improved the clinical outcomes for patients compared to those receiving standard of care chemotherapy, Dacarbazine.

Nivolumab, also known by the trade name Opdivo, is an antibody immune checkpoint inhibitor immunotherapy. It functions to block checkpoint proteins on cells in the immune system. By blocking these proteins, Nivolumab boosts the immune system response, unleashing its activity to fight cancer and destroy cancerous cells.



Ian, Checkmate 066 clinical trial patient, with Dina Cherfi, Clinical Trial Study Coordinator Oncology Research. Photo Credit: Darren James.

Principal Investigator for the Checkmate 066 trial and Ian’s oncologist, A/Prof Brady, led the study at Cabrini. He described the Checkmate 066 trial as “the gold standard in clinical trial design”.

“It was a double-blinded, international, multicentre, prospective trial,” A/Prof Brady said.

“Cabrini was the largest recruiting site in the world, our patients and team contributed greatly to what really is a landmark oncology trial.”

The term ‘landmark’ is not used lightly to describe oncology trials, it is only bestowed on those which significantly change the landscape of cancer therapy. They are studies of the highest impact, which lead to changes in current clinical practice.

Although the study was double-blinded, meaning the doctor and patient didn’t know what treatment they were receiving, Ian had a feeling he might have been on Nivolumab.

“I had a scan after nine weeks of being on treatment. My main lesions had shrunk 30 to 50 per cent, a remarkable response I was told. Every scan after that was either stable or shrinking. Eventually it got to the point where there was no longer detectable metastatic cancer in my lungs, a truly amazing outcome that the research team were so excited and amazed by, and my family incredibly grateful for. I most likely wouldn’t be here today without Nivolumab,” Ian said.

A/Prof Brady described the Checkmate 066 trial as the beginning of the end of chemotherapy in cancer.

#### Journal Reference

Robert C, Long GV, Brady B, Dutriaux C, Maio M, Mortier L, Hassel JC, Rutkowski P, McNeil C, Kalinka-Warzocho E, Savage KJ, Hernberg MM, Lebbé C, Charles J, Mihalcioiu C, Chiarion-Sileni V, Mauch C, Cognetti F, Arance A, Schmidt H, Schadendorf D, Gogas H, Lundgren-Eriksson L, Horak C, Sharkey B, Waxman IM, Atkinson V, Ascierto PA. (2015) Nivolumab in previously untreated melanoma without BRAF mutation. *N Engl J Med.* 372(4):320-30. doi:10.1056/NEJMoa1412082.

“We demonstrated that Nivolumab was able to extend the lives of patients with metastatic advanced melanoma, the first therapy ever to do so,” he said.

“Nivolumab has probably led to a cure in some advanced melanoma patients. Many of the original patients in this study are still alive eight years later. This is a remarkable change in patient outcomes, as not too long ago we would have estimated they only had months to live. Ian is one of these patients. Nivolumab has saved his life.”

The Checkmate 066 trial at Cabrini recruited 23 patients, the largest cohort from a single trial site in the world. A/Prof Brady was an author on its publication in the prestigious journal, *New England Journal of Medicine*. Nivolumab, developed by the Bristol Myers Squibb pharmaceutical company, was the very first immunotherapy approved in the world, receiving regulatory approval from the Pharmaceuticals and Medical Devices Agency (PMDA) in Japan to treat advanced melanoma on 4 July 2014, followed soon after by approvals from the USA Food and Drug Administration (FDA) in November, and in Europe and Australia in 2015.

“I WOULD HAVE CRAWLED OVER BROKEN GLASS TO GET ON THE TRIAL AND RECEIVE NIVOLUMAB... ....I MOST LIKELY WOULDN’T BE HERE TODAY WITHOUT NIVOLUMAB”

# INFORMING FUTURE CANCER AND PALLIATIVE CARE PROVISION DURING CRISES

CABRINI MONASH UNIVERSITY DEPARTMENT OF NURSING RESEARCH

The COVID-19 pandemic has impacted us all in ways we could never have imagined. Patient care has been disrupted in a variety of ways, resulting in increased stress for patients and caregivers. A new study at Cabrini, supported by an Alan Jackson Nursing Research Grant, will explore the experiences of people with cancer and their caregivers to inform future cancer and palliative care provision during crises.

Associate Professor Philip Russo, Director of the Cabrini Monash University Department of Nursing Research, together with Dr Lucy Kerr, a postdoctoral research fellow, is leading a collaborative project with Cabrini and Monash University researchers to explore experiences of people with cancer and their caregivers during COVID-19 to better prepare for the next pandemic.

Dr Kerr who is also a specialist cancer nurse said “The illness experiences of people with cancer and their caregivers are likely to have been detrimentally affected by the COVID-19 pandemic; however, given the emerging nature of this problem, little is currently known.”

“This research seeks to address this gap and help to improve cancer and palliative care service provision into the future.”

The advent of COVID-19 has introduced unprecedented change in hospitals across Australia. Routine healthcare services have been put aside to allow preparation for a potential surge of patients with COVID-19 requiring hospital care. Elective surgery, outpatient and pathology services have all been severely disrupted, affecting patients and healthcare workers (HCW) alike.

This alteration in work processes has even resulted in some cases in a complete change of employment role, or requests to take leave. There has also been an incredible influx of recommendations and guidelines from Commonwealth and state health departments, colleges, societies and associations, occasionally resulting in contrary guides and mixed messages.

We can learn so much from those who are directly responsible for the care of patients in an infectious disease crisis. Fears of infection, uncertainty and reliance on personal protective equipment, keeping updated on management guidelines and the wellbeing of colleagues and families have been identified as major concerns for HCW in recent studies.

The study at Cabrini involves a series of interviews with key informants such as those providing direct healthcare (nurses, doctors and allied health) from a variety of cancer service settings at Cabrini. These interviews provided crucial information for the next phase of the study, in-depth interviews from people with cancer and their caregivers.

“The findings from this study will inform future planning of cancer services during crisis management at Cabrini. Emerging infectious diseases, such as other novel viruses, and the emergence of multi-resistant organisms, pose an ongoing threat to our community. We can expect to see other COVID like pandemics in the future,” A/Prof Russo said.



*A/Prof Philip Russo,  
Director Cabrini  
Monash University  
Department of Nursing  
Research.*



*Dr Lucille Kerr,  
Postdoctoral Research  
Fellow, Cabrini Monash  
University Department of  
Nursing Research.*



“THE ILLNESS EXPERIENCES OF PEOPLE WITH CANCER AND THEIR CAREGIVERS ARE LIKELY TO HAVE BEEN DETRIMENTALLY AFFECTED BY THE COVID-19 PANDEMIC; HOWEVER, GIVEN THE EMERGING NATURE OF THIS PROBLEM, LITTLE IS CURRENTLY KNOWN”

Demis Balamatsias, Senior Clinical Trial Study Coordinator Oncology Research (left) with Leslie, an oncology clinical trial participant. Photo Credit: Darren James

# ADDRESSING CANCER PATIENTS NEEDS THROUGH COMMUNITY CARE

SZALMUK FAMILY PSYCHO-ONCOLOGY RESEARCH UNIT

Academic psychiatrist, psycho-oncology researcher and author, Professor David Kissane AC, believes there is a clear need for more support for patients suffering from cancer-related depression in our community.

“Clinical depression is the most prevalent psychological condition affecting cancer patients, but many patients do not receive treatment for their depression, due to a chronic shortfall in the hospital-based psycho-oncology workforce,” said Prof Kissane.

Recognising the need to improve access to psychology services in the community, Prof Kissane, Head of the Szalmuk Family Psycho-oncology Research Unit at Cabrini Research, led a Monash Partners Comprehensive Cancer Consortium (MPCCC) collaborative pilot that looked at a novel shared care model for cancer-related depression.

Shared care is based on a team-driven approach, in which a multidisciplinary group of healthcare professionals work in a co-ordinated fashion and are empowered to maximise the care of an individual patient. Shared care holds potential to relieve the care burden on acute hospital settings and to provide affordable services for patients and their families, close to where they live.

Funding from the Victorian Department of Health and Human Services allowed Prof Kissane and the research team to test a shared care model for cancer-related depression. They trained and mentored community-based psychologists to treat cancer-related depression and established a patient referral pathway from the acute hospital setting to community-based services. It enabled cancer patients to access services closer to where they lived. Run across the Monash Partners health services, including Cabrini Health (Brighton), Monash Cancer Centre, Monash Health (Moorabbin) and Peninsula Health (Frankston), the study brought together hospital-based oncologists and psycho-oncologists, specialty-trained community-based psychologists and general practitioners (GPs) to provide a coordinated system of care.

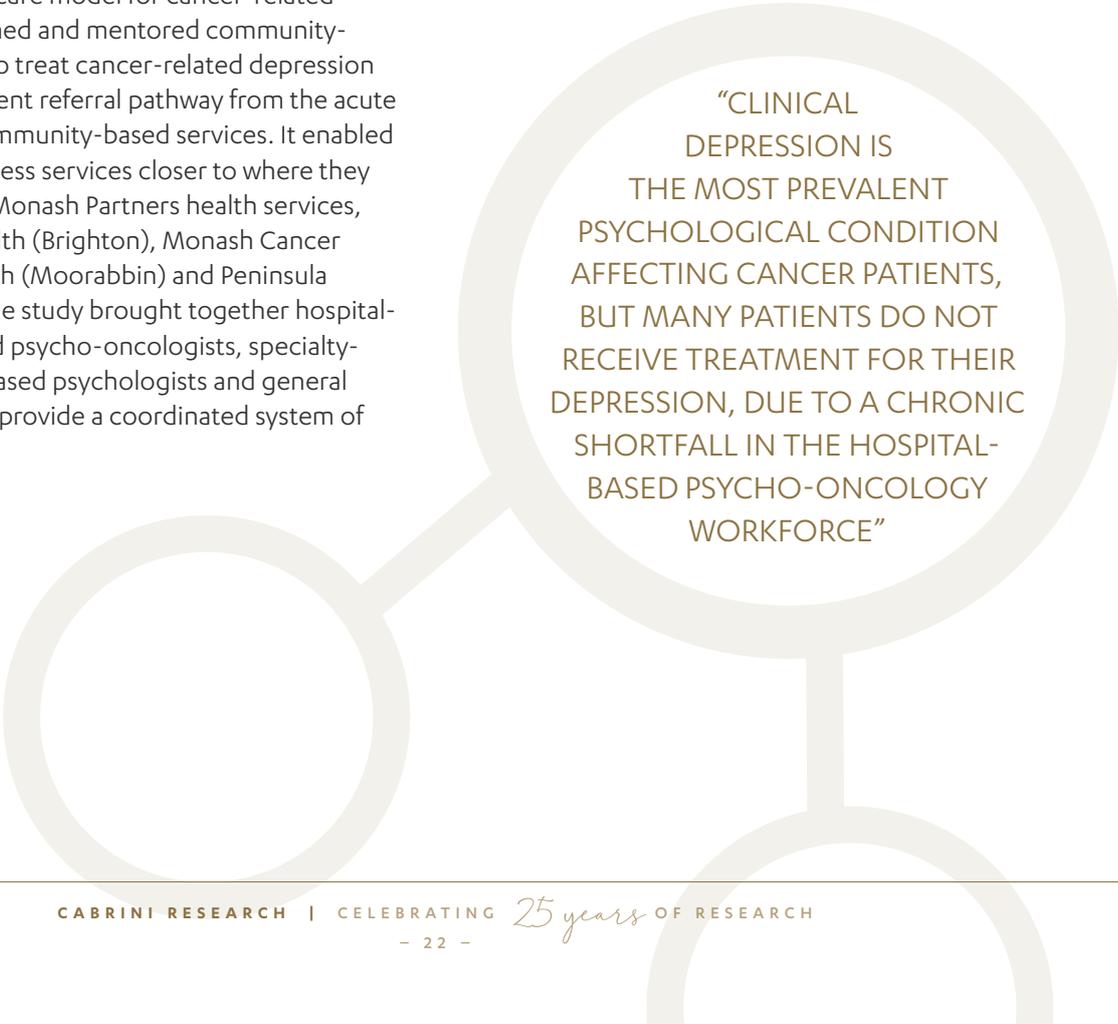
The shared care cancer-related depression pilot was extremely successful and had clear outcomes. Most cancer patients who participated found it to be effective and acceptable. It provided them with timely and affordable access to high-quality, cancer-specialised psychology services close to where they lived.

It was an effective way to upskill community-based psychologists using specialist training and expanded professional networks.

Prof Kissane says implementing the model would benefit hospitals by improved workforce capacity, and patients would have greater access to clinicians who can provide specialised treatment for cancer-related depression. Oncology teams in hospitals would be supported, allowing them to address the needs of their patients in a timely, affordable manner that is convenient to patients.

“This collaborative care model increases the confidence of community-based psychologists to treat patients with cancer, and it helps GPs to feel more confident about increased dosage of antidepressant medication when this is needed,” Prof Kissane said.

“Psycho-oncology services remain inadequate in Melbourne – this is one model of care that improves outcomes.”



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Team members of the shared care model for cancer-related depression project (left to right) Genevieve Murphy, Oncology Research Nurse, Professor David Kissane AC, Director Szalmuk Family Psycho-oncology Research Unit, and Anne Loupis, Project Manager.

# PATIENTS CAN DRIVE IMPROVED OUTCOMES THROUGH MORE THERAPY

CENTRE FOR ALLIED HEALTH RESEARCH AND EDUCATION

We must ensure patients have enough therapy practice for the best inpatient rehabilitation outcomes. During rehabilitation, we know patients don't often receive enough therapy and actually spend most of the day sitting and lying down. Participating in more occupational therapy and physiotherapy during inpatient rehabilitation enables patients to achieve better function and quality of life, and return home sooner. Increasing the amount of supervised therapy is not always an option however, as extra staffing costs places considerable pressure on hospital budgets and resources.

My Therapy was an original program conceived and piloted at Cabrini, led by Dr Natasha Brusco, formally of the Centre for Allied Health Research and Education (CAHRE) at Cabrini Research. It is a consumer driven, self-management program designed to increase the amount of therapy participation by patients, through independent practice of exercise and activity in addition to usual care, without the need for additional staff. It is tailored to individual needs, prescribed by a patient's treating occupational therapist and physiotherapist, and is practiced within business hours, evenings or weekends. The pilot study demonstrated that patients participating in My Therapy can achieve 100 minutes of extra weekly practice alongside usual care inpatient rehabilitation. For every patient receiving usual care who achieved a minimal important difference in function from admission to discharge, two patients receiving My Therapy achieved the same improvement in function. The benefits were achieved without additional staff, adverse events or safety concerns.

Following dissemination of the Cabrini My Therapy pilot work there was a strong desire for My Therapy to be implemented across health services. It is hypothesised that through sustained change to patient and clinician behaviour, and enhanced patient self-management, the pilot study benefits will continue to be realised.



*Dr Natasha Brusco  
formerly of CAHRE,  
and project lead for the  
My Therapy research  
program.*

This interest led to a successful NHMRC Partnership Grant, with almost \$1 million in funding, across Alfred Health, Cabrini Health,

Eastern Health, Healthscope, and Monash and La Trobe Universities. Led by Dr Natasha Brusco and supported at Cabrini by Chief Investigator Dr Annemarie Lee, Director of CAHRE at Cabrini Research, the NHMRC Partnership Grant will evaluate scaled up implementation of the My Therapy program, with respect to effectiveness, cost effectiveness and factors influencing implementation, across inpatient rehabilitation wards in the public and private partner healthcare organisations. The project will couple knowledge generation and knowledge translation with cost-effectiveness analyses.

Dr Brusco says My Therapy has the potential to influence national and international models of rehabilitation.

“By collaborating with clinicians and patient consumers, we can increase the dosage of rehabilitation. We expect this will help patients achieve a higher functional status by discharge, empower our patients and improve their ability to self-manage their health, as well as reduce the health service cost and rehabilitation length of stay”.



## Journal Reference

Brusco NK, Tilley L, Walpole B, Kugler H, Li R, Kennedy E, Morris ME. (2019) Feasibility of increasing the dosage of inpatient occupational therapy and physiotherapy rehabilitation via independent tasks and exercises: 'My Therapy'. *Aust Occup Ther J.* 66(6):739-752. doi: 10.1111/1440-1630.12614.



PARTICIPATING IN  
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Dr Annemarie Lee, Director Centre for Allied Health Research and Education (CAHRE) Cabrini Research (left) and Louise Tilley, Research Assistant CAHRE.

# CHANGING THE FUTURE FOR THOUSANDS OF PROSTATE CANCER PATIENTS

DEPARTMENT OF UROLOGY

Prostate cancer is the second most common cancer in men worldwide and has a 30 per cent recurrence rate. One of the current treatments for men with prostate cancer is a radical prostatectomy, an operation to remove the prostate gland and tissues surrounding it. Following surgery, patients are monitored via blood tests to check for cancer recurrence. Soon to be published ground-breaking research looking at the best way to locate recurrent prostate cancer in patients will change the future for thousands of people.

Cabrini Urologist Professor Mark Frydenberg, Director of the Department of Urology at Cabrini Research, together with former Cabrini medical student Dr Kavitha Gnanasambantham, were part of the team researching how to locate recurrent prostate cancer in patients and whether it was localised recurrence or in another part of the body.

“Following a radical prostatectomy if the blood test result isn’t zero and is rising, we are concerned there are active cancer cells that have recurred,” Prof Frydenberg said.

“The problem now is we don’t know exactly where the cancer cells are located. It can be localised near the bladder or it could have spread to lymph glands or the bones. The treatment options are very different depending on where it is.”

Dr Gnanasambantham said patients were then usually treated with salvage radiotherapy to the prostatic bed for presumed localised disease, or by androgen deprivation therapy for presumed advanced disease.

“Each type of treatment has its own side-effects, they can include urinary incontinence, irritation, inflammation and erectile dysfunction,” she said.

“It’s important to treat the cancer but we don’t want patients exposed to unnecessary therapy. We want to make sure we know where the recurrence is. Unfortunately routine imaging using CT scans of the abdomen and pelvis and nuclear bone scans rarely provides an answer at low PSA levels”.

The study, which included 119 patients, looked at <sup>68</sup>Gallium-labelled prostate-specific membrane antigen positron emission tomography (<sup>68</sup>Ga-PSMA-11 PET) and multiparametric magnetic resonance imaging (mpMRI), new imaging modalities that have been proven to detect recurrent prostate cancer more accurately, and whether the addition of the mpMRI scan had a role to play in picking up local recurrence.

“We looked at the detection rate for each type of scan and it was quite clear that <sup>68</sup>Ga-PSMA-11 PET was good at detecting distant recurrence but less accurate for local recurrence,” Dr Gnanasambantham said.

“But the mpMRI was substantially better at detecting local recurrence compared to <sup>68</sup>Ga-PSMA-11 PET scanning. So pairing them together was the best option. Having both scans improved diagnosis and guided better treatment selection for patients.”

Prof Frydenberg said the research would ultimately change how patients with recurrent prostate cancer were treated.

“Whilst the novel imaging does not detect every microscopic recurrence, it is much better than conventional imaging and provides the patient some assurance that if salvage radiotherapy is being recommended, it is to treat a suspected or proven local recurrence. Distant disease, unlikely to be cured by local treatments, can then be identified and treated on its merits”.



*Prof Mark Frydenberg,  
Director Department of  
Urology.*



*Dr Kavitha  
Gnanasambantham,  
former Cabrini medical  
student.*

A microscopic image of cells, likely cancer cells, stained in shades of blue and teal. The cells are irregular in shape and contain dark, oval nuclei. Overlaid on the image are three white-outlined circles of varying sizes. A large circle in the upper right contains a quote. Two smaller circles are positioned to the left and bottom right of the large circle, connected to it by thin white lines, suggesting a flow or relationship between the text and the visual elements.

“IT’S IMPORTANT TO  
TREAT THE CANCER  
BUT WE DON’T WANT  
PATIENTS EXPOSED  
TO UNNECESSARY  
THERAPY”



*A/Prof David Brewster, Deputy Director and Head of Intensive Care Research at Cabrini, and the Clinical Dean for the Monash University Clinical School, and Shannon Simpson, ICU research coordinator.*

A NEW STUDY HAS HIGHLIGHTED JUST HOW SIGNIFICANT THE RISKS ARE WITH INTUBATING CRITICALLY ILL PATIENTS, WITH MORE THAN 40 PER CENT SUFFERING A LIFE THREATENING COMPLICATION.

# COMPLICATIONS OF INTUBATING CRITICALLY ILL PATIENTS

INTENSIVE CARE RESEARCH UNIT

Tracheal intubation is a high risk procedure commonly performed in critically ill patients who are suffering from severe respiratory problems requiring support to breathe. A new study published in JAMA in 2021 has highlighted just how significant the risks are with intubating critically ill patients, with more than 40 per cent of critically ill patients suffering a life threatening complication.

The International Observational Study to Understand the Impact and Best Practices of Airway Management in Critically Ill Patients (INTUBE), was conducted to gain a better understanding of the complications experienced by critically ill patients undergoing intubation in intensive care units (ICUs), emergency departments, and wards from October 1, 2018 to July 31, 2019. INTUBE is the largest study of intubations in critically ill patients ever conducted, and included 2964 patients from 197 sites in 29 countries across five continents.

Cabrini researcher Associate Professor David Brewster, Deputy Director and Head of Intensive Care Research at Cabrini, and the Clinical Dean for the Monash University Clinical School, was a co-author and the national coordinator for the INTUBE study in Australia and New Zealand.

A/Prof Brewster said the study shed light on the “significant morbidity and mortality risk associated with intubation in the critically ill as well as patient and operator factors associated with worse outcomes”.

“This is a major achievement” A/Prof Brewster said. “To have such a large international collaboration of researchers successfully creating this database shows that research on such a large scale is possible within the ICU community with regards to airway management. It is by far the largest study ever conducted on intubation outcomes and the first true multi-national study in this area.”

“We found major peri-intubation events occurred in a higher percentage of patients who later died in ICU (versus ICU survivors). This means that relevant outcomes were identified. Major peri-intubation events were more frequent in patients who required multiple intubation attempts. Worse outcomes for patients were less common amongst skilled and experienced operators and less common with the use of videolaryngoscopy.

This showed the outcomes are modifiable.” A/Prof Brewster said on a personal level, it was fantastic to be able to lead such a large trial in Australia and New Zealand.

“The support of the Australian and New Zealand Intensive Care Society (ANZICS) was crucial in recruiting sites and the ability to manage our national dataset from the Cabrini ICU was only possible given the hard work of our ICU research coordinator, Shannon Simpson”, he said.

## Key findings from the INTUBE study included:

- The main reason for intubation was respiratory failure in 52.3 per cent of patients, followed by neurological impairment in 30.5 per cent, and cardiovascular instability in 9.4 per cent.
- More than 45 per cent of patients experienced at least one life threatening complication during intubation.
- The most common complications following tracheal intubation was cardiovascular instability, experienced by 1172 patients (42.6 per cent), severe hypoxemia in 272 patients (9.3 per cent) and cardiac arrest in 93 patients (3.1 per cent).
- Overall ICU mortality was 32.8 per cent (966 patients).
- Patients who experienced a complication due to intubation were more likely to die (40.7 per cent) than those who did not experience a complication (26.3 per cent).
- First pass intubation success was achieved for 2360 patients (79.8 per cent). A second attempted intubation was achieved for 460 patients (15.6 per cent). More than two attempts at intubation were required for 133 patients (4.5 per cent). The rate of complications was significantly lower with first pass intubation success than it was for patients requiring two attempts and for patients requiring three or more attempts.

## Journal Reference

Russotto V, Myatra SN, Laffey JG, Tassistro E, Antolini L, Bauer P, Lascarrou JB, Szuldrzynski K, Camporota L, Pelosi P, Sorbello M, Higgs A, Greif R, Putensen C, Agvald-Öhman C, Chalkias A, Bokums K, Brewster D, Rossi E, Fumagalli R, Pesenti A, Foti G, Bellani G; INTUBE Study Investigators. (2021) Intubation Practices and Adverse Peri-intubation Events in Critically Ill Patients From 29 Countries. *JAMA*. 325(12):1164-1172. doi: 10.1001/jama.2021.1727.

# SCRIBES ENABLE EMERGENCY DOCTORS TO GET TO BEDSIDES MORE OFTEN

ALAN, ADA AND EVA SELWYN EMERGENCY DEPARTMENT

Emergency medicine provides one in 10 medical consultations in Australia. This is about 7.5 million consultations every year. Most acute care of urgent medical problems starts in an emergency department. The Alan, Ada and Eva Selwyn Emergency Department at Cabrini has been a leader in understanding how to enable emergency doctors to get to the bedsides of patients more often. The Scribe research program was led by former Cabrini emergency physician and researcher, Professor Katie Walker.

It is not widely known that an emergency doctor has to spend 48 per cent of their time during a clinical shift typing at a computer instead of seeing patients. A medical scribe is a trained assistant for a doctor. The aim of the scribe is to free the doctor from paperwork/typing and allow them to spend more time thinking about, and consulting, with their patients. They stand with the doctor at patients' bedsides, documenting consultations, arranging tests and appointments, completing electronic medical record tasks, finding information and people, booking beds, printing discharge paperwork, and doing clerical tasks. Despite the existence of the role in the USA for the last 20 to 30 years, there had been almost no independent evaluation of their effectiveness anywhere in the world. Cabrini emergency department brought this concept from the USA to Australia for the first time and tested the role critically, publishing a series of papers on their findings.

The research team initially tested the role in a pilot with an American scribe and then with an extended pilot. Following the successful pilot they developed a training program for Australian pre-medical and medical students and trained their scribes. Their research has demonstrated patients tolerate the presence of scribes well, and less than one per cent of consultations are inappropriate for scribes. Most doctors working with scribes support or strongly support their use, with 15 per cent preferring not to work with scribes.

In 2019 the researchers published the first multicentre randomised trial evaluating the effectiveness of scribes in



*Professor Katie Walker, Head of the Scribe Research Program and former Director of Emergency Medicine Research.*

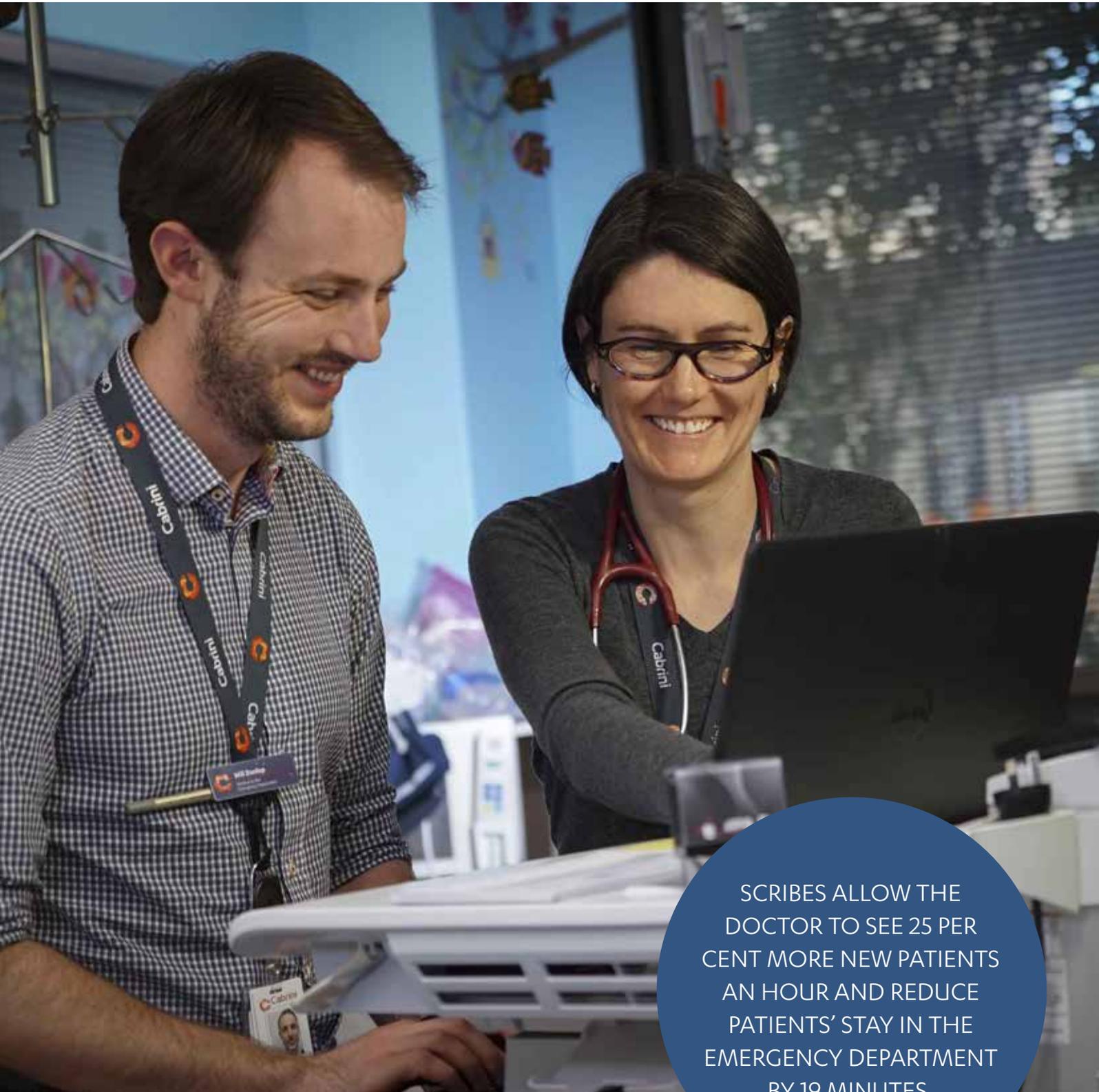
public and private emergency departments in the British Medical Journal. Scribe programs were implemented and tested in five Victorian emergency departments representative of public, private and rural services across a period of three years. Their work demonstrated that scribes allow the doctor to see 25 per cent more new patients an hour and reduce patients' stay in the emergency department by 19 minutes (both in public and private hospitals). This could allow doctors to see 9.4 million patients across Australia with the current medical workforce, if scribes were available in every emergency department.

The greatest gains were achieved by placing scribes with senior doctors at triage, the least by using them in sub-acute/fast track regions. No significant harm involving scribes was reported. The cost-benefit analysis based on productivity and throughput gains, showed a favourable financial position with use of scribes.

The work by Prof Walker and team received a lot of international interest in the scribe concept. More than 1.2 million people heard about the British Medical Journal paper via Twitter and they achieved the highest multi-channel media exposure for emergency medicine research in 2019.

## Journal Reference

*Walker K, Ben-Meir M, Dunlop W, Rosler R, West A, O'Connor G, Chan T, Badcock D, Putland M, Hansen K, Crock C, Liew D, Taylor D and Staples M. (2019) Impact of scribes on emergency medicine doctors' productivity and patient throughput: multicentre randomised trial. British Medical Journal 364: l121. doi: 10.1136/bmj.l121.*



SCRIBES ALLOW THE DOCTOR TO SEE 25 PER CENT MORE NEW PATIENTS AN HOUR AND REDUCE PATIENTS' STAY IN THE EMERGENCY DEPARTMENT BY 19 MINUTES.

*William Dunlop, Medical Scribe, and Professor Katie Walker, Head of the Scribe Research Program and former Director of Emergency Medicine Research.*

# BIG 1-98 CLINICAL TRIAL CHANGES THE PRACTICE OF HORMONAL ADJUVANT THERAPY

CABRINI MONASH UNIVERSITY DEPARTMENT OF MEDICAL ONCOLOGY –  
THE SZALMUK FAMILY DEPARTMENT OF MEDICAL ONCOLOGY

Breast cancer is the most commonly diagnosed cancer in Australia. More than 20,000 diagnoses are made each year, and more than 3000 people died from breast cancer in Australia in 2020. During the past 25 years, research has driven changes in how we detect, treat and care for patients with breast cancer, which has had an immense impact on survival rates. Five year survival rates for breast cancer are now 91 per cent. A continued commitment to research will ensure we keep making progress.

In early stage breast cancer there is a risk of cancer recurrence post-surgery, including distant metastases especially in the first three years. Distant metastatic cancers compose the majority of early recurrences and are a well-recognised predictor of breast cancer death. To counter this risk, anticancer treatment is given post-surgery to eliminate any tumor cells that might remain in the body. This type of therapy is called adjuvant therapy. Adjuvant therapy significantly decreases the chance that the cancer will return (or recur), and it also improves the chances of surviving breast cancer.

Oestrogen is a known key regulator of normal breast tissue growth and differentiation. It can also stimulate the growth of certain types of breast cancer, known as oestrogen receptor (ER) positive breast cancer. About 75 per cent of all breast cancers are ER positive. Oestrogen is primarily produced in the ovaries. Following menopause, the ovaries cease to make oestrogen but the body can still produce a small amount by using an enzyme called aromatase, which turns other sex hormones called androgens into oestrogen. Reducing the production of oestrogen helps to keep ER positive breast cancer from growing.

From as early as 1985, tamoxifen was the gold standard adjuvant treatment for ER positive early breast cancer in postmenopausal women. Tamoxifen is a selective oestrogen receptor modulator, which prevents cancer cells from accessing oestrogen that they need to grow and multiply.

The third generation aromatase inhibitor, letrozole, marketed as Femara, was approved in the late 1990's for postmenopausal ER positive breast cancer.



*Professor Gary Richardson OAM, BIG 1-98 clinical trial Principal Investigator, Group Director Cabrini Research, and Director Cabrini Monash University Department of Medical Oncology, Szalmuk Family Department of Medical Oncology.*

Letrozole lowers the level of oestrogen in the body by inhibition of aromatase enzymes, stopping the conversion of androgens to oestrogen.

The Breast International Group 1-98 (BIG 1-98) clinical trial looked at whether letrozole was more effective as an initial adjuvant therapy or as sequential therapy with tamoxifen in either order when given for five years. From 1998 to 2003, 8010 women were enrolled into the trial for a median time of 8.1 years. The study demonstrated that letrozole was more effective than tamoxifen in improving breast cancer survival and preventing recurrence among women with breast cancer, including a significant reduction in the risk of distant metastases.

The BIG 1-98 trial was a landmark study for adjuvant hormonal treatment. Globally, it changed clinical practice of adjuvant therapy, establishing aromatase inhibition as the gold standard of care for postmenopausal women with early ER positive breast cancer.

Cabrini played a key role in Australia's contribution to the global study, enrolling 24 patients on the study, a large cohort for a single site. Professor Gary Richardson OAM, Principal Investigator for the BIG 1-98 trial at Cabrini, said the trial, along with other similar aromatase inhibitor trials carried out at the same time worldwide, had "revolutionised the treatment of early breast cancer, benefiting millions of women around the globe".

## Journal Reference

Coates AS, Keshaviah A, Thürlimann B, Mouridsen H, Mauriac L, Forbes JF, Paridaens R, Castiglione-Gertsch M, Gelber RD, Colleoni M, Láng I, Del Mastro L, Smith I, Chirgwin J, Nogaret JM, Pienkowski T, Wardley A, Jakobsen EH, Price KN, Goldhirsch A. (2007) Five years of letrozole compared with tamoxifen as initial adjuvant therapy for postmenopausal women with endocrine-responsive early breast cancer: update of study BIG 1-98. *J Clin Oncol.* 25(5):486-92. doi: 10.1200/JCO.2006.08.8617.

THE TRIAL, ALONG WITH OTHER SIMILAR AROMATASE INHIBITOR TRIALS CARRIED OUT AT THE SAME TIME WORLDWIDE, “REVOLUTIONISED THE TREATMENT OF EARLY BREAST CANCER, BENEFITING MILLIONS OF WOMEN AROUND THE GLOBE”.



Oncology Research Clinical Trials team members (left to right) Kate Chandler, Kate Hurford and Timothy Colgan.  
Photo Credit: Darren James.

# CALL TO ACTION TO ADDRESS GLOBAL OVERMEDICALISATION OF LOW BACK PAIN

MONASH-CABRINI DEPARTMENT OF CLINICAL EPIDEMIOLOGY

Low back pain is the leading cause of disability worldwide, affecting an estimated 540 million people at any one time. The burden of back pain has doubled in the past 25 years. It can affect anyone at almost any age, and almost everyone will experience it at some stage of their life. Treatment varies widely, but use of low value treatments such as bed rest and dangerous drugs as well as surgery and overuse of imaging is rife across the world, including in low- and middle-income countries.

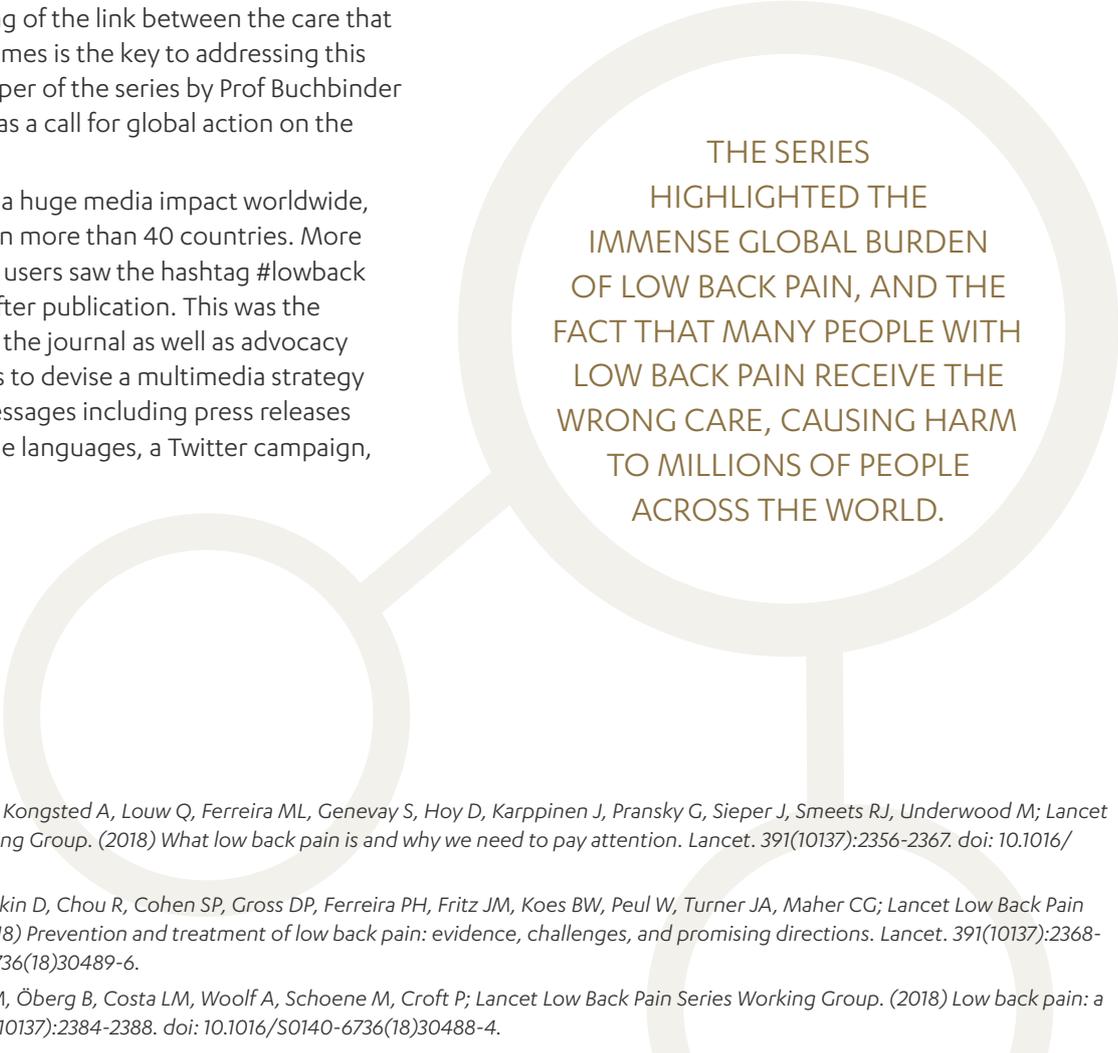
Professor Rachelle Buchbinder AO, Director of the Monash-Cabrini Department of Clinical Epidemiology led an international group of 32 authors from 12 countries in writing a groundbreaking series of three papers outlining the issues and proposing solutions. Published in the prestigious and influential *Lancet* in March 2018, the series highlighted the immense global burden of low back pain, and the fact that many people with low back pain receive the wrong care, causing harm to millions of people across the world and wasting valuable healthcare resources.

A better understanding of the link between the care that is delivered and outcomes is the key to addressing this problem. The third paper of the series by Prof Buchbinder and her colleagues, was a call for global action on the problem.

The *Lancet* series had a huge media impact worldwide, with media coverage in more than 40 countries. More than 15 million Twitter users saw the hashtag #lowbackpain in the first days after publication. This was the result of working with the journal as well as advocacy and policy consultants to devise a multimedia strategy to disseminate the messages including press releases translated into multiple languages, a Twitter campaign,

country media focal points, and email banners. The series has also contributed to catalysing changes in several countries, while the World Health Organisation (WHO) is now developing guidelines for the management of chronic primary low back pain in adults, with Prof Buchbinder among the Guideline Development Panel members.

Prof Buchbinder was recognised in the Australia Day Honours 2020 and became an Officer of the Order of Australia in recognition of her outstanding contribution to epidemiology and rheumatology research and medical education. For the past three years she has been listed on the Highly Cited Researchers list from Clarivate Analytics. This list recognises world-class researchers selected for their exceptional research performance, demonstrated by the production of multiple highly cited papers that rank in the top one per cent by citations for a given field in the last decade in Web of Science. Prof Buchbinder's field is "cross field", meaning across more than one research field.



THE SERIES HIGHLIGHTED THE IMMENSE GLOBAL BURDEN OF LOW BACK PAIN, AND THE FACT THAT MANY PEOPLE WITH LOW BACK PAIN RECEIVE THE WRONG CARE, CAUSING HARM TO MILLIONS OF PEOPLE ACROSS THE WORLD.

## Journal References

Hartvigsen J, Hancock MJ, Kongsted A, Louw Q, Ferreira ML, Genevay S, Hoy D, Karppinen J, Pransky G, Sieper J, Smeets RJ, Underwood M; *Lancet Low Back Pain Series Working Group*. (2018) What low back pain is and why we need to pay attention. *Lancet*. 391(10137):2356-2367. doi: 10.1016/S0140-6736(18)30480-X.

Foster NE, Anema JR, Cherkin D, Chou R, Cohen SP, Gross DP, Ferreira PH, Fritz JM, Koes BW, Peul W, Turner JA, Maher CG; *Lancet Low Back Pain Series Working Group*. (2018) Prevention and treatment of low back pain: evidence, challenges, and promising directions. *Lancet*. 391(10137):2368-2383. doi: 10.1016/S0140-6736(18)30489-6.

Buchbinder R, van Tulder M, Öberg B, Costa LM, Woolf A, Schoene M, Croft P; *Lancet Low Back Pain Series Working Group*. (2018) Low back pain: a call for action. *Lancet*. 391(10137):2384-2388. doi: 10.1016/S0140-6736(18)30488-4.



Prof Rachelle Buchbinder AO (centre) with A/Prof Manuela Ferreira and Prof Chris Maher. Prof Buchbinder is leading a global call to action on back pain treatment, which three new studies in the Lancet show is ineffective and often harmful. March 2018.  
Photo Credit: Eddie Jim | The Sydney Morning Herald and The Age Photos.

# EARLY ACCESS TO NOVEL TREATMENTS VIA CLINICAL TRIALS SAVES LIVES

CABRINI MONASH UNIVERSITY DEPARTMENT OF MEDICAL ONCOLOGY –  
THE SZALMUK FAMILY DEPARTMENT OF MEDICAL ONCOLOGY

June 2021 was an incredible milestone for Han Tsai and his oncologist Associate Professor Jeremy Shapiro. It marked the 10 year anniversary since Han was enrolled on the PREVAIL clinical trial for advanced prostate cancer, a trial evaluating a novel hormone therapy called MDV3100. As Han's prostate cancer had spread, and become resistant to all other treatments, his prognosis was guarded. He knew that half the patients in his situation would not survive beyond two years. A/Prof Shapiro suggested he consider a new clinical trial that just opened at Cabrini. Han would either be receiving a new hormone tablet (MDV3100) or a placebo tablet. If this trial was not effective, the plan was to switch to chemotherapy.

Han agreed, and within weeks of starting the study medication his PSA began to fall, and he began to feel healthier. Even better, the medication did not cause him any side-effects. By the six month mark his PSA was undetectable, and by the one year, all evidence of cancer had disappeared from his scans. When the study results were made available, Han was informed he was receiving the hormone tablet. He was offered the opportunity to continue to receive the medication, funded by the study team. He readily accepted. He has continued on this treatment ever since, with no evidence of recurrent cancer now at the 10 year mark.

Han was one of the first Australian patients to access this novel hormone therapy, now known as enzalutamide. Fast forward to 2021, and enzalutamide is now a routine drug for treating advanced prostate cancer, however it is still not yet PBS funded for most patients until after they have tried chemotherapy. Despite the excellent outcomes seen with Han, and many other patients in the PREVAIL trial, patients must either accept the side-effects of chemotherapy or self fund this expensive medication (\$50,000 per year).

"Han's story is truly a testament to early access of novel treatments via clinical trials," A/Prof Shapiro, Principal Investigator for the PREVAIL trial at Cabrini, said.

"Not only have the results been amazing for Han, but it has also allowed all other trial participants access to an



A/Prof Jeremy Shapiro, oncologist and PREVAIL clinical trial Principal Investigator. Photo Credit: Darren James.

expensive and unfunded agent earlier in their disease course, delaying the need to commence chemotherapy, and thereby improving quality of life."

Prostate cancer is the most commonly diagnosed cancer and the sixth leading cause of cancer-related death among men worldwide. Prostate cancer is an androgen-dependent malignancy. Although medical or surgical castration is effective initially, the cancer eventually becomes resistant and requires additional treatment, usually chemotherapy. Enzalutamide is taken orally and works by blocking the effect of the hormone testosterone on prostate cancer cells. The PREVAIL study examined the benefit of enzalutamide versus placebo in men with metastatic prostate cancer who had progressed despite androgen deprivation therapy but had not yet received chemotherapy. A total of 1717 patients were enrolled at 207 sites globally between 2010 and 2012. The results of the PREVAIL trial were published in the New England Journal of Medicine in 2014. Results showed significant improvement in overall survival for patients taking enzalutamide compared with placebo, and also allowed a long delay before chemotherapy was required. The outcomes were so favourable that the trial was halted prematurely to offer all patients initially enrolled on placebo, an opportunity to receive enzalutamide.

## Journal Reference

Beer TM, Armstrong AJ, Rathkopf DE, Loriot Y, Sternberg CN, Higano CS, Iversen P, Bhattacharya S, Carles J, Chowdhury S, Davis ID, de Bono JS, Evans CP, Fizazi K, Joshua AM, Kim CS, Kimura G, Mainwaring P, Mansbach H, Miller K, Noonberg SB, Perabo F, Phung D, Saad F, Scher HI, Taplin ME, Venner PM, Tombal B; PREVAIL Investigators. (2014) Enzalutamide in metastatic prostate cancer before chemotherapy. *N Engl J Med.* 371(5):424-33. doi: 10.1056/NEJMoa1405095.



“HAN’S STORY IS TRULY A TESTAMENT TO EARLY ACCESS OF NOVEL TREATMENTS VIA CLINICAL TRIALS.”

*Han, PREVAIL clinical trial patient, has brought flowers for A/Prof Shapiro’s secretary every time he has visited for the past ten years.*

# THE POWER OF DATA – DRIVING BENCH TO BEDSIDE DISCOVERIES IN BOWEL CANCER

CABRINI MONASH UNIVERSITY DEPARTMENT OF SURGERY



Professor Paul McMurrick, Director Cabrini Monash University Department of Surgery.

“THE DATABASE  
ALLOWS SURGEONS  
TO HAVE A GREATER  
IMPACT ON PATIENT  
OUTCOMES. IT IS NO LONGER  
JUST ABOUT THE PERSON THEY  
WERE SEEING THAT DAY IN  
SURGERY, THEY CAN IMPACT  
THE COMMUNITY IN A  
BROADER SENSE”

Bowel cancer is the third most common type of newly diagnosed cancer in Australia and is the second biggest cancer killer. It is stage dependent, meaning if treated early, people do very well, but if not then the outcomes can be very poor.

For decades Cabrini has been treating more patients with bowel cancer than any other private or public hospital in Victoria. In 2006 the planning for a Cabrini Monash Colorectal Neoplasia Database (CMCND) commenced, led by Professor Paul McMurrick, head of the Cabrini Monash University Department of Surgery. It was envisioned that a bowel cancer clinical data management system would be the centerpiece of Cabrini’s contemporary bowel cancer treatment service.

The CMCND was implemented in 2010, and is now a well-established registry capturing data on patients with either bowel cancer or benign bowel neoplasia surgically treated at Cabrini Health and other Monash affiliated hospitals, including The Alfred, Peninsula Health and Monash Medical Centre in Dandenong. It is used successfully as a platform for clinical translational research, is a source of high quality data on the clinical treatment and outcomes of patients, and provides reports on the quality of clinical work of both individuals and of unit clusters. In 2014 Prof McMurrick and database manager Karen Oliva, together with members of the

Cabrini Monash University Department of Surgery, successfully published the first paper based on data from the CMCND. The paper addressed the data collection of the first 1000 patients, which was delivered at 100 per cent completion, reflecting over 27,000 data points. The CMCND has facilitated extensive research ever since.

The Cabrini Monash University Department of Surgery has published numerous research papers detailing factors that influence or predict patient outcomes after colorectal cancer surgery.

“The database allows surgeons to have a greater impact on patient outcomes. It is no longer just about the person they were seeing that day in surgery, they can impact the community in a broader sense. The collection of high quality data in the CMCND will have an impact on improving health for the Australian community,” Prof McMurrick said.

The structure and success of the CMCND collection model led the Colorectal Surgical Society of Australia and New Zealand (CSSANZ) to adopt it as the Binational Colorectal Cancer Audit (BCCA) in 2013.



Karen Oliva, Cabrini Monash Colorectal Neoplasia Database Manager (2010-2021).

To ensure scalability, BCCA modified the CMCND to allow participation at the level of the current data set (“Extended Data Set”) or at a minimum data set level, allowing participation by smaller, and less well supported clinical centres. There has been enthusiastic uptake by multiple centres. Now, almost 100 sites across Australia and New Zealand are contributing data from more than 38,000 patients. The registry allows surgeons to benchmark their performance amongst their peers, ensuring a commitment to the highest standards of patient care.

One of the recent developments for the CMCND was the incorporation of a standardised set of colorectal cancer patient reported outcome measures (PROMs). The new development allows direct patient entry of data relating to all aspects of quality of life and functional outcomes following surgical treatment for bowel cancer. What matters most are the outcomes that patients experience and this data will provide a feedback loop between the patient and the clinician to ensure optimised treatment for all patients.

#### Journal Reference

McMurrick PJ, Oliva K, Carne P, Reid C, Polglase A, Bell S, Farmer KC, Ranchod P. (2014) The first 1000 patients on an internet-based colorectal neoplasia database across private and public medicine in Australia: development of a binational model for the Colorectal Surgical Society of Australia and New Zealand. *Dis Colon Rectum*. 57(2):167-73. doi: 10.1097/DCR.0000000000000041.

CMCND tissue banking provides an incredibly powerful platform for clinical research. The Cabrini Monash University Department of Surgery collaborates with the Monash Biomedicine Discovery Institute’s Epithelial Regeneration Laboratory, led by Professor Helen Abud. The collaboration brings together a powerful partnership of clinical and basic research expertise to drive rapid translation of research into the clinic. Data and tissue collected in the clinic can be tested in the lab, and the findings taken straight back to clinical care, so that they become available to patients as quickly as possible.

The major challenge with the CMCND is funding. It crosses both clinical care and discovery research, meaning it doesn’t necessarily come under the funding arrangements for either of these two groups. Since the beginning, the CMCND has been entirely funded by the Cabrini Monash University Department of Surgery. They are incredibly thankful for the benevolent support from donors and supporters that maintains this very important work.

# PREVENTING HOSPITAL ACQUIRED INFECTIONS – LEARNINGS FROM COVID-19

CABRINI MONASH UNIVERSITY DEPARTMENT OF NURSING RESEARCH

The infection prevention challenges presented by COVID-19 are unprecedented and have resulted in a heightened awareness of hospital acquired infections. To prepare for the admission and treatment of patients with or suspected with COVID-19, a number of new and modified initiatives have been implemented across Cabrini and other healthcare organisations. An increased emphasis on infection prevention education for all healthcare workers, hand hygiene, cleaning, and the use of personal protective equipment (PPE) are some of the interventions that have been implemented.

Outside of COVID-19 the use of PPE, hand hygiene and cleaning are fundamental in every infection prevention program, yet deficits in implementation and compliance have persisted. Some of the barriers to compliance include environmental factors (lack of convenient hand basins), insufficient knowledge, lack of PPE and risk behaviours. Incorrect removal of PPE can also put healthcare workers at risk of self-contamination. The heightened awareness COVID-19 has introduced may mean there is increased compliance and diligence. Whilst preventing the spread of COVID-19, the new and modified activities implemented during the pandemic should also prevent many other types of infection.

Funded by an Alan Jackson Research Grant, a new study at Cabrini will measure the impact that infection prevention interventions implemented for COVID-19 has on other healthcare associated infections. Associate Professor Philip Russo, Director of the Cabrini Monash University Department of Nursing Research is leading the research, and is joined by members of his research team Dr Lucille Kerr and Elizabeth Todio, and Cabrini Research biostatistician Associate Professor Wei Wang.

They are collaborating with Robyne Renton, Infection Control Coordinator for Cabrini Health, Professor Brett Mitchell from the University of Newcastle, and Dr Andrew Stewardson from Alfred Health. The study will retrospectively review three years of laboratory data of infections recorded from inpatients at Cabrini Malvern, Brighton and Ashwood. Data from February 2018 to January 2020 will be compared to data collected from February 2020 to January 2021, in order to identify if increased infection prevention awareness brought about by COVID-19 has impacted on hospital infection rates. Data will also be collected from the infection control team on the type, timing and location of various COVID-19 specific interventions that were implemented during 2020 to identify changes that could be implemented permanently to reduce hospital acquired infections.

THE INFECTION  
PREVENTION  
CHALLENGES PRESENTED BY  
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AND HAVE RESULTED IN A  
HEIGHTENED AWARENESS  
OF HOSPITAL ACQUIRED  
INFECTIONS.



*A/Prof Philip Russo,  
Director Cabrini  
Monash University  
Department of Nursing  
Research.*



*Dr Lucille Kerr,  
Postdoctoral Research  
Fellow, Cabrini Monash  
University Department of  
Nursing Research.*



Oncology Research Clinical Trials team members (left to right) Dina Cherfi, Demis Balamatsias and Timothy Colgan. One of the COVID-19 initiatives implemented was the use of masks across Cabrini.



Elizabeth Todio,  
Research Assistant,  
Cabrini Monash  
University Department  
of Nursing Research.



A/Prof Wei Wang,  
Biostatistician Cabrini  
Research.

# LEADING THE WAY IN MUSCULOSKELETAL RESEARCH EXCELLENCE

MONASH-CABRINI DEPARTMENT OF CLINICAL EPIDEMIOLOGY



*The Hon Greg Hunt MP, Minister for Health and Aged Care, speaking at the ANZMUSC Clinical Trial Network CRE official opening.*



*Prof Rachelle Buchbinder AO and the Hon Greg Hunt MP, Minister for Health and Aged Care, at the ANZMUSC Clinical Trial Network CRE official opening.*

Arthritis and musculoskeletal conditions are an immense burden on the world's population, accounting for 18.3 per cent of years lived with a disability globally.

In Australia, these conditions are the most common chronic disorder, affecting 28 per cent (or 6.1 million) of Australians, and making up almost one-quarter of the total disability burden.

The Australia and New Zealand Musculoskeletal (ANZMUSC) Clinical Trials Network aims to optimise musculoskeletal health through high quality, collaborative research. Formed to emulate other successful clinical trial networks in Australia, ANZMUSC had an inaugural summit in Melbourne in 2015, attended by more than 100 clinical researchers, clinicians, consumer representatives, policy makers and funders, who came together and agreed on the vision, mission, values and first year goals towards establishing the network.

ANZMUSC is now a multidisciplinary network of more than 300 members from 30 universities, 31 hospitals and 17 research institutes involving over 30 disciplines. As well as executive and scientific committees, it also has a consumer advisory committee who form an integral part of the network. In 2018, ANZMUSC was awarded an NHMRC Centre for Research Excellence (CRE), received funding worth \$2.5 million, and the NHMRC ANZMUSC Clinical Trials Network CRE was officially opened by the Federal Minister for Health and Aged Care the Hon Greg Hunt MP on 22 March 2018 at Cabrini Research. The network now boasts an osteoarthritis and back pain

special interest group (the latter supported by its own ANZBACK CRE) and is in the process of setting up a basic science special interest group.

The NHMRC ANZMUSC Clinical Trial Network endorses and promotes high quality clinical trials that address important evidence gaps. It builds research capacity through practitioner and postdoctoral fellowships and PhD scholarships, fosters links between clinical and consumer groups, advocates for musculoskeletal research, and enables effective transfer of research outcomes into clinical practice and health policy for improved patient outcomes. It is also formulating NHMRC-endorsed Australian Living Guidelines for the pharmacologic management of inflammatory arthritis and separate living guidelines of juvenile idiopathic arthritis, partly supported by two large Australian Department of Health grants. It has also formulated national living guidelines for COVID-19 vaccination in people with autoimmune inflammatory diseases taking immunosuppressant medication and these continue to be updated as new evidence becomes available.

Founding member, Professor Rachelle Buchbinder AO, Director of the Monash-Cabrini Department of Clinical Epidemiology, continues to lead and oversee ANZMUSC as the founding Chair of the Executive Committee.

"ANZMUSC is now considered the gold standard of musculoskeletal research networks in the world. Several other countries, including Finland, Sweden and Denmark, are already forming similar networks based upon our example," Prof Buchbinder said.



THE NHMRC ANZMUSC CLINICAL TRIAL NETWORK ENDORSES AND PROMOTES HIGH QUALITY CLINICAL TRIALS THAT ADDRESS IMPORTANT EVIDENCE GAPS..... ANZMUSC IS NOW CONSIDERED THE GOLD STANDARD OF MUSCULOSKELETAL RESEARCH NETWORKS IN THE WORLD.

*Prof Rachelle Buchbinder AO, Director Monash-Cabrini Department of Clinical Epidemiology, speaking at the ANZMUSC Clinical Trial Network CRE official opening.*



# BREAKTHROUGH FOR BRCA-MUTATED EARLY STAGE BREAST CANCER

CABRINI MONASH UNIVERSITY DEPARTMENT OF MEDICAL ONCOLOGY –  
THE SZALMUK FAMILY DEPARTMENT OF MEDICAL ONCOLOGY

Breast cancer remains one of the most common cancers globally. About five per cent of all patients with breast cancer carry a BRCA gene mutation, which means they are at high-risk of developing breast cancer and often present with aggressive features with a high-risk for recurrent disease, even when diagnosed in the early stages.

BRCA1 and BRCA2 genes produce proteins that are responsible for repairing damaged DNA and play an important role in maintaining the genetic stability of cells. Mutations in the BRCA genes cause the protein products to either not be made, or to not function properly, leading to unrepaired DNA damage and cell instability. The instability within BRCA mutated cells means they are more likely to develop additional genetic alterations that lead to cancer development. PARP inhibitors exploit the cell instability of BRCA mutated cells to target and kill cancer cells.

PARP inhibitors are targeted therapies that block poly ADP ribose polymerase, an enzyme involved in many cell functions, including repair of damaged DNA. Olaparib is a potent oral PARP inhibitor that induces double-stranded DNA breaks, which cannot be accurately repaired. It works to selectively kill BRCA mutated tumour cells (or other cells deficient in repairing damaged DNA) by exploiting the multiple DNA damage repair deficiencies, causing cancer cell death by synthetic lethality.

Olaparib has been shown to be effective in treating advanced BRCA1 or BRCA2 associated breast, ovarian, prostate and pancreatic cancers.

The OlympiA study, led by Associate Professor Yolanda Antill at Cabrini, was the first time Olaparib was tested as an adjuvant therapy for breast cancer, and the first time

in any adjuvant setting (adjuvant treatment is given in addition to primary therapy). OlympiA enrolled women diagnosed with high-risk, early stage, HER2-negative breast cancer with BRCA1/BRCA2 mutations to receive one year of adjuvant therapy with either Olaparib or a placebo. The OlympiA study's first interim analysis was presented at the international ASCO meeting in 2021 and was published simultaneously in the prestigious *New England Journal of Medicine* in June 2021. At a median follow up of just three years, the use of Olaparib resulted in a 42 per cent reduction in the risk of breast cancer recurrence compared to placebo. This includes local and distant recurrences of breast cancer, new cancers and death due to any cause (iDFS 85.9 per cent for the Olaparib group and 77.1 per cent in the placebo group) or an absolute difference of nearly nine per cent.

To date, Olaparib has also resulted in fewer women dying of breast cancer, but as the follow up time is short, the result is immature and not yet statistically significant. Importantly, the use of Olaparib was associated with mild to moderate side effects, most of which were treatable.

A/Prof Antill said a number of Cabrini patients participated in the OlympiA trial. Their enrolment in the trial contributed to what both the presenters and reviewers believe will change clinical practice for women with BRCA1/2 related breast cancers in the future.

"OlympiA is really exciting news," A/Prof Antill said.

"It will undoubtedly be practice changing, not only for women at high risk of breast cancer relapse, but the results also provide an increased rationale for germline testing for BRCA1 and BRCA2 in women with early breast cancer to allow an understanding of best practice for their treatment."

## Journal Reference

Tutt ANJ, Garber JE, Kaufman B, Viale G, Fumagalli D, Rastogi P, Gelber RD, de Azambuja E, Fielding A, Balmaña J, Domchek SM, Gelmon KA, Hollingsworth SJ, Korde LA, Linderholm B, Bandos H, Senkus E, Suga JM, Shao Z, Pippas AW, Nowecki Z, Huzarski T, Ganz PA, Lucas PC, Baker N, Loibl S, McConnell R, Piccart M, Schmutzler R, Steger GG, Costantino JP, Arahmani A, Wolmark N, McFadden E, Karantza V, Lakhani SR, Yothers G, Campbell C, Geyer CE Jr; OlympiA Clinical Trial Steering Committee and Investigators. (2021) Adjuvant Olaparib for Patients with BRCA1- or BRCA2-Mutated Breast Cancer. *N Engl J Med.* 384(25):2394-2405. doi: 10.1056/NEJMoa2105215.

“OLYMPIA IS REALLY EXCITING NEWS. IT WILL UNDOUBTEDLY BE PRACTICE CHANGING, NOT ONLY FOR WOMEN AT HIGH RISK OF BREAST CANCER RELAPSE, BUT THE RESULTS ALSO PROVIDE AN INCREASED RATIONALE FOR GERMLINE TESTING FOR BRCA1 AND BRCA2 IN WOMEN WITH EARLY BREAST CANCER TO ALLOW AN UNDERSTANDING OF BEST PRACTICE FOR THEIR TREATMENT.”



*A/Prof Yoland Antill, oncologist and OlympiA clinical trial Principal Investigator (right) and Kate Hurford, Associate Team Leader, Oncology Research.*

# FROM LETHAL TO AN EFFECTIVE TREATMENT – THE INCREDIBLE IMPACT OF A DRUG

CABRINI MONASH UNIVERSITY DEPARTMENT OF MEDICAL ONCOLOGY –  
THE SZALMUK FAMILY DEPARTMENT OF MEDICAL ONCOLOGY

Almost nine people die from breast cancer every day in Australia, but incredibly the number of deaths is decreasing.

Breast cancer is not a single disease. It is a group of tumour subtypes with different biology and characteristics, each requiring a different treatment approach. Amplification of the HER2 gene or overexpression of the HER2 protein, or both, defines one of the tumour subtypes called HER2-positive breast cancer. Representing 20 to 30 per cent of all breast cancer diagnoses, HER2-positive breast cancers are extremely aggressive in their capacity to grow and metastasise, even in early stage breast cancer. Up until the late 1990s, HER2-positive breast cancer was associated with poorer outcomes and higher death rates than any other breast cancer subtype.

During the past two decades, there has been a dramatic shift in treatments and outcomes for patients with HER2-positive breast cancer. Trastuzumab (Herceptin), sometimes referred to as the ‘miracle drug’, has had an incredible impact, taking HER2-positive breast cancer from an often lethal disease to one that can often be effectively treated.

HERA was a ground-breaking clinical trial for women with early stage HER2-positive breast cancer. It tested trastuzumab in the adjuvant setting (treatment that is given in addition to primary therapy) and enrolled women who had completed all types of primary therapy (including, surgery, chemotherapy, and radiotherapy). Patients were randomly assigned to either receive trastuzumab for one year, or for two years, or to an observation group.

The HERA results clearly showed that the addition of trastuzumab produces a better outcome, improving overall survival and disease-free survival. The risk of disease returning was reduced by an incredible 46 per cent. It was effective regardless of the type of primary therapy received or the extent of nodal involvement, making the results relevant to many parts of the world. One year of trastuzumab treatment was found to be optimal, with a two-year course not improving outcomes and associated with more side effects.

## Journal Reference

Piccart-Gebhart MJ, Procter M, Leyland-Jones B, Goldhirsch A, Untch M, Smith I, Gianni L, Baselga J, Bell R, Jackisch C, Cameron D, Dowsett M, Barrios CH, Steger G, Huang CS, Andersson M, Inbar M, Lichinitser M, Láng I, Nitz U, Iwata H, Thomssen C, Lohrisch C, Suter TM, Rüschoff J, Suto T, Grotzer V, Ward C, Straehle C, McFadden E, Dolci MS, Gelber RD; Herceptin Adjuvant (HERA) Trial Study Team. (2005) Trastuzumab after adjuvant chemotherapy in HER2-positive breast cancer. *N Engl J Med.* 353(16):1659-72. doi: 10.1056/NEJMoa052306.



Professor Gary Richardson OAM, HERA clinical trial Principal Investigator, Group Director Cabrini Research, and Director Cabrini Monash University Department of Medical Oncology, Szalmuk Family Department of Medical Oncology. Photo Credit: Darren James.

Globally, 478 clinical sites enrolled more than 5000 women between December 2001 and March 2005. It was one of the largest adjuvant studies ever carried out among breast cancer patients and the first time Australian sites had participated in a trial in the adjuvant setting. The trial was run at Cabrini by Principal Investigator Professor Gary Richardson OAM.

“The discovery of trastuzumab was one of the most exciting events in my lifetime as an oncologist,” he said. “A truly personalised therapy that turned one of the most aggressive forms of breast cancer into one of the most curable”.

The HERA trial delivered one of the most important breakthroughs for breast cancer, changing practice around the world. Since October 2006 it has been made available for Australian women and men with early-stage breast cancer via the Pharmaceutical Benefits Scheme.

“THE DISCOVERY OF TRASTUZUMAB WAS ONE OF THE MOST EXCITING EVENTS IN MY LIFETIME AS AN ONCOLOGIST. A TRULY PERSONALISED THERAPY THAT TURNED ONE OF THE MOST AGGRESSIVE FORMS OF BREAST CANCER INTO ONE OF THE MOST CURABLE”.



Oncology Research Clinical Trials team members (left to right) Simer Khaira, Rochelle Woods and Dina Cherfi.  
Photo Credit: Darren James.

# TISSUE MICROARRAYS AND BIOMARKERS PAVE THE WAY FOR PERSONALISED MEDICINE

CABRINI MONASH UNIVERSITY DEPARTMENT OF SURGERY

Colorectal cancer is one of the leading causes of cancer-related deaths worldwide. Patients diagnosed with colorectal cancer often experience different clinical outcomes and drug responses, even when controlled for similar pre-operative features, tumour stage and pathological characteristics.

The research team within the Cabrini Monash University Department of Surgery, led by Professor Paul McMurrick, aims to personalise treatment for colon cancer patients through understanding the role of predictive and prognostic biomarkers through the tissue microarray program. Tissue microarrays are a platform that allow for high throughput analysis of multiple tissue samples, simultaneously.

Senior Research Fellow, Dr Christine Koulis is co-ordinating the construction of the tissue microarrays, through collaborations with Monash Histology platform, with more than 1200 patients currently enrolled in the program. Each tissue microarray comprises of normal and tumour tissue taken from the patient at the time of surgery. This valuable resource will be correlated with patient outcome information stored on the Cabrini Monash Colorectal Neoplasia Database.

“The ability to combine biomarker information with clinical outcome data provides a powerful research tool that has the potential to transform and personalise the management of colorectal cancer,” Dr Koulis said.

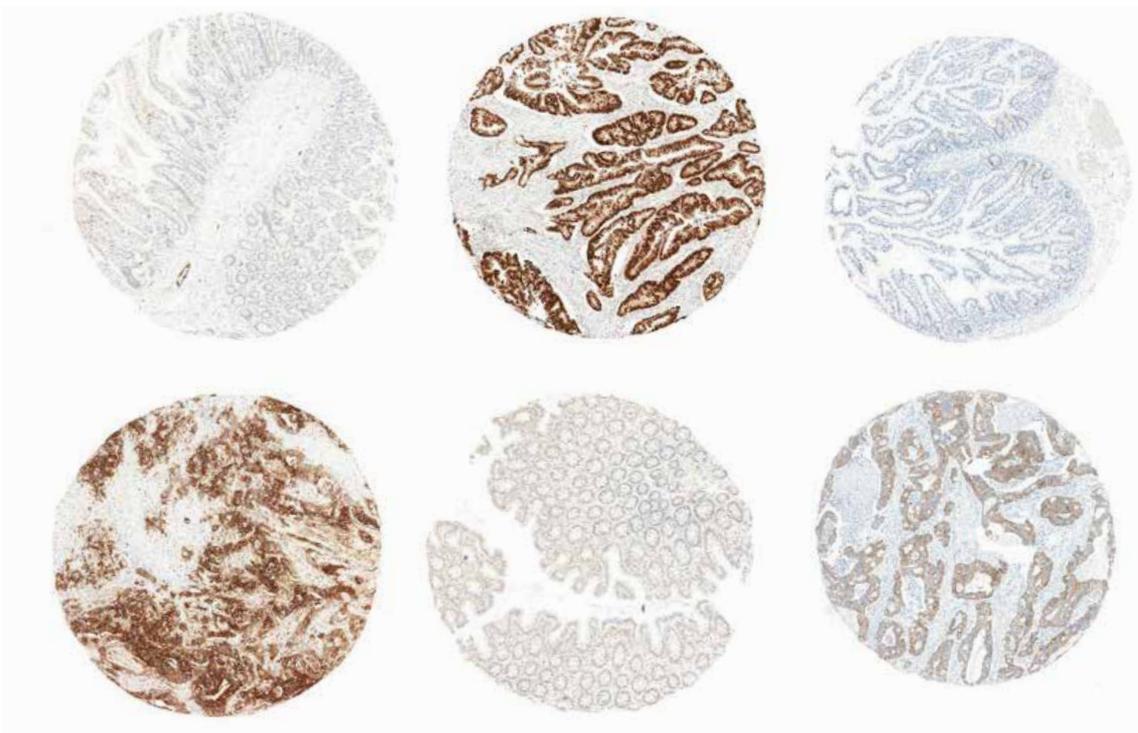


*Prof Paul McMurrick,  
Director Cabrini Monash  
University Department of  
Surgery.*

In collaboration with Monash University partners, including Professor Helen Abud and Dr Anne Fletcher’s laboratories, tissue microarrays will undergo analysis

of specific tissue biomarkers, including the analysis of molecular subtypes along with markers of stem cells, niche cells and regulators of the immune response. The results from this program will enable researchers to define mechanistic treatment ‘rules’ based on the expression of specific biomarkers.

Supported by funding from Margaret Walkom Trust, Rick Smith Trust, Alan, Ada and Eva Selwyn Cabrini Foundation Grant and Cabrini charity Let’s Beat Bowel Cancer, the information gained from this research will allow the team of scientists, surgeons, oncologists and pathologists to predict the most effective treatment option for each patient, while reducing the incidence of drug resistance and toxicity, paving the way to personalised medicine.



*Immunostained  
tissue microarrays.*

# The predictive and prognostic role of p53, GLUT1 and TRAP1 in Stage IV colon cancer

Christine Koulis<sup>1</sup>, Simon Wilson<sup>1</sup>, Ayesha Khan<sup>1</sup>, Anandha Rajan<sup>1</sup>, Paul J. Mitchell<sup>1</sup>

## Background

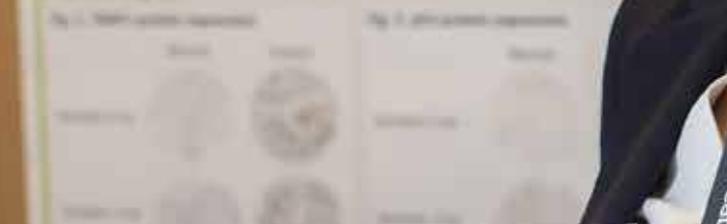
Colorectal cancer (CRC) is one of the leading causes of cancer-related death worldwide. Colorectal cancer is a heterogeneous disease, with approximately 20% of CRC patients having microsatellite instability (MSI) and 80% having microsatellite stable (MSS). These differences in genetic background may lead to different clinical outcomes and allow for the identification of biomarkers that can be used to predict prognosis and response to treatment.

**Aim**  
To determine whether microsatellite instability (MSI) and protein expression of p53, GLUT1 and TRAP1 are associated with clinical outcomes in patients with colorectal cancer.

**Method**  
The expression of p53, GLUT1 and TRAP1 in colorectal cancer were analysed in 100 patients with MSS and 100 patients with MSI. Immunohistochemistry (IHC) and Western blot analysis were performed to determine protein expression levels.

## Results

Patients with colorectal cancer who were identified as the MSI group had a significantly longer overall survival (OS) compared to patients with MSS. The expression of p53, GLUT1 and TRAP1 were significantly associated with OS in MSS patients, with high levels of p53 expression demonstrating a significant association with poor OS (Fig. 1). High p53 expression significantly increased OS in MSI patients (Fig. 2).



# The role of pre-operative colorectal cancer.

Dr. Simon Wilson<sup>1</sup>, Simon Wilson<sup>1</sup>, Ayesha Khan<sup>1</sup>, Anandha Rajan<sup>1</sup>, Paul J. Mitchell<sup>1</sup>

## Background

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## Aim

The primary aim of this study was to determine whether a pre-operative biomarker panel could be used to predict prognosis and response to treatment in patients with colorectal cancer.

**Method**  
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Dr Christine Koulis, Senior Postdoctoral Research Fellow, Cabrini Monash University Department of Surgery.



“THE ABILITY TO COMBINE BIOMARKER INFORMATION WITH CLINICAL OUTCOME DATA PROVIDES A POWERFUL RESEARCH TOOL THAT HAS THE POTENTIAL TO TRANSFORM AND PERSONALISE THE MANAGEMENT OF COLORECTAL CANCER”.

# DOUBLING THE POWER OF IMMUNE TARGETING IN ADVANCED RENAL CELL CARCINOMA

CABRINI MONASH UNIVERSITY DEPARTMENT OF MEDICAL ONCOLOGY –  
THE SZALMUK FAMILY DEPARTMENT OF MEDICAL ONCOLOGY

Kidney cancer is the seventh most commonly diagnosed cancer in Australia. Renal cell carcinoma (RCC) is the most common kidney cancer type, accounting for 90 per cent of all diagnoses. Advanced or metastatic RCC has a poor prognosis, with patients having less than 12 per cent chance of surviving more than five years. Until recently, the only first line therapy options available for patients with advanced RCC were drugs that targeted vascular endothelial growth factor (VEGF) and serine/threonine kinase pathways, as traditional chemotherapy did not work like other cancers. Although often effective in treating low risk early RCC, patients with advanced high risk RCC often responded poorly to these treatments. Patients diagnosed with advanced RCC are usually advised it is a challenging disease. There is only one in ten chance of surviving, and most die in a very short period of time.

During the past five years incredible advances in drug development and drug combination approaches have transformed the treatment landscape for advanced RCC, providing more promising outcomes for patients. Contributing greatly to this new era of RCC treatment were the findings from the Checkmate 9ER study, sponsored by Bristol Myers Squibb, and published this year in the prestigious *New England Journal of Medicine*. The novel study looked at the impact of a first line treatment regime that combined a tyrosine kinase inhibitor (TKI) with immunotherapy.

The Checkmate 9ER study took advantage of a new and very effective TKI, cabozantinib, and combined it with the checkpoint inhibitor immunotherapeutic nivolumab in the first line setting. Both drugs had only ever been used as single therapies for second line treatment of RCC. The new treatment strategy was compared to sunitinib, an older TKI which has been the standard of care for the past 15 years.

The results were astounding. The combination of nivolumab with cabozantinib was superior to sunitinib for first line treatment of advanced RCC. The combination approach reduced the risk of death or disease



A/Prof David Pook,  
oncologist and  
Checkmate 9ER  
clinical trial Principal  
Investigator.

progression by almost 50 per cent. Importantly, the superior clinical outcomes were also accompanied by patients reporting a significantly better quality of life, which is important for any patient undergoing treatment for this challenging disease.

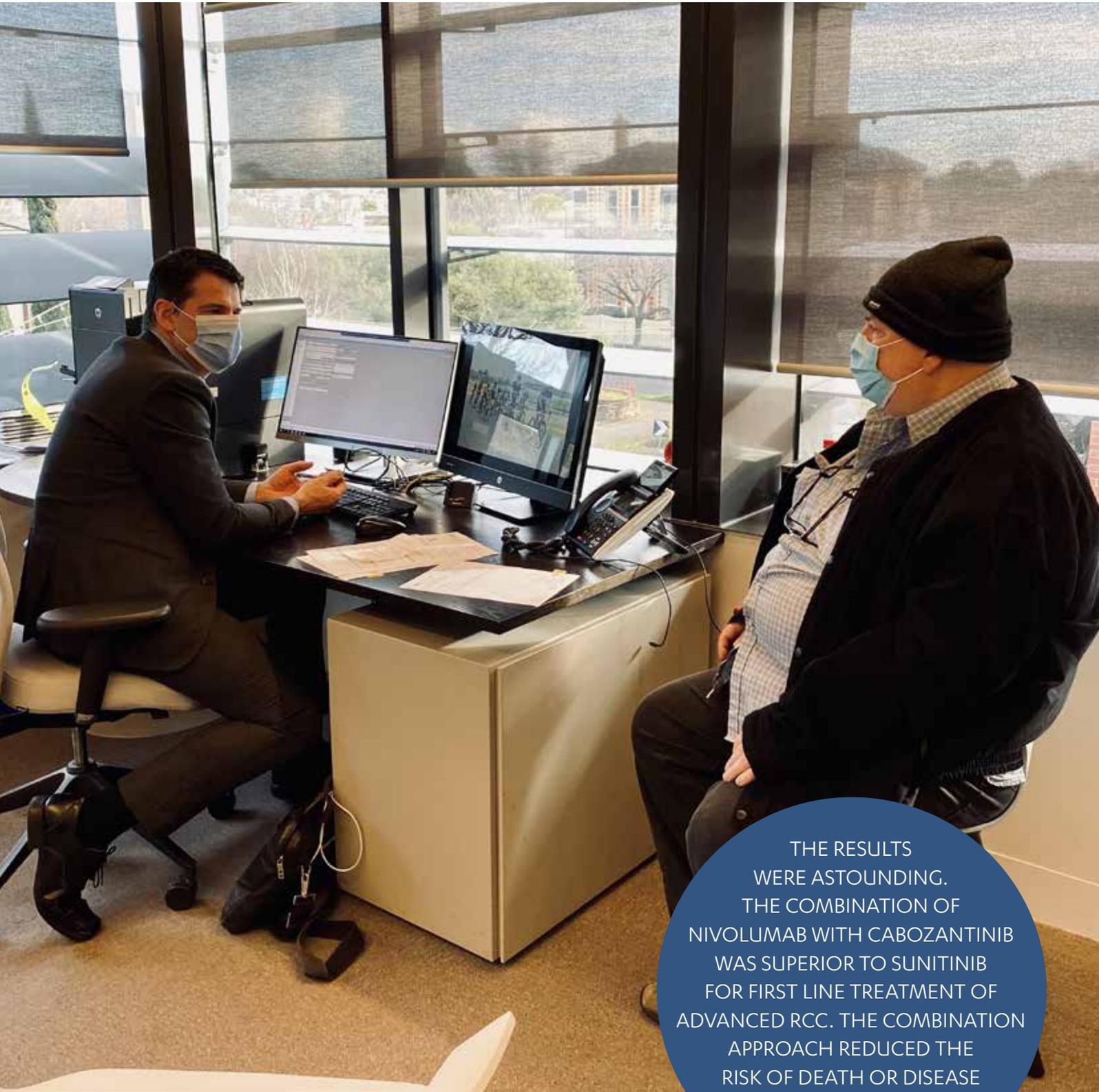
Between September 2017 and May 2019, a total of 651 patients were enrolled in the study across 125 sites in 18 countries. Cabrini contributed greatly to the study, enrolling nine patients. Associate Professor David Pook was Principal Investigator at Cabrini and co-author of the *New England Journal of Medicine* publication. Checkmate 9ER is one of a few recent trials that have successfully combined TKIs and immunotherapies to produce significant outcomes in advanced RCC. The combination of nivolumab with cabozantinib was approved for the first line treatment of advanced RCC by the USA Food and Drug Administration (FDA) in January 2021, and further applications are under review with health authorities globally.

A/Prof Pook said the study was an example of the immense benefit of precision medicine.

“The combination of two targeted treatments showed synergistic effect on tumour response and led to improvement in all measures of patient benefit.”

## Journal Reference

Choueiri TK, Powles T, Burotto M, Escudier B, Bourlon MT, Zurawski B, Oyervides Juárez VM, Hsieh JJ, Basso U, Shah AY, Suárez C, Hamzaj A, Goh JC, Barrios C, Richardet M, Porta C, Kowalyszyn R, Feregrino JP, Żołąnierek J, Pook D, Kessler ER, Tomita Y, Mizuno R, Bedke J, Zhang J, Maurer MA, Simsek B, Ejzykiewicz F, Schwab GM, Apolo AB, Motzer RJ; CheckMate 9ER Investigators. (2021) Nivolumab plus Cabozantinib versus Sunitinib for Advanced Renal-Cell Carcinoma. *N Engl J Med.* 384(9):829-841. doi: 10.1056/NEJMoa2026982.



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*A/Prof David Pook, oncologist and Checkmate 9ER clinical trial Principal Investigator with Gary, an oncology clinical trial participant.*

# THE POWER OF A MASS MEDIA CAMPAIGN TO CHANGE BACK PAIN BELIEFS

MONASH-CABRINI DEPARTMENT OF CLINICAL EPIDEMIOLOGY

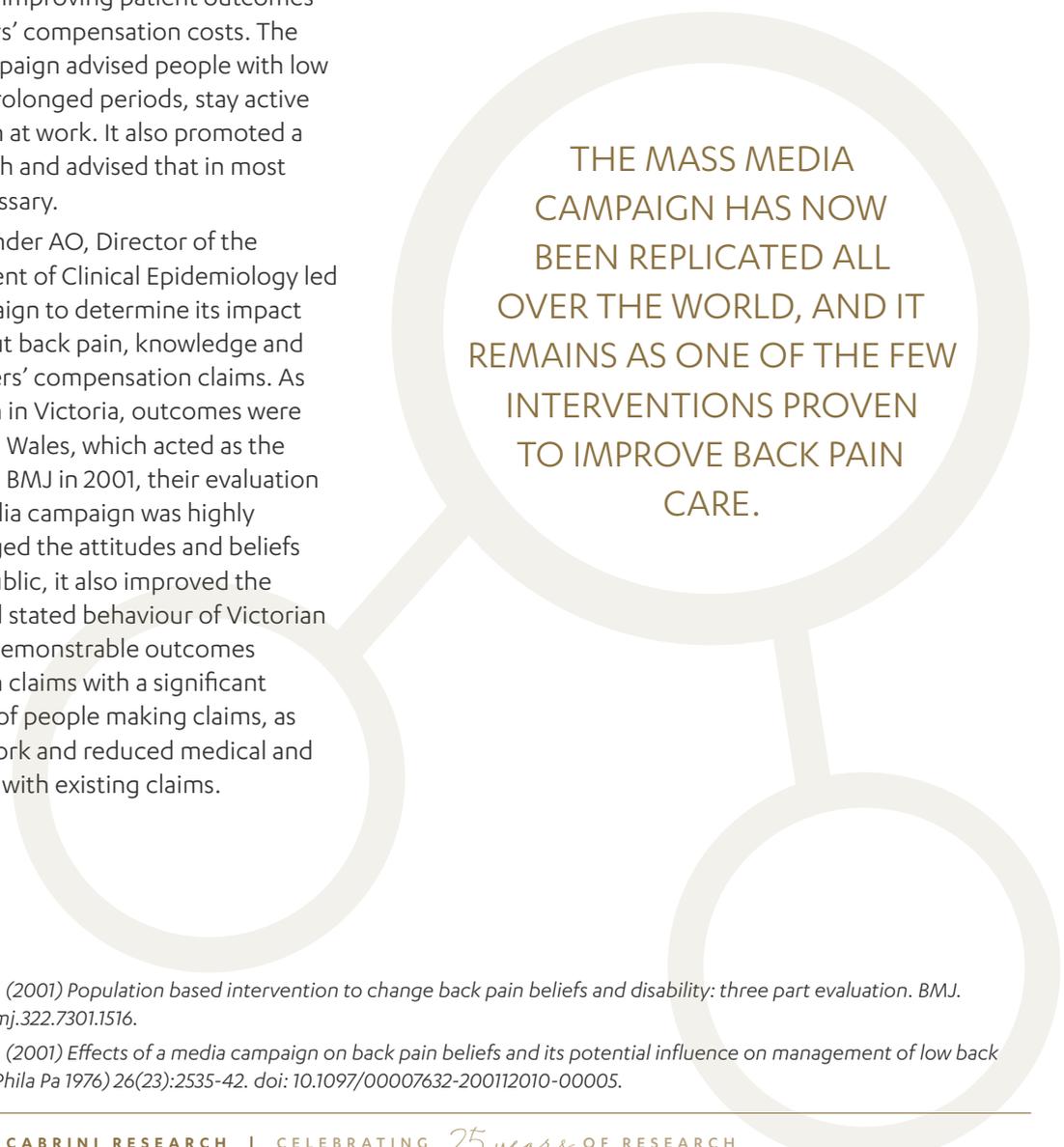
Low back pain is the world's most disabling health condition, costing the health service more than cancer and diabetes combined.

By the 1990s there was considerable evidence indicating that low back pain should be treated by staying active and continuing ordinary activities rather than resting, and early investigations or referrals to specialists are unwarranted in most cases. Yet the evidence was failing to be translated into the clinic. The Victorian WorkCover Authority was faced with rapidly increasing costs in compensation payouts for low back pain, with payouts having tripled in the past decade. In 1997 they embarked on a state-wide public health campaign: "Back Pain: Don't Take it Lying Down", which ran for two years. The multimedia campaign was aimed at altering the general population's attitudes and beliefs about back pain, changing clinician behaviour towards more evidence-based care, and ultimately improving patient outcomes and bringing down workers' compensation costs. The main messages of the campaign advised people with low back pain to not rest for prolonged periods, stay active and exercise and to remain at work. It also promoted a self-management approach and advised that in most cases imaging was unnecessary.

Professor Rachelle Buchbinder AO, Director of the Monash-Cabrini Department of Clinical Epidemiology led an evaluation of the campaign to determine its impact on population beliefs about back pain, knowledge and attitudes of GPs and workers' compensation claims. As the campaign was only run in Victoria, outcomes were compared with New South Wales, which acted as the study control. Published in *BMJ* in 2001, their evaluation showed that the mass media campaign was highly effective. It not only changed the attitudes and beliefs of the Victorian general public, it also improved the knowledge and beliefs and stated behaviour of Victorian doctors. There were also demonstrable outcomes on workers' compensation claims with a significant reduction in the numbers of people making claims, as well as reduced time off work and reduced medical and overall costs among those with existing claims.

These effects were sustained for at least five years after the end of the campaign. There were no changes over time in NSW during the same period.

The mass media campaign has now been replicated all over the world, and it remains as one of the few interventions proven to improve back pain care. Prof Buchbinder has since been involved in similar studies in the Netherlands and Japan. Prof Buchbinder and colleagues were awarded the prestigious Volvo Award in 2001 for this work, based upon a second publication in the journal *Spine*. The Volvo Award recognises the best back pain clinical paper published each year. This work also resulted in Prof Buchbinder being awarded the Monash University Mollie Holman Medal for the best PhD thesis in the Faculty of Medicine, Nursing and Health Sciences in 2006, as well as a Commendation for the Victorian Premier's Award for Medical Research in 2007.



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## Journal References

Buchbinder R, Jolley D, Wyatt M. (2001) Population based intervention to change back pain beliefs and disability: three part evaluation. *BMJ*. 322(7301):1516-20. doi: 10.1136/bmj.322.7301.1516.

Buchbinder R, Jolley D, Wyatt M. (2001) Effects of a media campaign on back pain beliefs and its potential influence on management of low back pain in general practice. *Spine (Phila Pa 1976)* 26(23):2535-42. doi: 10.1097/00007632-200112010-00005.



| Prof Rachelle Buchbinder AO, Director Monash-Cabrini Department of Clinical Epidemiology.

# MANAGING HIGH RISK CARDIAC SURGERIES SAFELY

## – TRICS III TRIAL

INTENSIVE CARE RESEARCH UNIT

The avoidance of unnecessary blood transfusion is a high priority. Red-cell transfusions can be life-saving in many contexts, but unnecessary transfusions carry considerable morbidity and mortality, as well as increasing costs. Patients undergoing cardiac surgery are among the highest recipients of red-cell transfusion, but it is unclear whether the safe threshold for transfusions in this group could be lowered.

The Transfusion Requirements in Cardiac Surgery (TRICS) III trial was an international, open-label, randomised, controlled, non-inferiority trial that compared whether a restrictive approach to intraoperative and postoperative transfusion in cardiac surgery patients with an elevated perioperative risk of death safely achieves outcomes similar to those achieved by means of a more liberal approach. Patients in the restrictive group received a red-cell transfusion if the haemoglobin concentration was less than 7.5g/dL intra-operatively or post-operatively. Patients in the liberal group received a red-cell transfusion at a higher haemoglobin threshold, at a concentration less than 9.5g/dL intra-operatively or post-operatively or less than 8.5g/dL in the non-ICU ward. Haemoglobin level was measured pre-operatively, intra-operatively and post-operatively at specified intervals. If the haemoglobin fell below the threshold, 1 unit of red cells was administered followed by reassessment of the level.

Globally, 73 clinical sites across 19 countries enrolled more than 5000 people between January 2014 and March 2017. The trial was run at Cabrini by Principal Investigator Associate Professor David Brewster, with assistance from ICU research coordinator Shannon Simpson.

Outcomes from the trial and data from six months of follow up were published in the prestigious *New England Journal of Medicine*. The restrictive transfusion strategy was found to be non-inferior to the liberal transfusion strategy in cardiac surgery patients with a moderate-to-high risk of death with regards to a composite outcome of death and major disability, meaning post-cardiac surgery patients can safely be managed with haemoglobins as low as 7.5g/dL. The successful outcomes from the trial have added to a growing body of evidence that restrictive transfusion protocols are not harmful in critically ill patients. Ultimately the study concluded that a restrictive strategy is feasible, safe, and leads to fewer units of blood transfused.

“This study was an example of excellent researcher initiated research by the collaborative group of international researchers that designed the TRICS III study. We were delighted to contribute to such a large trial. This shows how our ICU has developed its research capacity over the last five to ten years to now contribute valuable data to such important studies.” said A/Prof Brewster.

### Journal References

Mazer CD, Whitlock RP, Fergusson DA, Hall J, Belley-Cote E, Connolly K, Khanykin B, Gregory AJ, de Médicis É, McGuinness S, Royse A, Carrier FM, Young PJ, Villar JC, Grocott HP, Seeberger MD, Fremes S, Lellouche F, Syed S, Byrne K, Bagshaw SM, Hwang NC, Mehta C, Painter TW, Royse C, Verma S, Hare GMT, Cohen A, Thorpe KE, Jüni P, Shehata N; TRICS Investigators and Perioperative Anesthesia Clinical Trials Group. (2017) Restrictive or Liberal Red-Cell Transfusion for Cardiac Surgery. *N Engl J Med* 377(22):2133-2144. doi: 10.1056/NEJMoa1711818.

Mazer CD, Whitlock RP, Fergusson DA, Belley-Cote E, Connolly K, Khanykin B, Gregory AJ, de Médicis É, Carrier FM, McGuinness S, Young PJ, Byrne K, Villar JC, Royse A, Grocott HP, Seeberger MD, Mehta C, Lellouche F, Hare GMT, Painter TW, Fremes S, Syed S, Bagshaw SM, Hwang NC, Royse C, Hall J, Dai D, Mistry N, Thorpe K, Verma S, Jüni P, Shehata N; TRICS Investigators and Perioperative Anesthesia Clinical Trials Group. (2018) Six-Month Outcomes after Restrictive or Liberal Transfusion for Cardiac Surgery. *N Engl J Med* 379(13):1224-1233. doi: 10.1056/NEJMoa1808561.

RED-CELL  
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*A/Prof David Brewster, Deputy Director and Head of Intensive Care Research at Cabrini, and the Clinical Dean for the Monash University Clinical School, and Shannon Simpson, ICU research coordinator.*

# LARGE HIGH QUALITY DATA SETS ALLOWS US TO PREDICT SURGICAL OUTCOMES

CABRINI MONASH UNIVERSITY DEPARTMENT OF SURGERY

Clinical data registries, when designed well with high quality data, have the potential to make real world quality improvements. They are an essential tool allowing surgeons and other healthcare professionals to benchmark their performance amongst their peers. Their wider use comes from the ability to aggregate large data sets and analyse trends or patterns in treatments and outcomes.

The Cabrini Monash Colorectal Neoplasia Database (CMCND) commenced in 2010 and is now an extensive resource, enabling researchers to identify a particular cohort of patients and analyse their outcomes, and in some cases, identify whether particular factors affect a particular group of patients. The strength of the CMCND is evidenced by the increasing number of published papers based on its dataset.

A 2016 study, led by colorectal surgeons Mr Raymond Yap and Professor Paul McMurrick and researcher Dr Simon Wilkins of the Cabrini Monash University Department of Surgery, used the CMCND to examine the risk of diabetes on the perioperative outcomes of colorectal cancer surgery patients. There are approximately 1.3 million Australians with diabetes, and reports in the literature were conflicting and varied considerably as to the effect of diabetes on the outcomes of colorectal cancer patients. CMCND data of 1725 patients analysed over 1745 treatment episodes showed that although the outcome of patients with diabetes was worse than patients without diabetes, including an increased risk of postoperative morbidity and increased length of stay, it was not significant after adjusting for other factors except in the area of surgical complications.

Patients with diabetes had significantly higher co-morbidities than patients without diabetes and it is likely that the myriad of co-morbidities that patients with diabetes have contributed more appreciably to their perioperative risk, rather than the diabetes itself. The study highlighted that the long-term control of diabetes to reduce the incidence and severity of associated pre-morbid conditions, including chronic renal failure and ischaemic heart disease, is probably more important than the short-term control of diabetes at the time of surgery.

A 2018 study led by colorectal surgeons and researchers Mr Stephen Bell and Prof McMurrick of the Cabrini Monash University Department of Surgery, used the CMCND to evaluate the effect of body mass index (BMI) on the clinical and oncological outcomes of surgery for colon and rectal cancer. Obesity is common in Western countries and its prevalence is increasing.

Surgery for colorectal cancer and laparoscopic surgery for rectal cancer is technically more challenging in obese patients. CMCND data of 1483 treatment episodes in 1464 patients showed that surgical complications occurred more frequently in patients with a BMI greater than 30. It was also shown for the first time that colon and rectal cancer patients with a BMI greater than 30 are less likely to be offered keyhole (laparoscopic surgery) and are more likely to be converted from laparoscopic to open surgery.

Open surgery was associated with worse outcomes for patients. Patients with a BMI greater than 30 were also more likely to have surgical complications. Findings from the study led to the initiation of the ADIPOSE randomised controlled multicentre clinical trial being run in Australia and New Zealand. ADIPOSE investigated whether patients who lose weight prior to surgery to achieve a BMI less than 30 have better outcomes than those who do not lose weight.



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## Journal References

Yap R, Wilkins S, Staples M, Oliva K, McMurrick PJ. (2016) The Effect of Diabetes on the Perioperative Outcomes of Colorectal Cancer Surgery Patients. *PLoS One*. 11(12):e0167271. doi: 10.1371/journal.pone.0167271.

Bell S, Kong JC, Wale R, Staples M, Oliva K, Wilkins S, McMurrick P, Warriar SK. (2018) The effect of increasing body mass index on laparoscopic surgery for colon and rectal cancer. *Colorectal Dis*. 20(9):778-788. doi: 10.1111/codi.14107.



| Mr Stephen Bell performing surgery.



Prof Paul McMurrick, Director  
Cabrini Monash University  
Department of Surgery.



Mr Raymond Yap, Colorectal and  
Academic Surgeon, Research  
Fellow, Cabrini Monash University  
Department of Surgery.



Dr Simon Wilkins, Senior  
Postdoctoral Research Fellow,  
Cabrini Monash University  
Department of Surgery.

# COMBINED IMAGING MAY REDUCE NEED FOR INVASIVE PROSTATE CANCER PROCEDURES

DEPARTMENT OF UROLOGY

Prostate cancer remains among the most commonly diagnosed cancers worldwide.

Management of localised prostate cancer relies on accurately determining the risk a tumour presents for a patient. The decision to biopsy and subsequently treat, or wait and watch (active surveillance), is complex. Multiparametric magnetic resonance imaging (mpMRI) has started to be used before biopsies and is helping to reduce the overdiagnosis of insignificant prostate cancer, however the rates of clinically significant disease missed and undertreatment still need to be minimised. Assurance is required that negative imaging truly indicates the absence of clinically significant disease. More recently, the clinical value of <sup>68</sup>Gallium-labelled prostate-specific membrane antigen positron emission tomography (<sup>68</sup>Ga-PSMA-11 PET) as a staging tool in prostate cancer has been recognised and approved. The quantification measure maximum standardised uptake value (SUVmax) can identify the highest radiotracer <sup>68</sup>Gallium uptake within a tumour, which correlates with greater cellular PSMA expression, and higher tumour grade. Its utility in characterising primary prostate cancer however, had remained unclear until recently.

The Department of Urology, led by Professor Mark Frydenberg, investigated the utility of <sup>68</sup>Ga-PSMA-11 PET and SUVmax. Published in the *European Urology Oncology* journal in 2021, it is the largest published series comparing <sup>68</sup>Ga-PSMA-11 PET and mpMRI in quantifying biopsy pathology in men with localised prostate cancer. They found <sup>68</sup>Ga-PSMA-11 PET had a high sensitivity for detecting clinically significant prostate cancer, and that the higher Gleason Grade (GG) group 3–5 tumours were associated with higher SUVmax than lower grade GG 1–2 tumours and benign lesions. In addition, SUVmax predicted GG 3–5 disease, independent of clinical and mpMRI findings. When combined with mpMRI, <sup>68</sup>Ga-PSMA-11 PET improved the already excellent sensitivity of mpMRI for GG 3–5 disease. This improvement was less prominent for lower grade GG 2–5 cancer.

The results suggest that SUVmax holds diagnostic utility alongside existing clinical variables and that <sup>68</sup>Ga-PSMA-11 PET may be a useful adjunct to mpMRI in better risk stratification of intermediate-risk prostate cancer. The combined diagnostic approach may be a further step forward to assist in accurate risk stratification.

“We would hope that this combined modality imaging may provide additional information so that men with low risk cancer on biopsy can be assured that a higher grade component has not been missed, and more appropriately assign men to either active surveillance as a treatment, or alternatively to active treatment,” Prof Frydenberg said. “<sup>68</sup>Ga-PSMA-11 PET may also be able to be used in men unable to have an MRI scan due to claustrophobia, or contraindications such as metallic foreign bodies, pacemakers or heart valves.”

“WE WOULD HOPE THAT THIS COMBINED MODALITY IMAGING MAY PROVIDE ADDITIONAL INFORMATION SO THAT MEN WITH LOW RISK CANCER ON BIOPSY CAN BE ASSURED THAT A HIGHER GRADE COMPONENT HAS NOT BEEN MISSED, AND MORE APPROPRIATELY ASSIGN MEN TO EITHER ACTIVE SURVEILLANCE AS A TREATMENT, OR ALTERNATIVELY TO ACTIVE TREATMENT.”

## Journal Reference

Kalapara AA, Ballok ZE, Ramdave S, O'Sullivan R, Ryan A, Konety B, Grummet JP, Frydenberg M. (2021) Combined Utility of <sup>68</sup>Ga-Prostate-specific Membrane Antigen Positron Emission Tomography/Computed Tomography and Multiparametric Magnetic Resonance Imaging in Predicting Prostate Biopsy Pathology. *Eur Urol Oncol.* S2588-9311(21)00040-7. doi: 10.1016/j.euo.2021.02.006.



| Prof Mark Frydenberg, Director Department of Urology.

# RESTORING HOPE, MORALE AND MEANING TO CANCER PATIENTS

SZALMUK FAMILY PSYCHO-ONCOLOGY RESEARCH UNIT

Advanced cancer creates an existential crisis that can lead to psychological distress in many patients.

One domain of particular study is the phenomenon and experience of demoralisation, wherein patient morale is lowered and their coping potentially challenged by the stress of their cancer diagnosis and treatment. Professor David Kissane AC, a recognised world leader in the field of psycho-oncology research, has shown that patients are at risk of becoming demoralised when they feel trapped by what is happening because of their illness.

The demoralisation can occur as a stand-alone psychological state of distressed coping or it can develop into a co-morbid clinical depression. In both states, when patients feel hopeless and helpless, they may begin to wonder about the value and point of their life, with the risk they give up prematurely in striving to have their illness treated.

Prof Kissane and his team from the Szalmuk Family Psycho-oncology Research Unit at Cabrini Research, are looking at a novel psychological intervention called Meaning and Purpose (MaP) Therapy as a way to treat demoralisation and restore hope, morale and meaning to the life of cancer patients. MaP therapy is a six week psychological treatment that looks to enhance meaning-based coping through a life review that focuses on the value and worth of the person, key relationships, sources of fulfillment, roles, and future priorities in living life out fully.

The primary aim is to restore meaning to the life of the person, empowering them to live out their life as fully as possible, despite any disability resultant from their illness. The six one hour weekly sessions of MaP Therapy are delivered by a mental health clinician in the clinic in face to face sessions in addition to usual care. The mental health clinician can be a psychologist, social worker or psychiatrist who has been specifically trained to deliver this model of therapy.

The initial pilot study of MaP Therapy of patients with advanced cancer showed great promise from the intervention, so much so that Prof Kissane and the team have embarked on a formal randomised controlled trial to confirm the genuine patient benefit of MaP therapy. Such trials are labour intensive as they involve the training, supervision and fidelity maintenance of the therapy as it is delivered across several weeks by a number of psychologists. The study is currently running across Cabrini Health and St Vincent's Sydney.

"Our therapists find the manual easy to follow," Prof Kissane said.

"They like the model of therapy. And importantly, our patients enjoy the optimism of the experience, the continuity that the homework delivers, and the constructive additions that the therapy brings to their lives. This approach is a winner."



"OUR PATIENTS ENJOY THE OPTIMISM OF THE EXPERIENCE, THE CONTINUITY THAT THE HOMEWORK DELIVERS, AND THE CONSTRUCTIVE ADDITIONS THAT THE THERAPY BRINGS TO THEIR LIVES. THIS APPROACH IS A WINNER."

## Journal Reference

Kissane DW, Lethborg C, Brooker J, Hempton C, Burney S, Michael N, Staples M, Osicka T, Sulistio M, Shapiro J, Hiscock H. (2019) Meaning and Purpose (MaP) therapy II: Feasibility and acceptability from a pilot study in advanced cancer. *Palliat Support Care*. 17(1):21-28. doi: 10.1017/S1478951518000883.



*Prof David Kissane AC, Director Szalmuk Family Psycho-oncology Research Unit, with Ingrid Kuebler, carer for her mother, Elizabeth Kuebler, who peacefully passed away at home. They are talking with Kathy Hauser of Cabrini Health's palliative and support services.  
Photo Credit: Peter Casamento The Catholic Weekly.*

# REDUCING THE USE OF A HARMFUL PROCEDURE WORLDWIDE

MONASH-CABRINI DEPARTMENT OF CLINICAL EPIDEMIOLOGY

Osteoporosis refers to thin, fragile bones that are highly susceptible to fracture. Osteoporotic vertebrae fractures are fractures in the spine and are one of the common types of fracture in a patient with osteoporosis. They can often cause severe pain and disability initially, although this improves over time, and treatment consists of providing pain relief and support until symptoms improve.

Vertebroplasty, a surgical procedure developed in the late 1980s, involves the injection of polymethylmethacrylate (PMMA), a medical grade cement, into the fracture under light sedation or general anaesthesia. The cement hardens in the bone space to form an internal cast. Early studies and reports suggested vertebroplasty could bring immediate and sustained pain relief and the procedure became the preferred treatment for these painful fractures, sometimes being performed by surgeons and sometimes by interventional radiologists.

As a result, the number of vertebroplasties performed quickly escalated, yet the efficacy of the procedure had never been proven in methodologically robust clinical trials. There were also risks of very serious complications including spinal cord compression due to cement leaking out of the bone resulting in paraplegia, cement leaking into the blood stream resulting in pulmonary embolism, and perforations of the heart, rib fractures, infections in the spine, and even death.

In 2009, Professor Rachele Buchbinder AO, Director of the Monash-Cabrini Department of Clinical Epidemiology, published the results of a ground-breaking NHMRC-funded randomised placebo-controlled trial of vertebroplasty. Published in the prestigious *New England Journal of Medicine*, the results from the study contested two decades of reports that mostly supported the use of vertebroplasty. The trial found that vertebroplasty was no better than placebo in alleviating symptoms, meaning that it could harm people for no apparent worthwhile benefit. This was the first trial to use a placebo control to investigate the value of vertebroplasty. A second similar US trial published in the same edition of the *New England Journal of Medicine* reported almost identical findings. The trials were covered widely in the media, including the *New York Times* and the CBS evening news in the USA and the ABC's '7.30 Report' and 'Health Report' in Australia. The trial results were the topic of numerous editorials and commentaries in major international



Prof Rachele Buchbinder AO, Director Monash-Cabrini Department of Clinical Epidemiology, and Prof Stephen Hall, Medical Director Emeritus Research, Professor of Medicine Monash University, Rheumatologist Cabrini Health.

journals, focusing particularly on the fact that the treatment had been in widespread use, despite the lack of a strong evidence base to support that use.

The trial was incredibly hard and took four years to enrol enough patients. There was strong opposition from some quarters who believed in the procedure based upon their anecdotal experiences and therefore considered the trial to be unethical.

Prof Buchbinder said she was proud of the efforts and the perseverance of the research team.

"The trial not only showed we shouldn't be performing vertebroplasties, there was a much larger message," she said.

"It showed we shouldn't be offering new treatments to people in routine care before they have been proven to be of value in high quality trials."

Three further placebo-controlled trials have now been performed confirming the findings of the earlier placebo-controlled trials.

"Our work not only reduced use of this procedure worldwide, it also sparked discussion and debate about the need to ensure there is high certainty evidence of the benefits of surgery and other procedures prior to adopting them into practice, similar to the regulations that apply for new drugs. This should also apply to existing treatments that have not undergone rigorous evaluation – some of them might be doing more harm than good," Prof Buchbinder said.

There are now groups of surgeons around the world performing randomised placebo-controlled trials of different types of surgery and the methods for performing them continues to evolve. Prof Buchbinder also participated in an international workshop that developed guidance on how to conduct these trials, which was published in *The Lancet* in 2020.

## Journal Reference

Buchbinder R, Osborne RH, Ebeling PR, Wark JD, Mitchell P, Wriedt C, Graves S, Staples MP, Murphy B. (2009) A randomized trial of vertebroplasty for painful osteoporotic vertebral fractures. *N Engl J Med*. 361(6):557-68. doi: 10.1056/NEJMoa0900429.



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# PERSONALISING COLORECTAL CANCER TREATMENT THROUGH TARGETED THERAPY

CABRINI MONASH UNIVERSITY DEPARTMENT OF MEDICAL ONCOLOGY –  
THE SZALMUK FAMILY DEPARTMENT OF MEDICAL ONCOLOGY

Targeted therapies are developed based on the specific biology of cancer cells, characteristics which distinguish them from normal healthy cells. They are drugs or other substances that interfere specifically with ‘molecular targets’ to prevent growth, progression and spread of cancer.

The development and effective use of targeted therapies relies on information about an individual’s genes and proteins. It is not a ‘one size fits all’ approach like most standard chemotherapies. Targeted therapies are a cornerstone of precision medicine, which aim to recommend a specific treatment approach for each patient tailored to best target the cancer’s molecular profile. This would individualise treatment for each patient, rather than the current ‘one treatment fits all’ approach we use for most patients.

Cetuximab was the first targeted therapy developed for colorectal cancer. As a monoclonal antibody, cetuximab was designed to specifically target and bind the Epidermal Growth Factor Receptor (EGFR). EGFR is found on the surface of many normal and cancer cells. The EGFR gene is overexpressed in many patients with colorectal cancer and is associated with poor outcomes. Binding of cetuximab prevents EGFR from binding its ligands, and stops the cell from continuing to signal for pathways that promote cancer growth and spread.

Cabrini researcher and oncologist, Associate Professor Jeremy Shapiro, was a Principal Investigator on the international research team that developed cetuximab. He was also a key player in the development of a national coordinated clinical research program for gastro-intestinal cancer, the Australasian Gastro-Intestinal Trials Group (AGITG).

AGITG is a multidisciplinary collaborative group of medical and research professionals, which conducts clinical trials and related biological research to improve treatments for gastro-intestinal (GI) cancers. Cabrini patients were able to access cetuximab very early on through AGITG sponsored trials Co17, Co20, and ICECREAM, all led by A/Prof Shapiro at Cabrini. Results of these trials were published in major journals, including the New England Journal of Medicine.

As the results were analysed it appeared that only some patients were benefitting from the new medication, which also resulted in a troublesome skin rash for most patients. Further evaluation of the molecular profiles of patients on these types of trials revealed that only patients with a particular molecular alteration (KRAS wild-type) were benefitting from this treatment. This molecular test is now routinely used in all colon cancer patients around the world, allowing this agent to be reserved for those patients most likely to benefit, with other patients being able to move to other approaches more quickly.

The trials have been game changers in the treatment of advanced colorectal cancer, leading to improved patient outcomes and changes in treatment guidelines worldwide. Cetuximab was first approved by the Food and Drug Administration (FDA) for colorectal cancer in 2004. During the past two decades clinical trials have played an instrumental role in determining how cetuximab can be used by itself and in combination with other therapies to improve patient outcomes. The impact of cetuximab on colorectal cancer has been substantial. Almost 500,000 patients with metastatic advanced colorectal cancer have now received cetuximab-based therapy worldwide.

A/Prof Shapiro said the development of cetuximab, and the discovery of a molecular marker that could predict the chances of benefitting from it in advance of treatment was an exciting step in colon cancer treatment.

“Since then, other predictive targets have been identified, and more are under evaluation,” he said.

We are moving closer and closer to our goal of precision therapy in this disease. Clinical trials have allowed Cabrini patients early access to these novel treatment approaches, which have improved outcomes for our patients.

“WE ARE MOVING CLOSER AND CLOSER TO OUR GOAL OF PRECISION THERAPY IN THIS DISEASE. CLINICAL TRIALS HAVE ALLOWED CABRINI PATIENTS’ EARLY ACCESS TO THESE NOVEL TREATMENT APPROACHES, WHICH HAVE IMPROVED OUTCOMES FOR OUR PATIENTS.”



A/Prof Jeremy Shapiro, oncologist and cetuximab clinical trials Principal Investigator (left), with Demis Balamatsias, Senior Clinical Trial Study Coordinator Oncology Research, and Kate Hurford, Associate Team Leader, Oncology Research.  
Photo Credit: Darren James.

# A WORLD FIRST COMBINATION TREATMENT GIVES HOPE TO OVARIAN CANCER PATIENTS

CABRINI MONASH UNIVERSITY DEPARTMENT OF MEDICAL ONCOLOGY –  
THE SZALMUK FAMILY DEPARTMENT OF MEDICAL ONCOLOGY

Each year, about 1400 Australian women are diagnosed with ovarian cancer. Most are diagnosed with advanced disease (Stage III and Stage IV) and three quarters will relapse with progressive disease within the first three years of their initial treatment. The five-year survival rate is less than 30 per cent. First-line therapy with a combination of surgery and platinum-based chemotherapy, has been the standard of care for ovarian cancer for decades.

Almost half of all ovarian cancers have a BRCA1 or BRCA2 mutation or a similar genomic alteration that results in deficiencies in DNA damage repair. These mutated cells are susceptible to PARP inhibitors, which exploit the multiple DNA damage repair deficiencies to target and kill cancer cells. PARP inhibitors themselves act to block the poly ADP-ribose polymerase (PARP) enzyme, which is involved in the repair of damaged DNA. There is also a strong rationale to combine PARP inhibitors with ovarian first line treatments on the basis that platinum-based chemotherapy induces DNA damage, which should augment the efficacy of PARP inhibitors. Clinical trials have shown oral PARP inhibitors to have some success when used as single agents or as maintenance therapy in a number of cancers. However there have been challenges combining PARP inhibitors with first line chemotherapy due to patients not tolerating the toxicity.

The Velia trial, led by Professor Gary Richardson OAM at Cabrini, examined whether combining a new PARP inhibitor, veliparib, with first line chemotherapy, with or without veliparib maintenance therapy, could improve progression-free survival among patients with advanced ovarian cancer. It was the first ever phase 3 study to successfully combine a PARP inhibitor with first line chemotherapy.

A total of 1140 patients were enrolled across 202 sites in 10 countries from July 2015 through to July 2017. One third of the trial participants either received chemotherapy plus placebo followed by placebo maintenance (control group), chemotherapy plus veliparib followed by placebo maintenance (veliparib combination only), or chemotherapy plus veliparib followed by veliparib maintenance (veliparib throughout).

At the time of its publication in the New England Journal



*Prof Gary Richardson OAM, Velia clinical trial Principal Investigator, Group Director Cabrini Research, and Director Cabrini Monash University Department of Medical Oncology, Szalmuk Family Department of Medical Oncology. Photo Credit: Darren James.*

of Medicine in 2019, and after a median follow-up of 28 months, the results showed those patients who received veliparib throughout experienced a 32 per cent reduction in the risk of disease progression or death, compared with the control group who did not receive veliparib. The benefit was even more pronounced for those patients with BRCA mutations, increasing from an extra six months to 13 months before the cancer returned or worsened. Importantly, the study showed the potential toxicity of PARP and chemotherapy combination dosing was well managed, with veliparib patients still able to receive a high proportion of planned chemotherapy doses and patient reports on quality of life suggesting it was well tolerated.

Velia was unique in its trial design. Not only did it include PARP therapy from the start of chemotherapy, it also enrolled a broad patient population who may not have normally been eligible for other PARP maintenance trials, including patients with stable disease or refractory disease at the end of chemotherapy, or those without a deficiency in DNA damage repair mutation.

Prof Richardson said quite a few Cabrini patients with advanced ovarian cancer took part in the Velia trial.

“PARP inhibitors now play a pivotal role in the management of newly diagnosed ovarian cancer, and should be used as maintenance therapy after initial chemotherapy,” Prof Richardson said.

“Further work needs to be done to identify subgroups that benefit the most from this class of drug.”

## Journal Reference

Coleman RL, Fleming GF, Brady MF, Swisher EM, Steffensen KD, Friedlander M, Okamoto A, Moore KN, Efrat Ben-Baruch N, Werner TL, Cloven NG, Oaknin A, DiSilvestro PA, Morgan MA, Nam JH, Leath CA 3rd, Nicum S, Hagemann AR, Littell RD, Cella D, Baron-Hay S, Garcia-Donas J, Mizuno M, Bell-McGuinn K, Sullivan DM, Bach BA, Bhattacharya S, Ratajczak CK, Ansell PJ, Dinh MH, Aghajanian C, Bookman MA. (2019) Veliparib with First-Line Chemotherapy and as Maintenance Therapy in Ovarian Cancer. *N Engl J Med.* 381(25):2403-2415. doi: 10.1056/NEJMoa1909707.



IT WAS THE FIRST  
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CHEMOTHERAPY.”

Ioana Logan (left) and Emily Bove, Clinical Trial Study Coordinators Oncology Research.  
Photo Credit: Darren James.

# SUPPORTING RELIGIOUS AND CULTURAL ADVANCE CARE PLANNING DISCUSSIONS

CABRINI MONASH UNIVERSITY DEPARTMENT OF NURSING RESEARCH

Advance care planning (ACP) is the process of planning a person's current and future healthcare needs. Understanding their values, beliefs and preferences helps people to make end-of-life decisions about their care when they are not able to make those decisions themselves. Integration of ACP has been associated with improved quality of life, better adherence to patients' wishes, and reduced hospitalisations.

Although there are a large number of resources available to support ACP today, it was only six years ago when very few to no resources were available to meet the needs of multicultural and multifaith populations in Australia. Without appropriate resources, General Practitioners (GPs) and other healthcare providers struggle to have well informed ACP conversations about death, dying, and end-of-life care with people from religiously and culturally diverse backgrounds.

In early 2015, Professor Lee Boyd and Amanda Pereira-Salgado from the Centre for Nursing Research at Cabrini, secured funding from the Australian Government Department of Health to develop the ACPTalk website. The aim was to deliver a web-based resource that would support health professionals in conducting conversations within diverse religious and cultural populations. Website solutions were to include religious and cultural information, communication ideas, legal information and downloadable content. Christian and non-Christian faiths were to be included in the religion-specific content.

Extensive consultation and interviews were undertaken with 37 key stakeholders including representatives of religious and cultural organisations (n=29), healthcare (n=5), and community organisations (n=3) to establish the acceptability and usability of the ACPTalk website. The majority of stakeholders strongly agreed or agreed that the content developed for the website used appropriate language and tone (92 per cent, 34/37), would support health professionals (89 per cent, 33/37), and was accurate (83 per cent, 24/29). A total of 107 Australian-based users completed the website survey with similarly



Professor Lee Boyd, project lead on the ACPTalk website, former Executive Director Nursing and Cabrini Institute.

positive feedback. Interviews with Buddhist, Christian, Hindu, Islamic, Jewish, Sikh and Bahá'í leaders informed how people of different faiths understand and consider ACP and its implications, including how religion affects followers' approaches to end-of-life care and ACP, and their implications for healthcare.

The project successfully met all its deliverables and was completed in June 2017. Resource usage within the first nine months was 12,957 page views in 4260 sessions; the majority (83 per cent) were from Australia. ACPTalk was nominated for a Catholic Health Australia award in 2017 for Excellence in Pastoral Care.

Although the ACPTalk website couldn't be maintained without a constant source of funding, it was one of the first ACP resources that supported cultural and religious diversity. It has ultimately helped many healthcare workers to provide sensitive and appropriate care and paved the way for newer ACP educational resources that encompass cultural and religious differences.

## Journal References

Pereira-Salgado A, Mader P, O'Callaghan C, Boyd L. (2018) A Website Supporting Sensitive Religious and Cultural Advance Care Planning (ACPTalk): Formative and Summative Evaluation. *JMIR Res Protoc*. 7(4):e78. doi: 10.2196/resprot.8572.

Pereira-Salgado A, Mader P, O'Callaghan C, Boyd L, Staples M. (2017) Religious leaders' perceptions of advance care planning: a secondary analysis of interviews with Buddhist, Christian, Hindu, Islamic, Jewish, Sikh and Bahá'í leaders. *BMC Palliat Care*. 16(1):79. doi: 10.1186/s12904-017-0239-3.

ACPTALK WAS ONE OF THE FIRST ACP RESOURCES THAT SUPPORTED CULTURAL AND RELIGIOUS DIVERSITY. IT HAS ULTIMATELY HELPED MANY HEALTHCARE WORKERS TO PROVIDE SENSITIVE AND APPROPRIATE CARE AND PAVED THE WAY FOR NEWER ACP EDUCATIONAL RESOURCES.



Amanda Pereira-Salgado, project lead on the ACPTalk website, former Research Associate, Centre for Nursing Research at Cabrini.

# IMPROVING OUTCOMES FOR COLORECTAL CANCER PATIENTS THROUGH PATIENT FEEDBACK

CABRINI MONASH UNIVERSITY DEPARTMENT OF SURGERY

Colorectal cancers are characterised by high symptom, functional and emotional burdens. Furthermore, these outcomes can persist even after eradication of the tumour. It is critical that patients with colorectal cancer receive the best possible symptomatic, functional and psychological support throughout their treatment trajectory and into survivorship.

Currently, patients undergoing colorectal cancer treatment are not specifically asked to answer questions about their symptom and functional outcomes, well-being and their health-related quality of life. As a result, there is a need to provide survivorship care that is tailored to individual circumstances in order to improve patient and health system outcomes.

In 2021 the Cabrini Monash University Department of Surgery, led by Professor Paul McMurrick, launched the Patient-Reported Outcome Measures (PROMs) program. PROMs ask for a patient's assessment of how a health service or intervention has, over time, affected their quality of life through answering a series of questions regarding daily functioning, symptom severity, and other dimensions of health. The aim of this Victorian-first program is to provide clinicians with valuable insights regarding how a patient's life is affected by colorectal cancer treatment, which will allow for improved health service and enable patients to enjoy the best possible quality of life before, during and after treatment.

"We are interested in finding a way to understand not only the outcomes for patients at the end of treatment, but how their lives are affected during it," said Prof McMurrick, Head of the Cabrini Monash University Department of Surgery at Cabrini Health.

This program, funded by the Collie Foundation and Let's Beat Bowel Cancer, a not-for-profit Cabrini initiative, will provide a platform for patients with colorectal cancer, undergoing surgery, to voice their health-related concerns throughout the course of their treatment, through to survivorship. The PROMS questionnaire adopted in this program comprises of the International Consortium of Health Outcome Measure Colorectal Cancer Standard Set, in addition to questions relating to low-anterior resection syndrome score and patient satisfaction. The PROMs patient data will be integrated into the Cabrini Monash Colorectal Neoplasia Database, a prospectively maintained clinician-led database, adding a new dimension to the database.

"This invaluable information will allow for improvements in patient care by enhancing patient-clinician communication, clinical decision-making and improving symptom monitoring," said Dr Christine Koulis, Senior Research Fellow and PROMs Study Coordinator.

In summary, the implementation of this important program at Cabrini aims to improve survival for colorectal cancer patients by providing a platform for patients to voice their health-related concerns.

"WE ARE INTERESTED IN FINDING A WAY TO UNDERSTAND NOT ONLY THE OUTCOMES FOR PATIENTS AT THE END OF TREATMENT, BUT HOW THEIR LIVES ARE AFFECTED DURING IT."



*Prof Paul McMurrick,  
Director Cabrini  
Monash University  
Department of Surgery.*



*Dr Christine Koulis, Senior  
Postdoctoral Research  
Fellow, Cabrini Monash  
University Department of  
Surgery.*



| Nurse-researcher discusses the PROMs program with a patient.

# COMBATting THE RISING COST OF HEALTHCARE WORLDWIDE

MONASH-CABRINI DEPARTMENT OF CLINICAL EPIDEMIOLOGY

The cost of healthcare worldwide is rising unsustainably. Healthcare systems are being challenged by multiple threats to their capacity to deliver high-quality care. These include ageing populations, increasing rates of chronic and complex diseases, growing cost pressures from new medical technologies and medicines, wasteful spending on low-value care, inefficiencies arising from system fragmentation and limited use of data and evidence to support reform.

The NHMRC Partnership Centre for Health System Sustainability (PCHSS) was established in July 2017. It is jointly governed and funded to the value of \$10.7 million over five years by the NHMRC, Bupa Health Foundation, NSW Health Foundation, NSW Health, Department of Health Western Australia and the University of Notre Dame Australia. The Partnership Centre is made up of a collaborative network led by six research lead investigators, and includes system and system-based investigators, expert advisors and system implementation partners from across Australia. Collaborators come from all states and territories and work within many sectors, including academia, public health and hospitals, private health, health insurance, government, not-for-profit healthcare and consumer advocacy. Their vision is to produce research that contributes to the development of a resilient healthcare system – one that is affordable, cost effective, and delivers improved health outcomes for all Australians.

The PCHSS is exploring the challenges to health system sustainability and is identifying and evaluating a set of practical interventions that are appropriate from clinical, patient, and economic perspectives. There are three key research themes to deliver on these goals:

Theme 1 - Using analytics, technology and shared-data

Theme 2 - Reducing waste and low-value care

Theme 3 - Promoting better value for the health dollar

Cabrini is a PCHSS system implementation partner, and PCHSS research lead investigator Professor Rachelle Buchbinder AO, is co-leading Theme 2, which is focused on reducing waste and identifying alternate models of care, which deliver effective and appropriate services for the same or better outcomes but at a lower cost. The Monash-Cabrini team, also being led by Associate Professor Denise O'Connor, has identified alternative models of service delivery that are considered most promising for increasing value in the delivery of healthcare in Australia based upon a scoping review and Delphi study involving an expert panel of health policy,

clinical, academic and consumer stakeholders. However, most of these have not yet been proven to be as effective and or efficient than more traditional models.

Several of these are now being investigated further, including an exploration of the uptake of hospital in the home across all Australian hospitals based upon data from the Independent Hospital Pricing Authority (IHPA) being led by Ms Alexandra Gorelik. Three Cochrane systemic reviews are underway. The first is investigating the value of models for delivery of primary and/or specialist care to older adults living in residential aged care facilities, led by Dr Polina Putrik. The second is the delivery of intravenous anti-cancer therapy at home versus in hospital or community settings for adults with cancer, led by Dr Liesl Grobler. The third is a qualitative evidence synthesis investigating factors affecting early discharge hospital at home and admission avoidance hospital at home, led by Dr Jason Wallis. Dr Wallis is also leading a trial of an education package, which aims to increase uptake of rehabilitation in the home following hip or knee joint replacement at Cabrini Health, one alternative model that is supported by high quality evidence of equi-effective outcomes compared with inpatient rehabilitation, although it is unclear whether this is a cheaper alternative from the perspective of the healthcare provider. This trial is also being supported by a HCF Foundation grant.

THEIR VISION IS TO PRODUCE RESEARCH THAT CONTRIBUTES TO THE DEVELOPMENT OF A RESILIENT HEALTHCARE SYSTEM – ONE THAT IS AFFORDABLE, COST EFFECTIVE, AND DELIVERS IMPROVED HEALTH OUTCOMES FOR ALL AUSTRALIANS.





| Healthcare practitioners.



*Prof Rachelle Buchbinder AO, PCHSS research lead investigator, Director Monash-Cabrini Department of Clinical Epidemiology.*



*A/Prof Denise O'Connor, Deputy Director Monash-Cabrini Department of Clinical Epidemiology.*



*Dr Jason Wallis, Postdoctoral Research Fellow, Monash-Cabrini Department of Clinical Epidemiology.*

# GREATER TREATMENT CHOICES FOR NON-HODGKIN'S LYMPHOMA

CABRINI MONASH UNIVERSITY DEPARTMENT OF MEDICAL ONCOLOGY –  
THE SZALMUK FAMILY DEPARTMENT OF MEDICAL ONCOLOGY

Non-Hodgkin's lymphoma (NHL) is a type of cancer that begins in the lymphatic system, which plays an important role in the body's immune response. NHL is a group of more than 30 subtypes of lymphoma, distinguished by the type of white blood cell (lymphocyte) that is affected, T cells, B cells or NK cells. Slow growing subtypes are referred to as indolent NHL, and primarily affect B cells. They account for about 40 per cent of all NHL cases. Mantle cell lymphoma (MCL), also affecting B cells, is a rarer NHL subtype accounting for only five to ten per cent of all cases, and is typically more aggressive in nature.

Rituximab was first developed for the treatment of NHL. As a monoclonal antibody treatment, rituximab recognises and binds the CD20 cell surface protein found on B cells and causes cell death. Rituximab combination therapy regimens (rituximab plus cyclophosphamide, doxorubicin, vincristine and prednisone [R-CHOP] or rituximab plus cyclophosphamide, vincristine, and prednisone [R-CVP]) are standard first treatment options for people with indolent NHL and MCL. In the early 2000s however, clinical trials testing bendamustine, an anti-cancer alkylating agent that kills cells by interfering with the DNA and RNA, were showing promise as a treatment on its own and in combination with rituximab, suggesting it may be a potential alternative first treatment option for indolent NHL and MCL.

The BRIGHT clinical trial, led by Cabrini oncologist and researcher Dr Kirsten Herbert, compared R-CHOP and R-CVP standard of care treatments to a combination of bendamustine with rituximab (BR) as first time treatments in patients with advanced indolent NHL or MCL. BRIGHT enrolled 447 patients from seven countries between 2009 and 2012.

The study demonstrated that BR was noninferior to R-CHOP and R-CVP, meaning that BR was as effective as these standard of care treatments, showing similar complete response rates. When overall response rates were assessed, BR showed superiority to standard of care treatments, meaning it was more effective. Interestingly, BR demonstrated a very different safety profile to R-CHOP and R-CVP, with vomiting and drug-hypersensitivity reactions more common with BR



Dr Kirsten Herbert,  
oncologist and BRIGHT  
clinical trial Principal  
Investigator.

treatment, and peripheral neuropathy/paresthesia and alopecia more common with R-CHOP and R-CVP standard therapy regimens.

The BRIGHT study played an instrumental role in establishing BR as a first line therapy for indolent NHL and MCL, and still remains a preferred regimen more than 10 years later. The findings mean patients have a much wider range of treatment options, and their choice may be driven by preferences regarding the different safety profiles of the treatment types.

Dr Herbert said the BRIGHT study was a landmark practice-changing trial in the management of low-grade lymphoma.

"The bendamustine-based regimen was as efficacious as the older treatment regimen, and caused far less toxicity and improved quality-of-life," Dr Herbert said.

"The impact on patients with this condition has been enormous."

THE BRIGHT STUDY PLAYED  
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ESTABLISHING BR AS A FIRST LINE  
THERAPY FOR INDOLENT NHL  
AND MCL, AND STILL REMAINS A  
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## Journal Reference

Flinn IW, van der Jagt R, Kahl BS, Wood P, Hawkins TE, Macdonald D, Hertzberg M, Kwan YL, Simpson D, Craig M, Kolibaba K, Issa S, Clementi R, Hallman DM, Munteanu M, Chen L, Burke JM. (2014) Randomized trial of bendamustine-rituximab or R-CHOP/R-CVP in first-line treatment of indolent NHL or MCL: the BRIGHT study. *Blood*. 123(19):2944-52. doi: 10.1182/blood-2013-11-531327.



Oncology Research Clinical Trials team members (left to right) Koby Scarff, Simer Khaira and Team Leader Li Hoon Lai.  
Photo Credit: Darren James.

# NATIONAL GUIDELINES REDUCING THE RISK OF COVID-19 AEROSOL TRANSMISSION

INTENSIVE CARE RESEARCH UNIT

The COVID-19 pandemic placed healthcare workers at a heightened risk of infection. COVID-19 virus spreads via contact with contaminated surfaces, droplets and aerosols. Aerosol transmission is of particular concern because it can remain suspended in the air and is easily produced by actions such as coughing, sneezing, shouting and singing. This puts frontline healthcare workers at greatest risk.

In the healthcare setting there are a number of procedures which are known to be aerosol generating including intubation, extubation and tracheotomy. Of patients presenting with COVID-19, it has been reported that up to one fifth of cases required an ICU admission. Someone presenting with severe respiratory distress syndrome is likely to require emergency tracheal intubation and mechanical ventilation to support a potential recovery from their illness. The process of caring for patients with severe COVID-19 and performing procedures associated with aerosol generating events in this group thus present an increased risk of infection for healthcare workers.

COVID-19 was classified as a high consequence infectious disease, emphasising the significant risk to healthcare workers and the healthcare system. The consensus statement on Safe Airway Society principles of airway management and tracheal intubation specific to the COVID-19 adult patient group was planned on 11 March 2020, when an urgent need for guidance in Australia and New Zealand for both clinical practice and staff preparation for the COVID-19 pandemic was identified.

Led by Associate Professor David Brewster, Deputy Director and Head of Intensive Care Research at Cabrini, the Safe Airway Society board assembled 14 experts from Australia and New Zealand to prepare the statement. They first reviewed the current literature on COVID-19 relevant to airway practice, as well as relevant publications from the 2003 SARS epidemic. The consensus statement recommended safe, simple, familiar, reliable and robust practices that should be adopted for all episodes of airway management for patients with COVID-19.

These crucial national guidelines were immediately widely endorsed by all relevant specialty colleges and airway societies in Australia and New Zealand. The main recommendations were:

- Using specific equipment, such as videolaryngoscopy, during all intubations.
- Using checklists and newly designed cognitive aids that had been specifically modified for the COVID-19 patient group to keep staff and patients safe.
- Early intubation to prevent the additional risk to staff of emergency intubation and to avoid prolonged use of high flow nasal oxygen or non-invasive ventilation.
- Significant institutional preparation is required to optimise staff and patient safety in preparing for the airway management of the COVID-19 patient group.
- The principles for airway management should be the same for all patients with COVID-19 (asymptomatic, mild or critically unwell).
- Safe, simple, familiar, reliable and robust practices should be adopted for all episodes of airway management for patients with COVID-19.

The consensus statement was published in the Medical Journal of Australia in June 2020 and had over 350 citations in its first year. A/Prof Brewster who led the consensus statement said it has been the one of the most downloaded and cited papers in Australia in 2020 and “had more impact in the clinical space than we could ever have foreseen”.

“It was a real privilege to work with and lead a national panel of experts in our field to create something to guide all clinicians in Australia and New Zealand. The uptake of these guidelines has been phenomenal. A follow up paper we have done has shown these guidelines, and specifically their components such as simulation training for team preparation, or the use of the aids and checklists, were adopted by 97 per cent of hospitals for the airway management of COVID-19 last year. They have also been used as national guidelines in multiple other countries and helped places like Canada with the institution of national guidelines too. We definitely helped create a universal practice for the staff in ICU, theatre and emergency departments at a time of great clinician anxiety. It is an achievement of which we will always be proud,” said A/Prof Brewster.



“WE DEFINITELY HELPED CREATE A UNIVERSAL PRACTICE FOR THE STAFF IN ICU, THEATRE AND EMERGENCY DEPARTMENTS AT A TIME OF GREAT CLINICIAN ANXIETY. IT IS AN ACHIEVEMENT OF WHICH WE WILL ALWAYS BE PROUD.”

A/Prof David Brewster (left), Deputy Director of Intensive Care and Head of Intensive Care Research at Cabrini Health, and the Clinical Dean for the Monash University Clinical School, and A/Prof Vineet Sarode, Director of Intensive Care at Cabrini Health.

#### Journal Reference

Brewster DJ, Chrimes N, Do TB, Fraser K, Groombridge CJ, Higgs A, Humar MJ, Leeuwenburg TJ, McGloughlin S, Newman FG, Nickson CP, Rehak A, Vokes D, Gatward JJ. (2020) Consensus statement: Safe Airway Society principles of airway management and tracheal intubation specific to the COVID-19 adult patient group. *Med J Aust.* 212(10):472-481. doi:10.5694/mja2.50598

# BIG DATA TO IMPROVE OUTCOMES FOR PATIENTS WITH INFLAMMATORY ARTHRITIS

MONASH-CABRINI DEPARTMENT OF CLINICAL EPIDEMIOLOGY

Hundreds of thousands of Australians suffer with inflammatory arthritis, caused by an overactive immune system resulting in painful joint inflammation. The Australian Rheumatology Association Database (ARAD) was established in 2003 and collects important health information from individuals with inflammatory arthritis such as rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis and juvenile idiopathic arthritis. ARAD specifically looks at the long-term effectiveness and safety of biologic and targeted-synthetic disease modifying antirheumatic drugs (bDMARDs and tsDMARDs) and other therapies used to treat inflammatory arthritis, with the ultimate aim of providing better care and improving outcomes for patients.

More than 6000 participants have enrolled in ARAD to date, with data collected by questionnaires at 6 to 12 monthly intervals examining medical history, medication history, responses to medication, physical functioning and quality of life. ARAD also perform linkages to MBS and PBS data and state and national cancer and death registries. More than 30,000 years of follow up data have been collected, and patient outcome reports are regularly provided to participating rheumatologists.

ARAD supports and drives a number of collaborative research projects. In response to the COVID-19 pandemic, ARAD is collaborating with the COVID-19 Global Rheumatology Alliance to look at direct and indirect impacts of COVID-19 on individuals with inflammatory arthritis.

ARAD is also being upgraded to the Australian Arthritis and Autoimmune Biobank Collaborative (A3BC) to add biobanking capabilities and an expanded scope of data capture through the rollout of the A3BC-ARAD biobank-registry network. Recruitment

is currently targeted towards patients with rheumatoid arthritis, ankylosing spondylitis, juvenile arthritis, psoriatic arthritis, giant cell arthritis and gout.

ARAD is owned by the Australian Rheumatology Association (ARA) and its inception and management has been driven by former ARA President, Professor Rachele Buchbinder AO, Director of the Monash-Cabrini Department of Clinical Epidemiology, together with other collaborators Professors Lyn March, Marissa Lassere and Catherine Hill. The day-to-day management of ARAD is performed by Mr Ashley Fletcher, ARAD Project Manager and Ms Vibhasha Chand, ARAD Database Manager, both members of the Monash-Cabrini Department of Clinical Epidemiology. ARAD has been financially supported by a range of funding sources including an NHMRC Enabling Grant (2006 to 2012), unrestricted pharmaceutical company educational grants to ARA and in-kind support from Cabrini Research, Monash University, University of Sydney and the Royal North Shore Hospital.



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ARAD SPECIFICALLY  
LOOKS AT THE LONG-TERM  
EFFECTIVENESS AND SAFETY  
OF BIOLOGIC AND TARGETED-  
SYNTHETIC DISEASE MODIFYING  
ANTIRHEUMATIC DRUGS (BDMARDS  
AND TSDMARDS) AND OTHER  
THERAPIES USED TO TREAT  
INFLAMMATORY ARTHRITIS.

# MODIFYING THE EPIGENOME AS A NOVEL AVENUE FOR COLON CANCER PERSONALISED THERAPY

CABRINI MONASH UNIVERSITY DEPARTMENT OF SURGERY

Colorectal cancer is one of the most prevalent and fatal types of cancers. New therapeutic options and biomarkers to guide personalised treatment approaches are desperately needed to improve patient outcomes.

During the past couple of decades, epigenetic alterations have come to be known as important molecular hallmarks of cancer. Unlike genetic mutations, which are unmodifiable changes to the DNA sequence, epigenetic alterations control inheritable changes to gene expression without a change to the DNA sequence. Epigenetic factors include DNA methylation, histone modifications and non-coding RNAs. Due to their reversible nature they are key targets for therapeutic development and some have shown great success in the clinic as cancer treatments.

It is well known that genetic alterations play a major role in colorectal cancer, however it is becoming evident that epigenetic alterations also contribute to the disease pathogenesis. A \$2 million Victorian Cancer Agency (VCA) grant awarded in 2016, funded a collaborative effort between the Hudson Institute of Medical Research, Monash University and Cabrini Monash University Department of Surgery, to test a new suite of anti-cancer epigenetic modulating drugs called BET inhibitors. The aim was to identify which patients with bowel or prostate cancer would respond well to BET inhibitors. The long noncoding RNA colon cancer-associated transcript 1 (CCAT1) in colon cancer and PCAT1 in prostate cancer were being evaluated as biomarkers at the point of diagnosis to identify patients who are likely to benefit from BET inhibitors.

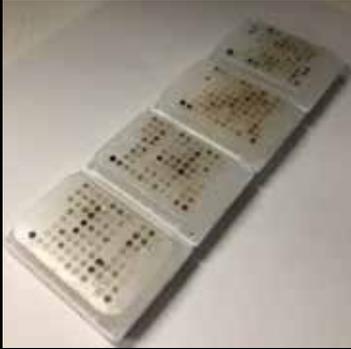
Bromodomain and Extra-Terminal motif (BET) proteins read epigenetic marks, binding acetylated histones and other proteins to positively regulate gene expression. Suppression of their activity by BET inhibitors leads to their displacement and results in down regulation of gene expression.

As chief investigators on the grant, Professor Paul McMurrick and Dr Simon Wilkins from the Cabrini Monash University Department of Surgery, created the tissue microarrays (TMAs) which were backed up by patient information from the Cabrini Monash Colorectal Neoplasia Database. The TMAs were provided to the team at the Hudson Institute of Medical Research to stain for the CCAT1 biomarker. The Cabrini Monash Department of Surgery also contributed fresh colon cancer tissue samples to the Monash Biomedicine Discovery Institute's Epithelial Regeneration Laboratory, led by Professor Helen Abud, to establish organoid models for BET inhibitor testing.

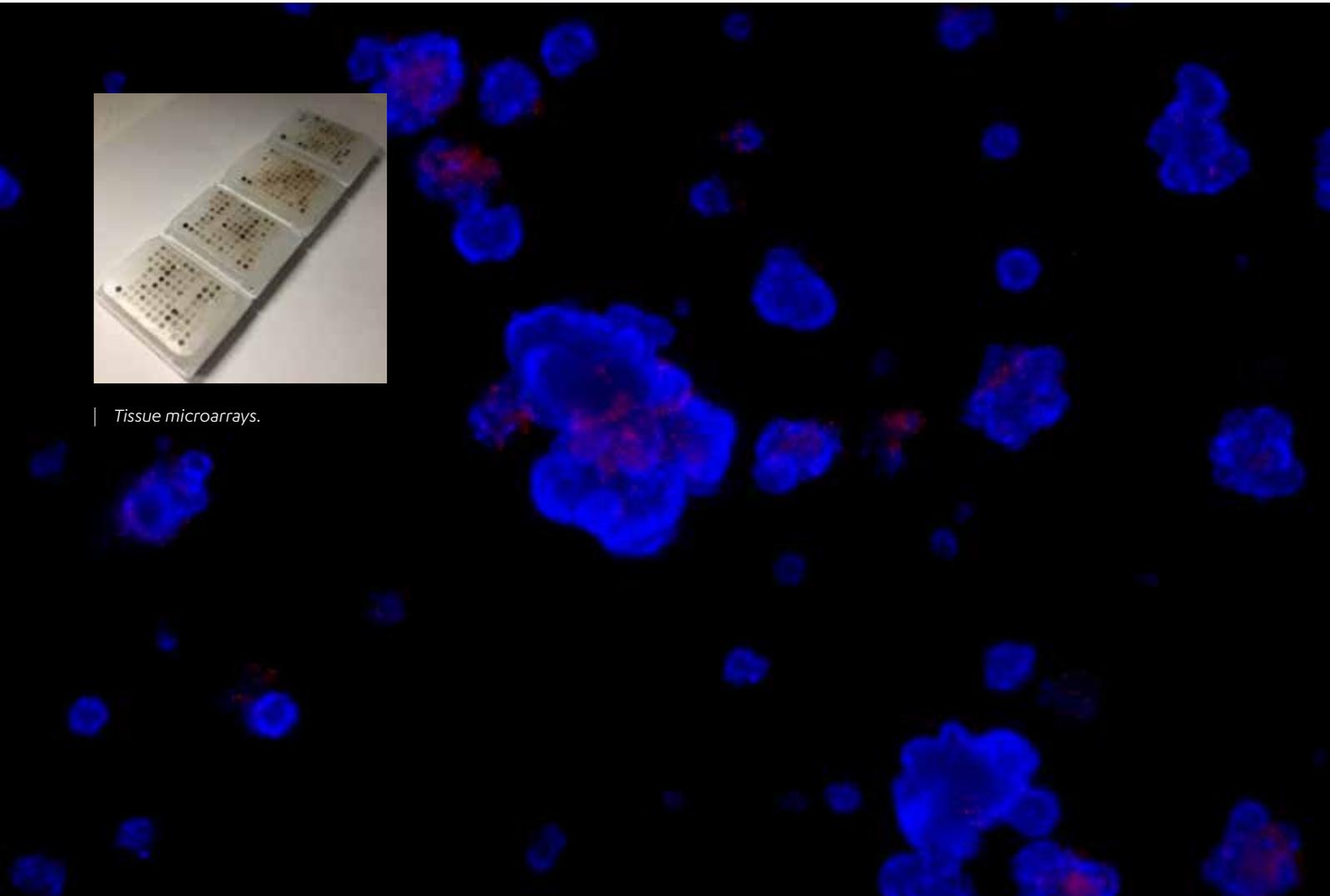
The overall outcomes from the grant were promising and a number of preclinical models have been successfully established through the collaborative efforts of the clinical and academic bench research teams. Clinically relevant and unique drug resistant prostate cancer and metastatic colon cancer preclinical models in both ex vivo (organoid) and in vivo (patient derived xenografts) forms have been created, enabling the exciting opportunity to test the response to BET inhibitors. Successful generation of the organoid models has translated into additional grant funding from Cancer Australia and the NHMRC and so far, at least two publications have been funded by the VCA grant. The tissue microarrays generated are an excellent resource for ongoing studies in biomarkers.

In the original VCA grant application the research teams had aimed to conduct an investigator initiated clinical trial of BET inhibitors in prostate and colon cancer patients, but a lack of pharmaceutical support to provide the BET inhibitors meant it couldn't be achieved. Instead, a Phase 1b GSK sponsored clinical trial (NCT03150056) was started with the first patient recruited in November 2017. This trial was open at Monash Health and was a world first in providing prostate cancer patients a chance to enrol in a study combining a BET inhibitor (GSK525762) with hormonal therapy. Although the trial didn't provide access to colon cancer patients, it will provide proof of concept data regarding PCAT1 testing and BET inhibitors in the clinic.

IT IS WELL KNOWN  
THAT GENETIC  
ALTERATIONS PLAY A  
MAJOR ROLE IN COLORECTAL  
CANCER, HOWEVER IT IS  
BECOMING EVIDENT THAT  
EPIGENETIC ALTERATIONS ALSO  
CONTRIBUTE TO THE DISEASE  
PATHOGENESIS.



| Tissue microarrays.



| Microscope image of tumour organoid labelled with fluorescent dyes to visualize live (Hoescht, blue) versus dead cells (PI, red).



| Dr Simon Wilkins, Senior Postdoctoral Research Fellow, Cabrini Monash University Department of Surgery.



| Prof Paul McMurrick, Director Cabrini Monash University Department of Surgery.

# IMMUNOTHERAPY, ENDOMETRIAL CANCER, AND MISMATCH DNA REPAIR DEFICIENCY STATUS

CABRINI MONASH UNIVERSITY DEPARTMENT OF MEDICAL ONCOLOGY –  
THE SZALMUK FAMILY DEPARTMENT OF MEDICAL ONCOLOGY

Endometrial cancer is a type of cancer that begins in the uterus or womb. It is the most common type of gynaecological cancer affecting women in developed countries such as Australia with the incidence increasing at alarming rates. Every year more than 3000 women are newly diagnosed and more than 600 die from endometrial cancer in Australia. Overall the survival rates are very good, with the chances of a woman surviving five years after her diagnosis being 83 per cent, however the number of women dying each year is increasing.

There are different types of endometrial cancer with some much more aggressive and for these tumours survival rates are often very poor whereas others have a very good prognosis with very little chance of recurrence. One type of endometrial cancer, known as mismatch repair deficient (dMMR), make up 15 to 30 per cent of all endometrial cancers. A hereditary cancer syndrome, known as Lynch Syndrome, makes up 5 to 10 per cent of this tumour type, while the others develop a genetic change in them as a result of time or life changes. Women with Lynch Syndrome are at much greater risk of developing endometrial cancer.

Treatment options for women with advanced or recurrent endometrial cancer are limited. Very few drugs have received approval in the last 50 years. The development of immunotherapy drugs in the last five to ten years provide a potentially new therapeutic avenue for women with endometrial cancer. Immunotherapy works by releasing the brakes on the body's immune system, activating it to target and kill cancer cells. dMMR endometrial cancers are predicted to respond well to immunotherapy due to the high level of immune cells in and around the tumour together with a high level of mutated antigens generated by dMMR which would attract a strong immune T cell response, a key effector in the immune response.

Associate Professor Yoland Antill from Cabrini together with a team of investigators from Australia developed and designed one of the very first studies looking at the use of immunotherapy in treating endometrial cancer. The PHAEDRA study (PHase 2 trial of Durvalumab in Advanced Endometrial Cancer) run through the Australia New Zealand Gynaecological Oncology Group (ANZGOG), examined the activity of the immunotherapeutic agent

durvalumab in women with advanced endometrial cancer that were either dMMR or pMMR.

Women with endometrial cancer with pMMR who had progressed after one to three lines of prior chemotherapy, and women with endometrial cancer with dMMR who had progressed after zero to three lines of prior chemotherapy were eligible. Almost equal numbers of women with dMMR or pMMR endometrial cancers (71 in total) were enrolled across 10 sites in Australia between February 2017 and September 2018.

PHAEDRA showed durvalumab to have promising efficacy in dMMR patients, with tumour shrinkage evident in 47 per cent of the patients (17/36), including six complete responses and 11 partial responses. In stark comparison, only three per cent of pMMR patients responded (1/35). In the dMMR patient group, a positive response was greater in those where durvalumab was their first-line of therapy. The median time to cancer progression was 8.3 months in the dMMR group compared to only 1.8 months in the pMMR group. Durvalumab was reasonably well tolerated, with only low grade immune-related adverse events reported. Cabrini contributed significantly to the study and still has one patient on trial who continues to maintain benefit from durvalumab treatment after several years.

PHAEDRA was one of the first studies to look at the use of immunotherapy in endometrial cancer patients. Interestingly the study demonstrated that mismatch repair deficiency status markedly determines the chances of responding well to durvalumab. A/Prof Antill said that "The encouraging outcomes are consistent with results coming out from other trials that have tested different immunotherapies in endometrial cancer, and certainly implies a change to the way we should consider treating dMMR endometrial cancers, but also points to the need for further research to understand how to improve on the response to immune therapy, particularly in the pMMR cancers.

The primary study results from PHAEDRA were presented at the international ASCO conference in 2019 as an oral abstract and were published in the Journal for Immunotherapy of Cancer in June 2021. Secondary results looking at the establishment of PDL1 cut points was accepted and presented as a poster at the 2021 ASCO conference.

## Journal Reference

Antill Y, Kok PS, Robledo K, Yip S, Cummins M, Smith D, Spurdle A, Barnes E, Lee YC, Friedlander M, Baron-Hay S, Shannon C, Coward J, Beale P, Goss G, Meniawy T, Lombard J, Andrews J, Stockler MR, Mileskin L; Australia New Zealand Gynaecological Oncology Group (ANZGOG). (2021) Clinical activity of durvalumab for patients with advanced mismatch repair-deficient and repair proficient endometrial cancer. A nonrandomized phase 2 clinical trial. *J Immunother Cancer*. 9(6):e002255. doi: 10.1136/jitc-2020-002255.



Prof Gary Richardson OAM with his patient Toan (centre) who is on the PHAEDRA clinical trial, and Oncology Research Clinical Trial Study Coordinator Ioana Logan.



A/Prof Yoland Antill, oncologist, Study Chair and Cabrini Principal Investigator for the PHAEDRA clinical trial.

PHAEDRA WAS ONE OF THE FIRST STUDIES TO LOOK AT THE USE OF IMMUNOTHERAPY IN ENDOMETRIAL CANCER PATIENTS. INTERESTINGLY THE STUDY DEMONSTRATED THAT MISMATCH REPAIR DEFICIENCY STATUS MARKEDLY DETERMINES THE CHANCES OF RESPONDING WELL TO DURVALUMAB.

# STOPPING THE VICIOUS CYCLE – DENOSUMAB REIGNS SUPERIOR

CABRINI MONASH UNIVERSITY DEPARTMENT OF MEDICAL ONCOLOGY –  
THE SZALMUK FAMILY DEPARTMENT OF MEDICAL ONCOLOGY

Bone is one of the most common metastatic sites for cancer. Patients with metastatic bone disease are at significant risk of complications including bone fractures, spinal cord compression, orthopedic surgery, and palliative radiation of the bone, collectively referred to as skeletal related events (SREs). SREs are indicators of poor prognosis and can cause substantial pain and suffering. They can also contribute to malignant hypercalcaemia (increased calcium released from the bone to the blood).

Bone is remodeled constantly, new bone is formed by osteoblast cells, and old bone is resorbed or ‘chewed up’ by osteoclast cells. Under normal conditions the opposing activities of the two cell types work harmoniously to remodel bone to maintain a healthy skeleton. A key mediator of osteoclast activity is receptor activator of nuclear factor kappa-B ligand (RANKL), a protein found on the surface of osteoblast cells, other cell types, and in soluble form.

Cancer metastasising to bone disrupts the normal bone remodelling process and initiates a so-called ‘vicious cycle’ of bone resorption and tumour proliferation in the bone space. Osteoclast cells are stimulated by the presence of the cancer cells to chew up more bone, and the degrading bone releases growth factors that provide nutrients for cancer cell growth, a vicious cycle that leads to SREs.

Zoledronic acid and denosumab are bone modifying agents that can modulate the activity of osteoclasts and prevent SREs. Zoledronic acid belongs to a class of drugs called bisphosphonates, which have been in use for almost three decades. Zoledronic acid binds directly to bone and inhibits osteoclast bone resorption activity. Denosumab is a newer class of targeted therapeutic, a monoclonal antibody that recognises and blocks RANKL, inhibiting osteoclast activity.

From 2006 to 2008, Cabrini participated in three identical Amgen clinical trials that compared denosumab with zoledronic acid in the treatment of bone metastases in breast cancer, prostate cancer, solid tumours and multiple myeloma. The studies, led by Principal Investigators Professor Gary Richardson OAM and Associate Professor Jeremy Shapiro, individually showed denosumab was either superior or non-inferior to zoledronic acid depending on the cancer type assessed.

In 2012, a study co-led by Prof Richardson combined the patient-level analyses from the three identical trials to have more power to fully evaluate the safety and efficacy of using denosumab and zoledronic acid.



*Professor Gary Richardson OAM, Group Director Cabrini Research, and Director Cabrini Monash University Department of Medical Oncology, Szalmuk Family Department of Medical Oncology.*

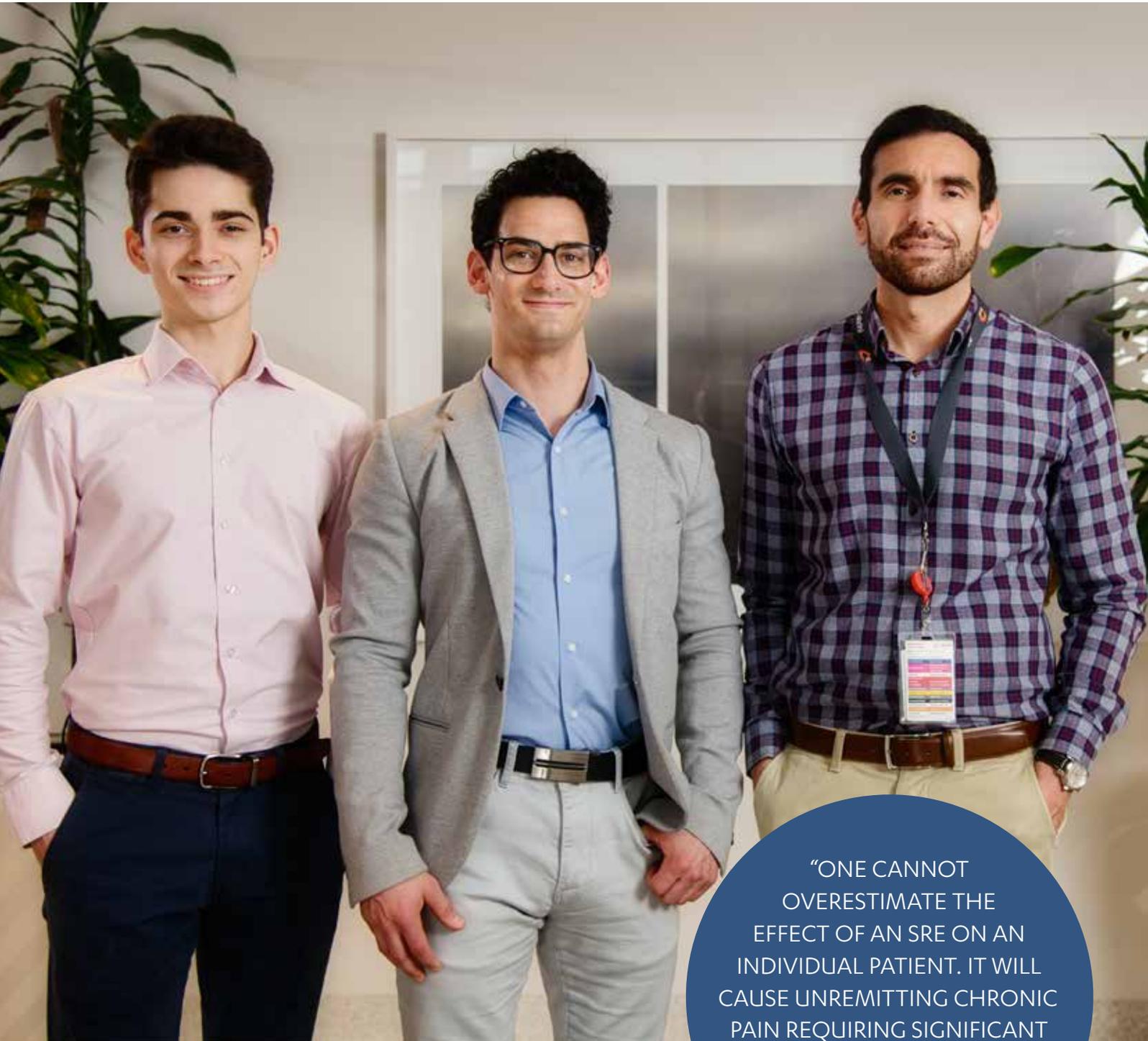
The study combined data from 5723 patients who had participated in one of the three trials conducted at 705 sites worldwide.

Importantly, the higher-powered study identified that denosumab was superior to zoledronic acid in delaying all types of SREs by more than eight months, and reduced the risk of a first on-study SRE by 17 per cent across all cancer diagnoses and sub groups of patients. Disease progression and overall survival had similar outcomes for both drugs. The large scale analysis increased the certainty around toxicities associated with the different drugs. They were able to show that denosumab had a better safety profile than zoledronic acid, having no effect on renal function and could be used without the need to dose adjust or monitor renal function. This was a significant finding given more than half of patients with advanced disease suffer from renal impairment. Hypocalcaemia was more common for denosumab, but its subcutaneous delivery method means it is not associated with acute-phase reactions, a known consequence of zoledronic acid.

“One cannot overestimate the effect of an SRE on an individual patient,” Prof Richardson said.

“It will cause unremitting chronic pain requiring significant analgesia, both of which have a profound impact on quality of life.”

“The combined study has made an incredible impact on our understanding of therapeutically preventing SREs, which in turn improves quality of life by preventing pain and debility, and eliminates the need for costly additional treatments, estimated to cost the health service ten’s of thousands of dollars every time a patient is seen for a SRE.”



Oncology Research Clinical Trials team members (left to right) Luka Keighley, Timothy Colgan and Demis Balamatsias. Photo Credit: Darren James.

“ONE CANNOT OVERESTIMATE THE EFFECT OF AN SRE ON AN INDIVIDUAL PATIENT. IT WILL CAUSE UNREMITTING CHRONIC PAIN REQUIRING SIGNIFICANT ANALGESIA, BOTH OF WHICH HAVE A PROFOUND IMPACT ON QUALITY OF LIFE.”

#### Journal Reference

Lipton A, Fizazi K, Stopeck AT, Henry DH, Brown JE, Yardley DA, Richardson GE, Siena S, Maroto P, Clemens M, Bilynskyy B, Charu V, Beuzeboc P, Rader M, Viniestra M, Saad F, Ke C, Braun A, Jun S. (2012) Superiority of denosumab to zoledronic acid for prevention of skeletal-related events: a combined analysis of 3 pivotal, randomised, phase 3 trials. *Eur J Cancer*. 48(16):3082-92. doi: 10.1016/j.ejca.2012.08.002.

# SUPPORTING OUR COVID-19 FATIGUED HEALTHCARE WORKERS

CABRINI MONASH UNIVERSITY DEPARTMENT OF NURSING RESEARCH

Frontline healthcare workers have never been more recognised for their work than throughout the COVID-19 crisis. They have worked tirelessly under extremely challenging and stressful conditions.

Data from around the world showed they had been at high risk of acquiring COVID-19 with workplace transmission possibly accounting for 10 to 20 per cent of all infections. The risk of being infected and/or transmitting it to loved ones, protocol changes, constant personal protective equipment (PPE) vigilance, long working hours and rapidly changing advice, were just some of the reasons leading to elevated anxiety, depression and stress within the workforce.

Cabrini is participating in the COVIC-HA project, looking to understand the needs of healthcare workers and how we safeguard their health and wellbeing during COVID-19 and future health threats. COVIC-HA aims to enrol more than 1500 Victorian frontline healthcare workers, both clinically facing and non-clinical facing, across multiple healthcare organisations including Ambulance Victoria, hospitals within the Monash Partners network, and primary care and aged care networks.

The study will question and monitor workers over time for mental health changes, impacts on physical health, and evidence of COVID-19 infection. Workplace preparedness and responses will also be investigated, to identify what worked well or performed poorly.

Associate Professor Philip Russo, Director of the Cabrini Monash University Department of Nursing Research at Cabrini Research, is playing a leading role in the study as a member of the scientific leadership team.



*A/Prof Philip Russo,  
Director Cabrini Monash  
University Department of  
Nursing Research.*

He said the COVIC-HA project and Cabrini's participation will inform future plans for outbreak management at healthcare services.

"Healthcare workers are critical to the containment and response to outbreaks, and this pandemic has highlighted the crucial role of all healthcare workers in the management, surveillance, policy, practice and education aspects," A/Prof Russo said.

"Therefore it is vital that we learn from these experiences and identify how we can put better supports in place."

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| Cabrini ICU clinical team.

# UP-TO-DATE INFORMATION ABOUT THE VALUE OF INTERVENTIONS FOR MUSCULOSKELETAL DISEASE

MONASH-CABRINI DEPARTMENT OF CLINICAL EPIDEMIOLOGY

Cochrane is an international not-for-profit and independent organisation, dedicated to making up-to-date, accurate information about the effects of healthcare readily available worldwide. It produces and disseminates what are considered to be the most trustworthy systematic reviews of healthcare interventions. Cochrane is an online resource for healthcare professionals, researchers and consumers. In Australia, the library is freely available to all residents.

Of the more than 50 currently registered review groups that make up Cochrane, Cochrane Musculoskeletal is one of the largest with more than 700 active healthcare professionals, researchers and consumer representatives from 26 countries. Since 2020, it has also taken over the responsibility for Cochrane Back and Neck. The impressive international collection of systematic reviews cover many musculoskeletal conditions including osteoarthritis, rheumatoid arthritis, psoriatic arthritis, axial spondyloarthritis, paediatric forms of arthritis, gout, systemic lupus erythematosus, systemic sclerosis, vasculitis, shoulder and other regional conditions, fibromyalgia as well as low back and neck pain.

Systematic reviews use highly rigorous methods to synthesise the available evidence for specific questions and Cochrane members have led the world in developing and refining these methods. Those who prepare the reviews are mostly healthcare professionals who volunteer to work in one of the many Cochrane groups, with editorial teams overseeing the preparation and maintenance of the reviews, as well as application of the rigorous quality standards for which Cochrane Reviews have become known.

The Monash-Cabrini Department of Clinical Epidemiology houses the international Cochrane Musculoskeletal editorial base tasked with editorial oversight of all Cochrane reviews in this area. It is under the direction of the Coordinating Editor, Professor Rachelle Buchbinder AO, and is coordinated by the Managing Editor, Dr Renea Johnston, with Dr Sheila Cyril in the role of Assistant Managing Editor. NHMRC funding supports Cochrane Musculoskeletal in Australia.

As coordinating editor of Cochrane Musculoskeletal since 2005, Prof Buchbinder has written more than 100 reviews and made significant contributions through editing reviews, training and supervising people in Australia and internationally in writing systematic reviews, and through advocacy for translation of Cochrane reviews into practice and policy.

“Cochrane is considered the benchmark around the world for the production of high quality, reliable, up-to-date and un-conflicted systematic reviews. Thus, we contribute by producing the best available evidence to inform decision-making in treating arthritis and musculoskeletal disorders,” Prof Buchbinder said.

Since 2017, the department has also housed the Australasian satellite of another review group, Cochrane Effective Practice and Organisation of Care (EPOC), under the direction of Satellite Director and editor, Associate Professor Denise O’Connor, also the Deputy Director of the Monash-Cabrini Department of Clinical Epidemiology, with Ms Jia-Xi (JC) Han in the role of Assistant Managing Editor. Cochrane EPOC publishes global evidence to guide health system decision-making to improve health services and population health outcomes, making its reviews also highly relevant to Cabrini Health.



*Prof Rachelle Buchbinder AO, Coordinating Editor Cochrane Musculoskeletal, Director Monash-Cabrini Department of Clinical Epidemiology.*



*Dr Sheila Cyril, Assistant Managing Editor Cochrane Musculoskeletal, Monash-Cabrini Department of Clinical Epidemiology.*



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AND MUSCULOSKELETAL  
DISORDERS.”

| Dr Renea Johnstone, Managing Editor Cochrane Musculoskeletal, Monash-Cabrini Department of Clinical Epidemiology.

# MELBOURNE ASHKENAZI JEWISH BOWEL CANCER STUDY DRIVEN BY CABRINI

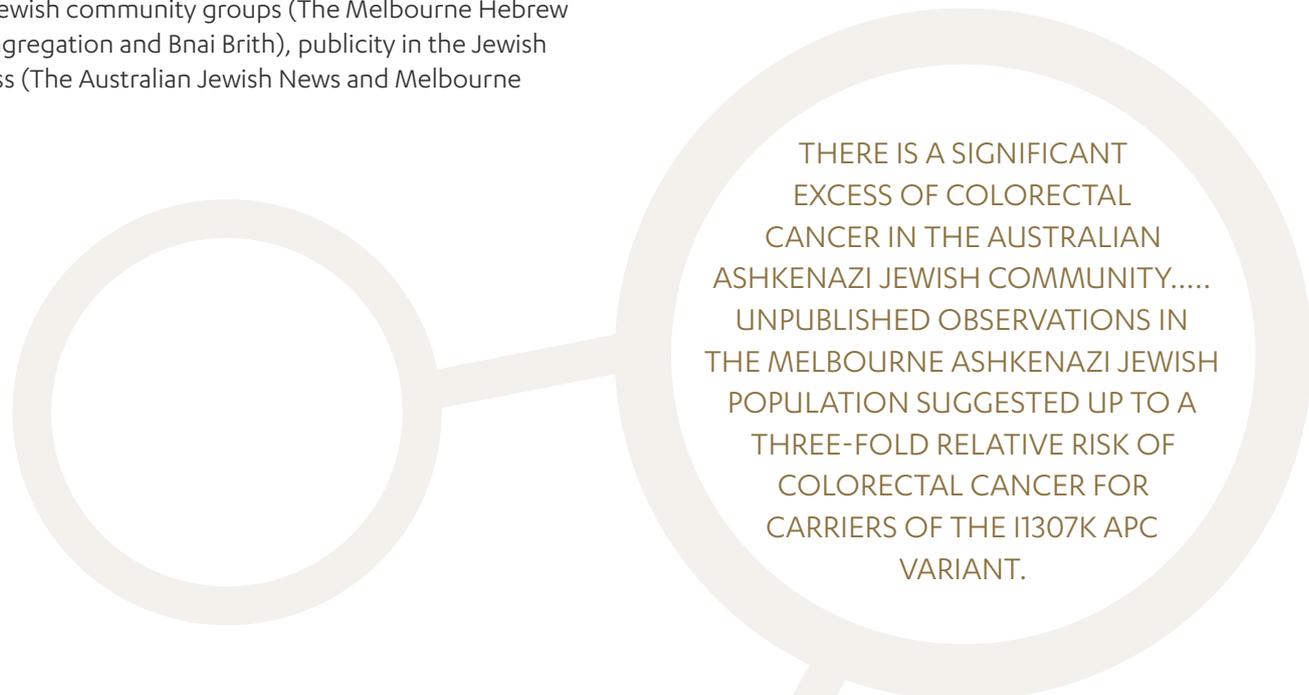
CABRINI MONASH UNIVERSITY DEPARTMENT OF SURGERY

There is a significant excess of colorectal cancer in the Australian Ashkenazi Jewish community. This was previously attributed to the fact that their diet is rich in animal fats and protein. However studies identified a mutation of the Adenomatous Polyposis Coli (APC) gene – the I1307K variant which led to the initiation of several studies around the world in an attempt to clarify the significance of the polymorphism in the development of colorectal cancer amongst Ashkenazi Jews. Research led by Associate Professor Henry Debinski of the Melbourne Gastrointestinal Investigation Unit and Professor Adrian Polglase of the Cabrini Monash University Department of Surgery at Cabrini formed part of these research efforts. Their unpublished observations in the Melbourne Ashkenazi Jewish population suggested up to a three-fold relative risk of colorectal cancer for carriers of the I1307K APC variant (which may translate into a 30 per cent or more lifetime risk), consistent with other research occurring around the world in the late 1990's and early 2000's.

By the early 2000's only sporadic clinical genetic testing was being offered for the APC I1307K variant. A/Prof Debinski and Prof Polglase looked at the acceptability of this testing in Melbourne's Ashkenazi Jewish population. Three hundred subjects were recruited by approaches to Jewish community groups (The Melbourne Hebrew Congregation and Bnai Brith), publicity in the Jewish press (The Australian Jewish News and Melbourne

Hebrew Congregation publication) and non-Jewish press (Leader newspapers, in areas of high Jewish population, and The Herald-Sun). Several recruitment days were also held at the Montefiore and Emmy Monash Homes for the Aged (both of which have primarily Jewish residents) and a stall was set up at a Jewish School Fete to directly recruit participants.

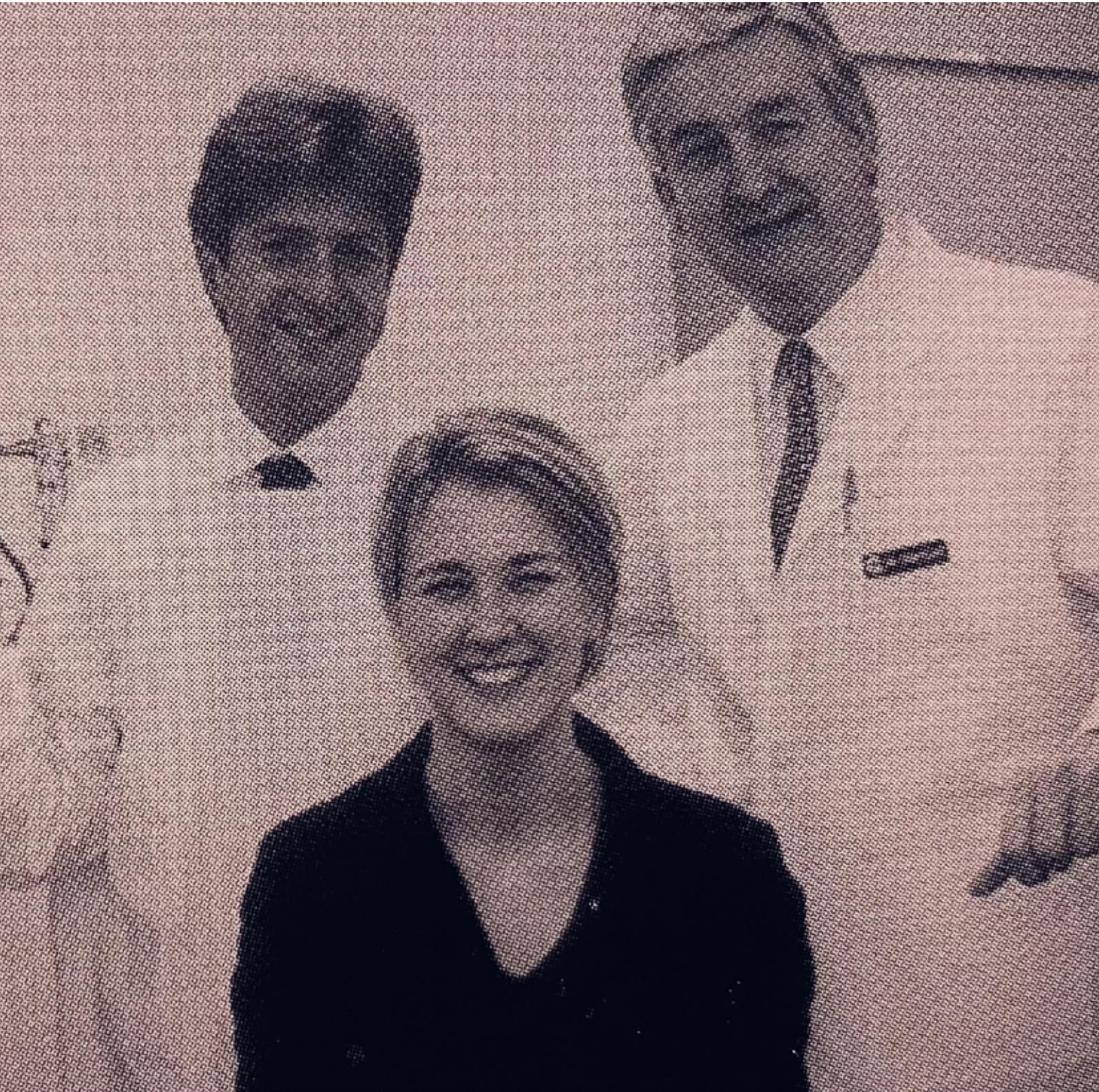
Their results showed a high acceptability to genetic testing with 94 per cent of participants saying they would have a test for predisposition to colorectal cancer and a majority would make this decision based on the desire for information for their families and to decrease their own cancer risk. Some concerns were noted about genetic testing for cancer predisposition, including insurance discrimination, test accuracy and confidentiality. The strong support for genetic testing was consistent with other research around the world which was showing Jewish communities strongly support genetic research and testing, including recent research at the time conducted in American Jews who showed acceptability for genetic testing for the I1307K variant specifically. The data from this study provided clinicians and counselors in Australia with useful information for working with the local Jewish population in genetic research and testing.



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## Journal Reference

Warner BJ, Curnow LJ, Polglase AL, Debinski HS. (2005) Factors influencing uptake of genetic testing for colorectal cancer risk in an Australian Jewish population. *J Genet Couns.* 14(5):387-94. doi: 10.1007/s10897-005-1623-3.



| A/Prof Henry Debinski (left), Lisette Curnow, Prof Adrian Polglase.

# GENETIC MAKEUP CAN HELP IDENTIFY BETTER TREATMENT OPTIONS

CABRINI MONASH UNIVERSITY DEPARTMENT OF MEDICAL ONCOLOGY –  
THE SZALMUK FAMILY DEPARTMENT OF MEDICAL ONCOLOGY

Long gone are the days where every cancer patient receives the same chemotherapy regime. As more research is undertaken and our knowledge grows, we progress further into the exciting era of personalised precision medicine, where we can tailor therapeutic options to each patient based on the specific biology of their cancer. Research and clinical trials are bringing us an increasing array of molecularly targeted therapies, and putting an increasing emphasis on knowing the genetic makeup of every individual patient.

Ten years ago the shift towards molecular therapies and the beginning of an era of genomic medicine drove the 'Cancer 2015' study. Cancer 2015 was designed to capture and track genomic and clinical information over time from a broad population of patients newly diagnosed with cancer. The main purpose was to determine how molecular genomic profiling could be incorporated into the routine care of cancer patients so that they could benefit from molecularly targeted therapies in place of often toxic and ineffective chemotherapy agents.

Funded by the Victorian Cancer Agency, the study recruited patients and collected data between November 2011 to September 2014. Cancer 2015 had originally aimed to enrol and sequence the genome of 1000 patients, but this was easily surpassed with 1685 patients with all different types of solid cancers participating. To establish a 'population' cohort that was not defined by a particular cancer group or from a specific hospital, the study collected data at five hospitals across Victoria, representing metropolitan and regional services. Cabrini was the only private hospital research partner, led by Professor Gary Richardson OAM. Prof Richardson and Professor Paul McMurrick, both from Cabrini, played key roles in the study and were co-authors on the publication in the *Journal of Personalized Medicine*.

The study population represented the expected major cancer types such as breast, lung, colorectal and prostate cancer. Importantly however, it also managed to recruit a substantial number of patients with less common cancers such as head and neck, bone/soft tissue, renal, bladder and, to a lesser extent, cancer of unknown primary. The data collected in these rarer groups will enable new



*Prof Gary Richardson OAM,  
Cancer 2015 Principal  
Investigator, Group Director  
Cabrini Research, and  
Director Cabrini Monash  
University Department of  
Medical Oncology, Szalmuk  
Family Department of  
Medical Oncology.*

avenues for investigation and treatment in these poor prognosis tumours.

Tumour samples were available from 90 per cent of patients enrolled, and genomic sequencing was conducted on more than 900 samples. At least one gene mutation was detected in 58 per cent of all patients, but in reality the actual number may be higher if the sequencing method were to have assessed more parts of the genome. Importantly, 90 advanced cancer patients were identified to have an actionable gene mutation, meaning they would be eligible for an approved targeted cancer therapeutic, or have increased access to clinical trials of new targeted therapies currently underway worldwide. The sequencing data also identified mutations in tumours not usually thought to harbor such genetic changes, raising new therapeutic opportunities for these patients.

"At the time Cancer 2015 was one of only a few population-based genomic cohorts being studied worldwide, and successfully provided evidence on the value of precision medicine to clinical practice," Prof Richardson said.

"It showed that an upscalable genomics testing platform could be established within a clinical setting, and is an approach that would help identify eligible participants for clinical trials of targeted therapies."

## Journal Reference

Parisot JP, Thorne H, Fellowes A, Doig K, Lucas M, McNeil JJ, Doble B, Dobrovic A, John T, James PA, Lipton L, Ashley D, Hayes T, McMurrick P, Richardson G, Lorgelly P, Fox SB, Thomas DM. (2015) "Cancer 2015": A Prospective, Population-Based Cancer Cohort-Phase 1: Feasibility of Genomics-Guided Precision Medicine in the Clinic. *J Pers Med.* 5(4):354-69. doi: 10.3390/jpm5040354.



| Oncology Research Clinical Trials team. Photo Credit: Darren James.

“AT THE TIME CANCER 2015 WAS ONE OF ONLY A FEW POPULATION-BASED GENOMIC COHORTS BEING STUDIED WORLDWIDE, AND SUCCESSFULLY PROVIDED EVIDENCE ON THE VALUE OF PRECISION MEDICINE TO CLINICAL PRACTICE.”

# BREAST CANCER MODELS - PREDICTING TREATMENT RESPONSES AND OVERCOMING DRUG RESISTANCE

CABRINI MONASH UNIVERSITY DEPARTMENT OF MEDICAL ONCOLOGY –  
THE SZALMUK FAMILY DEPARTMENT OF MEDICAL ONCOLOGY



Dr Tali Lang, Senior Postdoctoral Research Fellow, and breast surgeon, Mr Peter Gregory.



Mr Peter Gregory.



Dr Tali Lang.

In 2021 more than 20,000 Australian women are going to face a diagnosis of breast cancer. Breast cancer accounts for approximately 30 per cent of all new cancer diagnoses and 14 per cent of all cancer-related deaths. Despite significant advances in anti-cancer therapies up to 40 per cent of patients are either drug resistant at the beginning of treatment, or have minimal response to current treatment regimes. Recurrent tumour growth is also common, seen in up to 30 per cent of cases. This is largely due to significant differences in the biology of breast cancers, characterised by many sub-types.

To improve patient outcomes and the number of curative treatments, new insight into the biology of breast cancer sub-types is needed. The Breast Cancer Research Program at Cabrini aims to translate laboratory discoveries into improved outcomes for breast cancer patients. The collaboration is led by Director Professor Gary Richardson OAM, and researchers Dr Tali Lang and Dr Dilys Leung from the Szalmuk Family Department of Medical Oncology, with Cabrini breast surgeon Mr Peter Gregory, and Professor Helen Abud and Dr Thierry Jardé from the Monash University Biomedicine Discovery Institute.

The clinician and bench research partnership seeks to change approaches to breast cancer screening and treatment through powerful tools including breast organoids, whole exome sequencing and RNA sequencing for rapid high-throughput “omics” profiling. Patient-derived organoids are mini-tumours that grow in a 3D culture, and have recently emerged as powerful pre-clinical models. Organoids replicate the features of the patient’s own tissue, allowing the characteristics of the tumour to be studied on an individual patient level. The new models will accelerate clinical research studies, allowing an exploration of the molecular changes in the primary tumour with clinical outcome data from the Cabrini Breast Cancer Database, an extensive clinical resource managed by Melissa Vereker from the Szalmuk Family Department of Medical Oncology.

“Organoids gives us the opportunity to see how every individual patient responds to different drugs. They will help us identify biomarkers that influence treatments and prognosis. This could revolutionise the field of drug discovery and personalised medicine. Ultimately organoids will enhance our knowledge in cancer biology, immunology and genomics,” said Prof Richardson.



*Professor Gary Richardson OAM, Group Director Cabrini Research, and Director Cabrini Monash University Department of Medical Oncology, Szalmuk Family Department of Medical Oncology.*



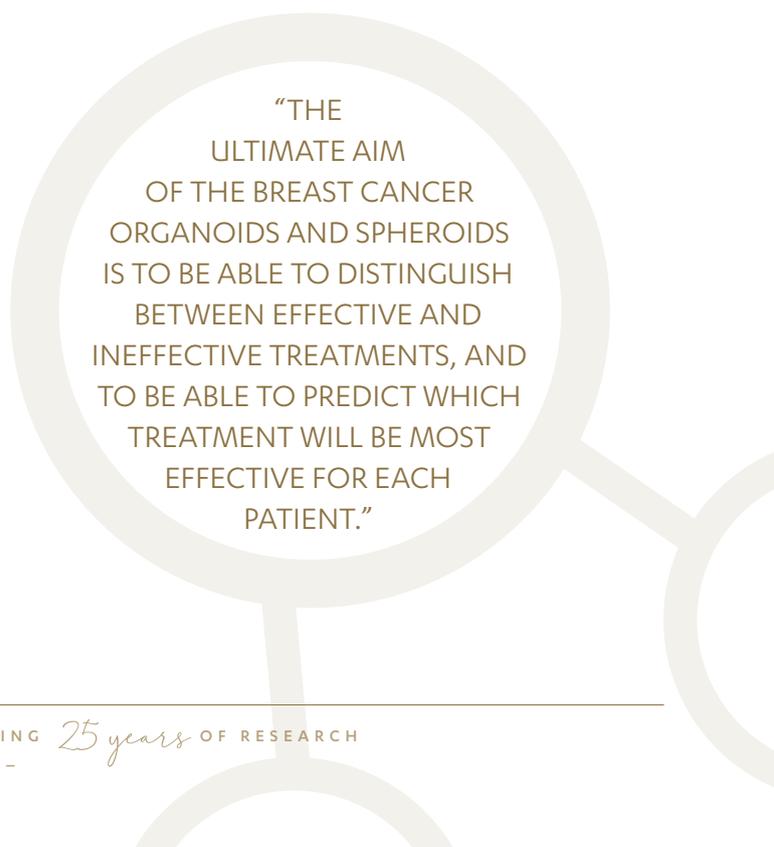
*Melissa Vereker, Cabrini Breast Cancer Database Manager.*

In 2021 the Breast Cancer Research Program expanded through a new research partnership with Dr Antonella Pappa and Dr Kelvin Yip from the Monash University Biomedicine Discovery Institute. Working with Dr Lang, the collaboration will seek to generate breast cancer spheroid models to compliment the organoid research program. Breast cancer spheroids, similar to organoids, are grown in a 3D culture system in the lab and recapitulate many characteristics of the primary tumour and microenvironment from which they were originally derived. Breast cancer spheroids can be grown quickly, within ten days, and can be used for molecular characterisation of the tumour, gene and protein expression studies, as well as pre-clinical, high throughput drug screens. Breast spheroids will be generated from a range of breast cancer sub-types to develop a rapid high-throughput pre-clinical test that can be utilised to determine the likelihood of a patient responding to specific treatments before they commence in the clinic.

“The ultimate aim of the breast cancer organoids and spheroids is to be able to distinguish between effective and ineffective treatments, and to be able to predict which treatment will be most effective for each patient,” said Dr Lang.

“This will ultimately spare patients receiving treatments from which they are unlikely to see benefit, reduce possible treatment side-effects, and tailor individual treatment plans for best clinical outcomes”.

Cabrini treats around 650 breast cancer patients each year and is uniquely positioned to deliver ground-breaking research through the Breast Cancer Research Program. The program is generating an extensive bioresource which includes matched non-cancerous and tumour patient-derived organoids, and paired blood specimens, all of which are linked to patient data on the Cabrini Breast Cancer Database. This database was established to collect hundreds of clinical parameters including co-morbidities/risk factors, family history/genetics, treatment regimens and long-term oncologic outcomes. Together, the Szalmuk Family Department of Medical Oncology and Monash Biomedicine Discovery Institute have developed a powerful resource with the potential to change the management of breast cancer.



“THE ULTIMATE AIM OF THE BREAST CANCER ORGANIDS AND SPHEROIDS IS TO BE ABLE TO DISTINGUISH BETWEEN EFFECTIVE AND INEFFECTIVE TREATMENTS, AND TO BE ABLE TO PREDICT WHICH TREATMENT WILL BE MOST EFFECTIVE FOR EACH PATIENT.”

# ‘REVIVAL’ CANCER STEM CELLS INFLUENCE HOW BOWEL CANCER PATIENTS RESPOND TO CHEMOTHERAPY

CABRINI MONASH UNIVERSITY DEPARTMENT OF SURGERY

In Australia, bowel cancer is the second most common cause of cancer related death in both men and women, with more than 5000 deaths reported each year. The majority of bowel cancer patients die due to reemergence of the cancer in distant new locations of the body (known as metastases) following chemotherapy treatment. If left untreated, the five year survival rate for a patient with metastases is as low as five per cent. Combination chemotherapy treatment, which includes the commonly used drug 5-fluorouracil, can help to improve the survival rate but more targeted and personalised therapies are required.

Bowel cancers are typically composed of multiple cell populations, but only a small fraction of cells initiate tumour activity. Cancer stem cells have been shown to play a crucial role in many cancer types, driving tumour growth, metastasis, resistance to chemotherapy, and cancer relapse. A cancer stem cell gene signature has been associated with worse overall survival and disease/recurrence-free survival of bowel cancer patients. Cancer stem cells are thus promising prognostic biomarkers and therapeutic targets. Recent studies in normal intestinal tissue have identified a novel population of ‘revival’ stem cells that are activated upon damage and can restore lost stem cells. It raised the question of whether a revival stem cell population also plays a role in bowel cancer.

Researchers from the Cabrini Monash University Department of Surgery (CMUDS), led by Professor Paul McMurrick and in collaboration with the Monash Biomedicine Discovery Institute at Monash University, identified a novel role for revival stem cells in bowel cancer and more specifically, how they influence chemoresistance. CMUDS Senior Research Fellow Dr Rebekah Engel was first author and led the studies published in the *Journal of Clinical Medicine*, together with senior authors Dr Thierry Jardé and Professor Helen Abud from Monash University.

Dr Engel used patient-derived bowel cancer organoids that were grown in the laboratory from small pieces of cancer tissue taken from patients, and their matching primary tumours to demonstrate that bowel cancers exhibit stem cell expression signatures, including markers of the revival stem cell population. They discovered that Clusterin, a marker of the ‘revival’ stem cell population, was significantly enriched following chemotherapy treatment in organoids, and high expression correlated



Dr Rebekah Engel, Senior Postdoctoral Research Fellow, CMUDS.

with chemotherapy resistance. They also demonstrated in patient outcome datasets that Clusterin is associated both with lower patient survival and an increase in disease recurrence.

Although the sample size was limited, the research provided a promising basis for future studies on the role of revival stem cells in progressive disease in bowel cancer patients. Dr Engel said the research demonstrated the incredible potential in using patient-derived bowel cancer organoids to study the complexities of the stem cell populations in bowel cancer.

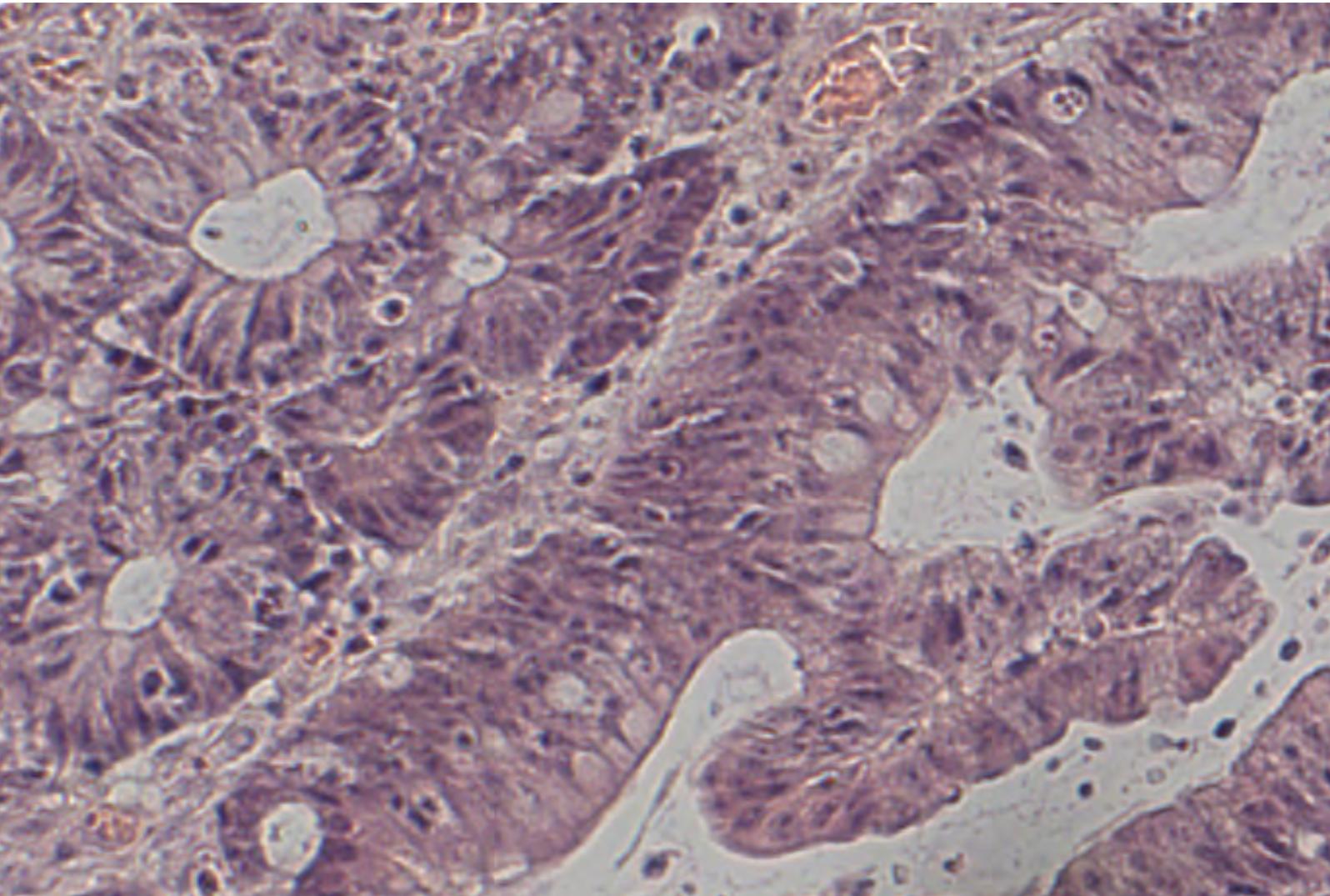
“Revival stem cells may be a potential therapeutic target and a biomarker for chemotherapy resistance in patients,” Dr Engel said.

“We are hopeful that our research will one day lead to new therapy options and biomarkers to help clinicians predict the best therapy regime for patients.”

Dr Engel received an Honourable Mention for her research and publication on revival stem cells in the 2020 Monash Partners Comprehensive Cancer Consortium Award for Outstanding Cancer Research. The award recognises the achievements of innovative and impactful Victorian mid-career cancer researchers, to reward research excellence and encourage future research leadership.

## Journal Reference

Engel RM, Chan WH, Nickless D, Hlavca S, Richards E, Kerr G, Oliva K, McMurrick PJ, Jardé T, Abud HE. (2020) Patient-Derived Colorectal Cancer Organoids Upregulate Revival Stem Cell Marker Genes following Chemotherapeutic Treatment. *J Clin Med*. 9(1):128. doi: 10.3390/jcm9010128.



Colorectal cancer tissue stained with hematoxylin and eosin.



Dr Thierry Jardé and Professor Helen Abud, Monash Biomedicine Discovery Institute, Monash University.



Professor Paul McMurrick, Director CMUDS.

“REVIVAL STEM CELLS MAY BE A POTENTIAL THERAPEUTIC TARGET AND A BIOMARKER FOR CHEMOTHERAPY RESISTANCE IN PATIENTS”

# ACKNOWLEDGEMENTS



## ANNE SPENCE

DIRECTOR OF INFRASTRUCTURE

A great organisation needs great people to deliver successes. One person that stands out and has contributed greatly to Cabrini Research is Anne Spence. Anne

has worked for Cabrini Research for almost 20 years, working with all four directors during that time. She has played an incredible role in shaping and delivering the Cabrini Research we know today. We thank you.



## DR EMMA BAKER

DIRECTOR OF RESEARCH

Authorship and photo compilation.

The 25th Anniversary of Cabrini Research is proudly supported by



## TIMELINE PHOTO REFERENCE

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Photo 1	Associate Professor Doug Lording AM	Photo 27	Prof Paul McMurrick
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Photo 3	Cabrini Clinical Education and Research Foundation official opening ( <i>left to right</i> ) A/Prof Doug Lording AM, Cabrini Health Board Chairman Ray Whelan, the Honorable Dr Michael Wooldrige, then Federal Minister for Health and Family Services, and the Most Reverend Sir Frank Little KBE	Photo 28	Prof Paul McMurrick
1997		Photo 29	Karen Oliva, Database Manager
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Photo 6	A/Prof Henry Debinski ( <i>left</i> ) and Prof Adrian Polglase	Photo 31	Mrs Patricia Peck and son Matthew Peck at the opening of the Patricia Peck Education and Research Precinct
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