POSTGRADUATE & EARLY CAREER RESEARCHER
SYMPOSIUM 2020

ABSTRACT BOOKLET & PROGRAM

FRIDAY 30 OCTOBER

Streamed virtually from
Chris O'Brien Lifehouse
Level 5, Education Centre

SYDNEY CATALYST
TRANSLATIONAL CANCER RESEARCH

Sydney Catalyst is supported by:

THE UNIVERSITY OF SYDNEY

Cancer Institute NSW
Translational Cancer Research Centre

WELCOME MESSAGE

DR CAROLYN MAZARIEGO & DR SEAN PORAZINSKI

On behalf of the Organising Committee, it is our pleasure to welcome you to the 2020 Sydney Catalyst Postgraduate & Early Career Researcher (PG&ECR) Symposium. As proud members of Sydney Catalyst, we are excited to be the co-chairs for this year's Symposium, an event which has gone from strength to strength to become a highlight of the Sydney Catalyst events calendar.

The annual PG&ECR Symposium underscores Sydney Catalyst's commitment to promoting collaboration and networking between researchers from different disciplines and institutions across the translational research spectrum. The PG&ECR Symposium showcases the diverse research of our network members spanning multiple disciplines from the basic sciences through to clinical and translational research. Through the challenges of 2020, the organising committee remained dedicated to find a way to continue to host this event as an opportunity for early career academics to showcase their research, network, and form collaborations with others. This has meant that the Symposium will now run in a hybrid format this year (virtual and face-to-face), and we are certain it will continue to be a fantastic event.

We are delighted to include two keynote speakers, A/Professor Thomas Cox (T1/T2) and Professor Alexandra Barratt (T2/T3) who will talk about their career journeys and share tips for a successful career in research. We will also hear from Cancer Voices NSW, a consumers in research organisation now celebrating their 20th anniversary, who will share the important work they do to ensure consumer involvement in both research and funding decisions, ultimately leading to improved outcomes and increased end value for people affected by cancer.

As in previous years, we have included our popular rapid-fire presentations, to ensure a wider breadth of research has the opportunity to be represented. These 3-minute presentations serve as a fun way to dynamically present diverse research succinctly and concisely.

We look forward to meeting you at this year's Symposium and hope that the day will provide you with inspiration, cutting-edge knowledge, facilitate new connections and enable new collaborations across the translational research spectrum.

WORKING GROUP

- Dr Carolyn Mazariego (Co-Chair) - The University of Sydney
- Dr Sean Porazinski (Co-Chair) - The Garvan Institute of Medical Research
- Jarem Edwards - Melanoma Institue Australia
- Dr Brooke Nickel - The University of Sydney
- Ann Livingstone - The University of Sydney
- Merilyn Heuschkel - Sydney Catalyst
- Cara McFarlane - Sydney Catalyst
- Divya Murthy - Sydney Catalyst

KEYNOTE SPEAKER

ASSOCIATE PROFESSOR THOMAS COX

Thomas leads the Matrix and Metastasis Group at the Garvan Institute of Medical Research. His team focuses on how the extracellular matrix (ECM) regulates resident cell behaviour and specifically how it contributes to cancer progression, metastasis and response to therapy. Recent work has focussed on how discrete subtypes of cancer associated fibroblasts (CAFs) within tumours underpin ECM remodelling programs that generate pro-invasive and pro-metastatic environments (Nature Communications 2019); the development of new techniques to image the ECM in health and disease (Nature Medicine 2017); and the systemic role of ECM remodelling in premetastatic niche formation (Nature 2015). The aim of Thomas' group is to establish targeting of ECM dynamics as a viable therapeutic approach in the treatment of solid tumours.

KEYNOTE SPEAKER

PROFESSOR ALEXANDRA BARRATT

Alexandra Barratt (MBBS, MPH, PhD) is a Professor of Public Health in the School of Public Health, University of Sydney. She has a background in epidemiological research spanning clinical epidemiology and public health epidemiology. She is recognised internationally for her research to quantify the benefits and harms (including overdiagnosis) of cancer screening, particularly breast cancer screening. She is a lead investigator on Wiser Healthcare, an NHMRC funded research collaboration to reduce overdiagnosis and overtreatment in healthcare. Overdiagnosis is one of the biggest drivers of iatrogenic harm, waste and opportunity cost in healthcare and is a serious challenge for citizens, patients and healthcare services around the world.

CONSUMER PRESENTATION

CANCER VOICES NSW

Cancer Voices NSW provides the independent voice of people affected by cancer in our state and beyond. It operates as the peak advocacy organisation.

Voting members are support and advocacy groups. Cancer Voices members include people with cancer and cancer survivors, carers, cancer care professionals and interested organsiations.

As a network, Cancer Voices NSW provides a forum for those affected by cancer to share their concerns, ideas and experiences. Our representatives offer broad, informed views on cancer issues at local, state and national levels – wherever decisions about us are made.

Since 2000, Cancer Voices NSW has been influential in improving cancer care, information, support and the direction of research in NSW.

PROGRAM
T1T2 RESEARCH

8.30am	Registration - Tea, coffee and light refreshments provided for those onsite
9.00am	**Introduction - Dr Sean Porazinski & Dr Carolyn Mazariego** Co-Chairs, Postgraduate & Early Career Researcher Symposium Working Group
9.05am	**Welcome - Professor Michael Boyer, Director of Sydney Catalyst**
9.10am	**Keynote Presentation - Associate Professor Thomas Cox** Group Leader - Matrix and Metastasis, The Garvan Institue of Medical Research
9.25am	Question time

SESSION 1

CHAIRED BY JAREM EDWARDS
Melanoma Institute Australia

9.30 - 10.20am	**ABSTRACT PRESENTATIONS (8 minutes + Questions)**
9.30am	**Josef Gillson** *The University of Sydney* Examining the chemoresistance mechanisms in pancreatic ductal adenocarcinomas
9.40am	**Brooke Pereira** *The Garvan Institute of Medical Research* Quantitative proteomics reveals cancer cell genotype can drive matrisomal changes associated with aggressive disease in pancreatic ductal adenocarcinoma (PDAC)
9.50am	**Michael Papanicolaou** *The Garvan Institute of Medical Research* Mapping the extracellular matrix through breast tumour progression
10.00am	**Amelia Parker** *The Garvan Institute of Medical Research* Extracellular matrix remodelling defines aggressive non-small cell lung cancer
10.10am	**Tuba Nur Gide** *Melanoma Institute Australia* Genomic and clinical profiles of patients with innate resistance to anti-PD-1-based immunotherapies in melanoma
10.20 - 10.30am	**RAPID FIRE PRESENTATIONS (3 minutes)**
Rapid Fire	**Rebecca Simpson** *Melanoma Institute Australia and The University of Sydney* Gut microbiota predicts response and adverse events during anti-PD1/anti-CTLA4 neoadjuvant immunotherapy

Rapid Fire	**Grace Attrill** *The University of Sydney and Melanoma Institute Australia* Tumour specific, tumour resident CD8 T cells are associated with reduced recurrence in adjuvant PD-1 treated melanoma
Rapid Fire	**Cecilia Chambers** *The Garvan Institute of Medical Research* Inhibition of the NPY signalling axis as a novel therapeutic option in pancreatic cancer
10.40am	**MORNING TEA/STRETCH BREAK**

SESSION 2

CHAIRED BY DR SEAN PORAZINSKI
The Garvan Institue of Medical Research

10.50 - 11.40am	**ABSTRACT PRESENTATIONS (8 minutes + Questions)**
10.50am	**Mark Schreuder** *Sydney Catalyst* Procoagulant platelets as a diagnostic predictor of thrombosis in lung cancer patients
11.00am	**Jessica Chitty** *The Garvan Institute of Medical Research* LOX family inhibition improves response to standard of care therapy in desmoplastic pancreatic cancer
11.10am	**Kendelle Murphy** *The Garvan Institute of Medical Research* Epithelial versus stromal targeting of FAK in pancreatic cancer: deconstructing treatment regimens according to Merlin status for improved outcome in personalized medicine
11.20am	**Daniel Reed** *The Garvan Institute of Medical Research* A Src-FRET biosensor mouse to predict cancer spread and response to anti-invasive therapies: Insights from intravital imaging
11.30am	**Thomas George Johnson** *ANZAC Research Institute* YB-1 knockdown inhibits the proliferation of mesothelioma cells through multiple mechanisms
11.40 - 11.50am	**RAPID FIRE PRESENTATIONS (3 minutes)**
Rapid Fire	**Fawaz Mayez Mahfouz** *The University of Sydney* Examination of small nerve fibre neuropathy in chemotherapy-treated patients using sudomotor function testing
Rapid Fire	**Ruth Allen** *The University of Sydney* Unravelling the role of immune cells targeted by immunotherapy

Rapid Fire	Elysse Filipe *The Garvan Institute of Medical Research* nanoP3 – A new class of nanocarriers for the treatment of breast cancer

CLOSING SESSION

11.50am	Consumer Presentation - Cancer Voices NSW
12.00pm	Awards and wrap up
12.10pm	Morning Symposium concludes. Lunch served for morning speaker/presenters.
12.40pm	Lunch concludes

VIRTUAL POSTERS

Please visit our website to view the extensive library of
virtual posters submitted by our members

PROGRAM
T2T3 RESEARCH

1.00pm	Registration - Lunch served for afternoon speakers/presenters
1.30pm	**Introduction - Dr Sean Porazinski & Dr Carolyn Mazariego** Co-Chairs, Postgraduate & Early Career Researcher Symposium Working Group
1.35pm	**Welcome - Professor Michael Boyer, Director of Sydney Catalyst**
1.40pm	**Keynote Presentation - Professor Alexandra Barratt** Professor of Public Health, The University of Sydney
1.55pm	Question time

SESSION 1
CHAIRED BY DR BROOKE NICKEL & DR CAROLYN MAZARIEGO
The University of Sydney

2.00 - 2.50pm	**ABSTRACT PRESENTATIONS (8 minutes + Questions)**
2.00pm	**Rebecca Venchiarutti** *SOuRCe, Royal Prince Alfred Hospital; The University of Sydney* 'The tyranny of distance': facilitators and barriers to early diagnosis and treatment of head and neck cancer
2.10pm	**Sabina Vatter** *The University of Sydney* Qualitative exploration of intention to change behaviour in patients undertaking genome sequencing
2.20pm	**Christina Stanislaus** *SOuRCe and IAS, Royal Prince Alfred Hospital* Short-term quality of life outcomes following robotic-assisted surgery
2.30pm	**Alison Young** *Sydney Catalyst* Adaptation and evaluation of a smoking cessation clinical pathway implemented within cancer services
2.40pm	**Clare Toms** *SOuRCe, Royal Prince Alfred Hospital* A cross-sectional investigation into quality of life and survival after resection for pancreatic cancer
2.50 - 3.00pm	**RAPID FIRE PRESENTATIONS (3 minutes)**
Rapid Fire	**Chloe Lim** *The University of Sydney* A thematic synthesis of qualitative research in colorectal cancer survivorship
Rapid Fire	**Olivia Fox** *SOuRCe, Royal Prince Alfred Hospital* Surgical outcomes and survival of local and remote patients undergoing pelvic exenteration

Rapid Fire	**Qamra Muaikel Alqahtani** *The University of Sydney* Information needs of children with cancer and their parents for managing cancer-related symptoms: Preliminary findings of a systematic review
3.10pm	**AFTERNOON TEA/STRETCH BREAK**

SESSION 2

CHAIRED BY ANN LIVINGSTONE
The University of Sydney

3.20 - 4.10pm	**ABSTRACT PRESENTATIONS (8 minutes + Questions)**
3.20pm	**Nicci Bartley** *PoCoG, The University of Sydney* Cancer patient experience of uncertainty while waiting for genome sequencing results
3.30pm	**Danielle Gessler** *The University of Sydney* Clinical strategies to building health literacy in adolescents and young adults with cancer and their families
3.40pm	**Jolyn Hersch** *School of Public Health, The University of Sydney* Treating (or monitoring?) low-risk ductal carcinoma in situ: focus groups about women's views
3.50pm	**Kim Tam Bui** *Concord Cancer Centre* Prevalence and severity of scanxiety in people with advanced cancers: final results of a multicentre survey
4.00pm	**Jasmine Yee** *The University of Sydney* Patterns and predictors of exercise following surgery for breast cancer
4.10 - 4.20pm	**RAPID FIRE PRESENTATIONS (3 minutes)**
Rapid Fire	**Catherine Seet-Lee** *The University of Sydney* The effect of aerobic exercise on tumour blood delivery: a systematic review of preclinical and clinical studies
Rapid Fire	**Tiffany Li** *The University of Sydney* Minimal clinically important differences in patient reported outcome measures used in chemotherapy-induced peripheral neuropathy

Rapid Fire	**Poorva Pradhan** *The University of Sydney* The role of cognitive biases in the context of cancer: A systematic review and meta-analysis

CLOSING SESSION

4.20pm	**Consumer Presentation - Cancer Voices NSW**
4.30pm	Awards and wrap up
4.45pm	Afternoon Symposium concludes

FEEDBACK

What did you think of the Sydney Catalyst Postgraduate & Early Career Researcher Symposium?
Did you enjoy the day but have some suggestions for how we can improve for next time?

Log into our online program evaluation and tell us what you thought!
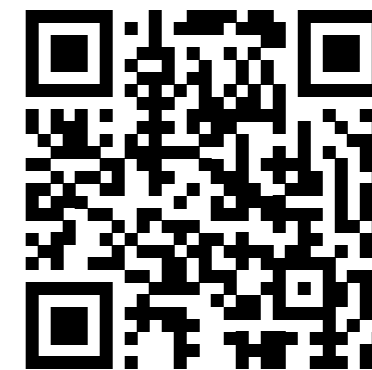
https://www.surveymonkey.com/r/PGECR2020

SYDNEY CATALYST
TRANSLATIONAL CANCER RESEARCH

JOSEF GILLSON

The University of Sydney

Examining the chemoresistance mechanisms in pancreatic ductal adenocarcinomas

Josef Gillson is a first year MPhil student located at the Kolling Institute, Royal North Shore Hospital, St. Leonards under the supervision of Dr. Sumit Sahni. His current project is aimed at investigating avenues of combination chemotherapy to overcome drug resistance in pancreatic cancer, the role of autophagy and the screening for novel biomarkers. He completed his Bachelor of Science and an honours project also with Dr. Sahni at the University of Sydney.

BROOKE PEREIRA

The Garvan Institute of Medical Research

Quantitative proteomics reveals cancer cell genotype can drive matrisomal changes associated with aggressive disease in pancreatic ductal adenocarcinoma (PDAC)

Brooke Pereira completed her PhD at Monash University within the Biomedicine Discovery Institute (BDI) under the supervision of Professor Gail Risbridger in late 2018. During her candidature she studied tumour-stroma interactions in localised prostate cancer using tissue engineering and quantitative mass spectrometry (MS)-based proteomics. Brooke is now a post-doctoral Research Officer at the Garvan Institute of Medical Research where she is investigating novel stromal targets in pancreatic cancer under the supervision of Associate Professor Paul Timpson. She is using a range of cutting-edge techniques such as patient-derived xenografting (PDX), LC-MS/MS, MALDI imaging and advanced microscopy to study the stroma of both murine and human pancreatic tumours.

MICHAEL PAPANICOLAOU

The Garvan Institute of Medical Research

Mapping the extracellular matrix through breast tumour progression

Michael Papanicolaou is a PhD student from Cancer Matrix and Metastasis at the Garvan Institute of Medical Research. Michael completed his Bachelor of Biomedical Science (1st Class Hons) at the University of Technology, where he pursued a project investigating the interaction between neutrophilic inflammation and brionchiolar extracellular matrix in chronic obstructive pulmonary disorder (COPD) with A/Prof Brian Oliver at the Woolcock Institute of Medical Research.

Michael's current work focuses on understanding how the tumour stroma, including the extracellular matrix, cancer associated fibroblasts and mechanobiology, affect breast cancer development and metastasis.

AMELIA PARKER

The Garvan Institute of Medical Research

Extracellular matrix remodelling defines aggressive non-small cell lung cancer

Dr Amelia Parker completed her Bachelor of Biomedical Engineering and Science (Biochemistry) degree at the University of Sydney before undertaking her PhD with the Children's Cancer Institute and University of New South Wales investigating the role of microtubule proteins in lung cancer aggressiveness.

Amelia furthered her interest in translational lung cancer research during her postdoctoral training at the National Cancer Institute, USA with Dr Curtis Harris focussing on biomarkers and mechanisms of lung cancer progression. Within the Cancer Matrix and Metastasis team led by Dr Thomas Cox, Amelia is applying her interdisciplinary expertise to further our understanding of the role of the extracellular matrix in lung cancer development and aggressiveness.

TUBA NUR GIDE

Melanoma Institute Australia

Genomic and clinical profiles of patients with innate resistance to anti-PD-1-based immunotherapies in melanoma

Dr Tuba Gide is a post-doctoral researcher at the Melanoma Institute Australia, The University of Sydney. She completed her PhD in 2019, focusing on the identification of biomarkers of response and resistance to anti-PD-1 based immunotherapies in metastatic melanoma. Her current research focuses on integrating cutting-edge technologies to identify the patients who will benefit from the standard-of-care immunotherapies and the patients who require treatment with novel drug combinations, ultimately enabling more accurate patient stratification into personalised treatments and improving patients' outcomes.

REBECCA SIMPSON

Melanoma Institute Australia and The University of Sydney

Gut microbiota predicts response and adverse events during anti-PD1/anti-CTLA4 neoadjuvant immunotherapy

Rebecca Simpson is a first year PhD candidate with the Melanoma Institute Australia, The University of Sydney. Her research focuses on how diet and intestinal microbes influence anti-tumour immune responses and the development of immune mediated toxicities during immunotherapy. Rebecca completed a Bachelor of Science (Advanced) with honours in Immunology in 2019 at the University of Sydney.

GRACE ATTRILL

The University of Sydney and Melanoma Institute Australia

Tumour specific, tumour resident CD8 T cells are associated with reduced recurrence in adjuvant PD-1 treated melanoma

Grace Attrill is a 2nd year PhD student at the University of Sydney and the Melanoma Institute Australia. Her research is focused on melanoma immunology, with a particular focus on the phenotyping of immune cells in human melanoma tissue. She primarily investigates the immune microenvironment of primary melanoma, and the phenotypes of anti-tumour CD8+ T cell populations.

CECILIA CHAMBERS

The Garvan Institute of Medical Research

Inhibition of the NPY signalling axis as a novel therapeutic option in pancreatic cancer

Cecilia Chambers is currently undertaking a PhD candidature in the Invasion and Metastasis group under Prof. Paul Timpson at the Garvan Institute of Medical Research. Her research sits within the T1/T2 end of the translational spectrum and is focussed on investigating the efficacy of inhibiting the Neuropeptide Y (NPY) signalling axis as a novel therapeutic strategy in Pancreatic Cancer. She uses a number of short-term in-vitro and in-vivo murine models alongside longer-term survival studies to elucidate the role NPY plays in pancreatic cancer progression and thus hopes to finetune the manipulation of this signalling pathway with the ultimate goal of identifying a novel therapeutic option for patients suffering from this devastating disease.

MARK SCHREUDER

Sydney Catalyst

Procoagulant platelets as a diagnostic predictor of thrombosis in lung cancer patients

Mark Schreuder is working at the Sydney Catalyst as a T1/T2 Research Fellow in the field of cancer biology. During his training he gained extensive experience in cardiovascular research and biochemistry and with his work he aims to bridge the gap between the bedside and the lab bench. At the CTC, Mark is researching cancer-associated thrombosis by utilising blood from Sydney Catalyst's Embedding Research (and Evidence) in Cancer Healthcare study to identify the role of procoagulant platelets.

Mark has previously worked at the Experimental Cardiology Department at Utrecht University and in the laboratory of Dr Andrew Hoy at the Sydney School of Medical Sciences. At the moment, Mark is completing his PhD in the laboratory of Dr Mettine Bos at the Leiden University in The Netherlands where he has unravelled the mechanisms by which specialized coagulation proteins found in the venom of the Australian Eastern brown snake exert their extreme effects on blood clotting.

JESSICA CHITTY

The Garvan Institute of Medical Research

LOX family inhibition improves response to standard of care therapy in desmoplastic pancreatic cancer

Jessica Chitty's PhD project was a collaboration with Prof. Bostjan Kobe and involved a combination of molecular and structural techniques. She joined Thomas Cox's lab to investigate Lysyl oxidase in order to further our understanding of its biochemical role in the extracellular matrix during cancer progression.

KENDELLE MURPHY

The Garvan Institute of Medical Research

Epithelial versus stromal targeting of FAK in pancreatic cancer: deconstructing treatment regimens according to Merlin status for improved outcome in personalized medicine

Dr Kendelle Murphy completed her Bachelor Degree in Pharmacology, Biochemistry and Molecular Biology at the University of Western Australia before undertaking an honours in the lab of Professor Paul Timpson at the Garvan Institute of Medical Research (University of New South Wales). Utilising state-of-the-art mutliphoton microscope, Kendelle completed her PhD investigating the potential of fine-tuned stromal manipulation to improve chemotherapeutic efficiency in Pancreatic Ductal Adenocarcinoma.

Kendelle is currently continuing this work with Professor Paul Timpson to unravel the complex interplay between tumour cells and the stromal architecture. Here, she is applying her knowledge of the extracellular matrix to streamline treatment regimes in a patient specific manner. She aims to determine if pulsed transient drug administration will alter the subtle ultrastructure of the extracellular matrix, rendering tumour cells increasingly vulnerable to subsequent chemotherapy whilst reducing metastatic potential.

DANIEL REED

The Garvan Institute of Medical Research

A Src-FRET biosensor mouse to predict cancer spread and response to anti-invasive therapies: Insights from intravital imaging

Daniel Reed is a research assistant and a PhD candidate at the Garvan. He is interested in using innovative cutting-edge imaging technologies to elucidate how cancer spreads throughout the body. Daniel uses pre-clinical animal and patient derived cancer models to optimise the efficacy of anti-invasive therapies to delay or block cancer spread.

THOMAS GEORGE JOHNSON

ANZAC Research Institute

YB-1 knockdown inhibits the proliferation of mesothelioma cells through multiple mechanisms

Thomas Johnson has recently completed his PhD at the ANZAC Research institute. His thesis focussed on the role of oncoprotein Y-box binding protein in mesothelioma. Since completing his doctorate, he has been working under A/Prof. Andrew Burgess in the Cell Division Laboratory at the ANZAC. He considers himself extremely lucky to have been supported by Sydney Catalyst throughout his PhD with a top-up scholarship and he appreciates the chance to continue his connection with the organisation.

FAWAZ MAYEZ MAHFOUZ

The University of Sydney

Examination of small nerve fibre neuropathy in chemotherapy-treated patients using sudomotor function testing

Fawaz Mayez Mahfouz is a PhD candidate at the University of Sydney, Faculty of Medicine and Health. His thesis centres around classifying chemotherapy induced peripheral neuropathy (CIPN) pain responses by using neurophysiological techniques, with the overarching aim to identify accurate tools for the assessment of painful CIPN leading to personalised treatment and pain management for cancer patients.

RUTH ALLEN

The University of Sydney

Unravelling the role of immune cells targeted by immunotherapy

Ruth Allen is a first year PhD student working in the Palendira lab at the University of Sydney. She is examining how immune infiltrates, in particular myeloid cells, regulate the tumour microenvironment in cancers of the skin. She seeks to apply this understanding to both immunotherapy and radiotherapy contexts.

ELYSSE FILIPE

The Garvan Institute of Medical Research

nanoP3 – A new class of nanocarriers for the treatment of breast cancer

Elysse Filipe moved to the Cancer Matrix and Metastasis laboratory at the Garvan after completing a PhD in bioengineering in the Applied Materials Group. At the Garvan, she is now applying her bioengineering skills in the cancer space, unravelling the interplay between the mechanical properties of tumours and their propensity to form metastasis. In close collaboration with the Applied Materials Group at the University of Sydney, Elysse is also developing a nanoparticle based therapy for the treatment of triple negative breast cancer which will be the focus of her presentation.

REBECCA VENCHIARUTTI

SOuRCe, Royal Prince Alfred Hospital; The University of Sydney

'The tyranny of distance': facilitators and barriers to early diagnosis and treatment of head and neck cancer

Rebecca Venchiarutti is a final year PhD candidate investigating patient and carer experiences of pathways to diagnosis and treatment of head and neck cancer. Her research interests include health services evaluation, cancer epidemiology, and variations in cancer care. In addition to undertaking a PhD, Rebecca is a research officer at the Surgical Outcomes Research Centre at the Royal Prince Alfred Hospital.

SABINA VATTER

The University of Sydney

Qualitative exploration of intention to change behaviour in patients undertaking genome sequencing

Dr Sabina Vatter is a postdoctoral researcher in psychology currently working on the Psychosocial Issues in Genomic Oncology (PiGeOn) research program. She completed her PhD in 2019 at the University of Manchester, UK exploring the impact of Parkinson's-related dementia on care partner outcomes. She is passionate about improving health, quality of life and well-being across the lifespan within diverse health conditions.

CHRISTINA STANISLAUS

SOuRCe and IAS, Royal Prince Alfred Hospital

Short-term quality of life outcomes following robotic-assisted surgery

Christina Stanislaus has worked in Robotic Surgery Research for 2 years with a background in Health Science and currently completing her Masters of Public Health. The robot within the Sydney Local Health District (SLHD) is governed by a research framework and Christina coordinates the SLHD robotic surgery database and assists in the management of robotic surgery research studies. She has experience working in various specialities that utilise the robot within the SLHD and assisting in speciality specific research to health systems research which includes cost and surgical team analysis.

ALISON YOUNG

Sydney Catalyst

Adaptation and evaluation of a smoking cessation clinical pathway implemented within cancer services

Alison Young has over five years of experience working in psycho-oncology research with both the Behavioural Sciences Unit at Sydney Children's Hospital and the Centre for Medical Psychology and Evidence-based Decision-making (CeMPED). Her clinical and research work has focused on supporting patients and their families in both adult and paediatric oncology. Alison's PhD research focuses on family communication, information needs, and genetic-related health professional's clinical practices working with families with a BRCA1 or BRCA2 pathogenic variant.

CLARE TOMS

SOuRCe, Royal Prince Alfred Hospital

A cross-sectional investigation into quality of life and survival after resection for pancreatic cancer

Clare Toms is a Master of Philosophy candidate at the University of Sydney, investigating the quality of life in pancreatic cancer patients.

Clare works at the Surgical Outcomes Research Centre (SOuRCe) at Royal Prince Alfred Hospital as a Research Officer/Data Manager for the Upper Gastrointestinal and Hepatobiliary Surgical Department. She is responsible for the management of the department's clinical database to determine the efficacy and surgical outcomes for the Morbidity & Mortality audit and other research areas, of interest to the surgical team. Clare's background is in anatomic science and public health. Her area of research interests include, pancreatic cancer management, quality of life in patients with UGI malignancy and surgical outcomes for UGI cancer patients.

CHLOE LIM

The University of Sydney

A thematic synthesis of qualitative research in colorectal cancer survivorship

Chloe Lim is a second year PhD Student at the School of Psychology, the University of Sydney, supervised by Prof Phyllis Butow, Dr Rebekah Laidsaar-Powell, and Prof Jane Young. Her PhD is exploring the psychosocial outcomes of early-stage and advanced colorectal cancer survivorship through a systematic review and multiple qualitative research studies.

OLIVIA FOX

SOuRCe, Royal Prince Alfred Hospital

Surgical outcomes and survival of local and remote patients undergoing pelvic exenteration

Olivia Fox has a background in Public Health Nutrition and recently graduated from a Masters of Global Health at the University of Sydney. She worked previously in community based organisations that aim to implement evidence based practice to improve health outcomes. Currently, she works as a Pelvic Exenteration Research Officer with the Surgical Outcomes Research Centre at Royal Prince Alfred Hospital. Her research in this role investigates quality of life measures and surgical outcomes for patients with colorectal cancer.

QAMRA MUAIKEL ALQAHTANI

The University of Sydney

Information needs of children with cancer and their parents for managing cancer-related symptoms: Preliminary findings of a systematic review

Qamra Muaikel Alqahtani is a full-time PhD student in Health Sciences at the University of Sydney and is currently work at King Saud University in Riyadh as a physiotherapy lecturer. Qamra has a master's degree from the United Kingdom and has had clinical experience of three years as a paediatric physiotherapist. Qamra's interests include childhood cancer rehabilitation and physical activity in general. Qamra's PhD research is exploring children with cancer and their parents' perspectives on cancer-related fatigue and physical activity during and after cancer treatment.

NICCI BARTLEY

PoCoG, The University of Sydney

Cancer patient experience of uncertainty while waiting for genome sequencing results

Nicci Bartley is a Research Officer on the Psychosocial issues in Genomic Oncology (PiGeOn) Project and PhD candidate with the Psycho-oncology Co-operative Research Group at the University of Sydney's School of Psychology. PiGeOn aims to understand the psychological, behavioural and ethical implications of genomic testing for cancer patients. Nicci's PhD research is aims to understand the cancer patients experience of uncertainty when undertaking genomic testing.

Nicci completed her Bachelor of Psychology (Honours) in 2006 at the University of Newcastle, and a Master of Evaluation in 2016 through the University of Newcastle. Having worked in research for 13 years across Australia, the UK, and Canada, Nicci began her PhD in 2018 under the supervision of Professor Phyllis Butow.

DANIELLE GESSLER

The University of Sydney

Clinical strategies to building health literacy in adolescents and young adults with cancer and their families

Danielle Gessler is a clinical psychology registrar who is passionate about translational clinical research in clinical psychology, medicine and public health. She has worked in psychiatry, neuroimaging and individual differences research, as well as public hospital roles at Royal North Shore Hospital and Westmead Hospital. Her current research investigates health literacy and shared decision-making in adolescents and young adults with cancer and she works with adolescents and their families in the Psychological Medicine department of the Children's Hospital at Westmead.

JOLYN HERSCH

School of Public Health, The University of Sydney

Treating (or monitoring?) low-risk ductal carcinoma in situ: focus groups about women's views

Dr Jolyn Hersch is a postdoctoral researcher at The University of Sydney School of Public Health and a member of Wiser Healthcare, a research collaboration for reducing overdiagnosis and overtreatment. Her research aims to improve communication to support people in making better informed healthcare decisions that are consistent with their personal values. Jolyn has led a landmark RCT with longitudinal quantitative and qualitative follow-up, examining how information about overdiagnosis influences women's decision making about breast cancer screening. Her postdoctoral project focuses on the under-researched topic of communication and decision making around managing screen-detected low-risk ductal carcinoma in situ.

KIM TAM BUI

Concord Cancer Centre

Prevalence and severity of scanxiety in people with advanced cancers: final results of a multicentre survey

Tam Bui is a medical oncologist who has recently completed her training through Concord Hospital and Chris O'Brien Lifehouse. In her clinical practice, she has often reviewed patients with scan-associated anxiety ('scanxiety'), which prompted her decision to pursue a PhD through the University of Sydney on the experiences around scans and with scanxiety in people with advanced cancer.

JASMINE YEE

The University of Sydney

Patterns and predictors of exercise following surgery for breast cancer

Jasmine Yee is a Postdoctoral Research Fellow (School of Psychology) and Academic Fellow (Exercise and Sport Science, School of Health Sciences) at the University of Sydney. Jasmine's research focuses on understanding the role of exercise to support physical and psychosocial wellbeing in people with cancer. Her PhD explored the effects of exercise in women living with metastatic breast cancer. Her current postdoctoral work aims to improve wellbeing for men with prostate cancer, working closely with the Radiation Oncology team at the Northern Sydney Cancer Centre.

CATHERINE SEET-LEE

The University of Sydney

The effect of aerobic exercise on tumour blood delivery: a systematic review of preclinical and clinical studies

Catherine Seet-Lee is a PhD student from the Faculty of Medicine and Health at the University of Sydney. She has an undergraduate degree in Exercise Physiology and completed an Honours degree looking at the safety and feasibility of intra-infusion exercise in patients with cancer. Her current research extends the findings from her Honours research and focuses on the effects of intra-infusion exercise on tumour vasculature.

TIFFANY LI

The University of Sydney

Minimal clinically important differences in patient reported outcome measures used in chemotherapy-induced peripheral neuropathy

Tiffany Li is a PhD candidate at the University of Sydney, Faculty of Medicine and Health, investigating outcome measures, risk factors and phenotypes of chemotherapy-induced peripheral neuropathy (CIPN) with a focus on haematological malignancies. Her thesis aims to identify optimal measures of CIPN for use in both the clinical and research settings as well as document the development, progression and recovery of CIPN for patients undergoing neurotoxic cancer treatment. Tiffany has been working in the field of clinical neurophysiology with A/Prof Susanna Park for over 4 years and has a background of Master of Biostatistics.

POORVA PRADHAN

The University of Sydney

The role of cognitive biases in the context of cancer: A systematic review and meta-analysis

Poorva Pradhan is a PhD candidate with the Psycho-oncology Co-operative Research Group at the University of Sydney's School of Psychology under the supervision of Professor Louise Sharpe, Professor Phyllis Butow and Dr Jemma Todd. Her current PhD project focuses on cancer survivorship issues and aims to examine cognitive biases in relation to Fear of Cancer Recurrence/Progression among cancer survivors. Poorva completed her Master in Psychological Studies (with Clinical Psychology as major) from University of Glasgow, UK.

ABSTRACTS T1T2

Examining the chemoresistance mechanisms in pancreatic ductal adenocarcinomas

Josef Gillson[a,b,c,d], Katia Gunther[b,c,e,f], Viive Howell[a,b,c,d], Jaswinder Samra[a,b,c,d], Anubhav Mittal[a,b,c,d], Sumit Sahni[a,b,c,d]

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Patients with pancreatic ductal adenocarcinoma (PDAC) are often diagnosed with advanced tumours due to late diagnosis from limited early onset symptoms. These advanced tumours are often highly resistant to current chemotherapeutic options.

The aim of this study is to further understand the mechanisms of action behind PDAC chemoresistance by examining changes in the proteomic and metabolomic profile due to development of chemoresistance.

Wild type (WT) PANC1 PDAC cells were sequentially incubated with increasing concentrations (0.1 – 5 μM) of standard chemotherapeutic gemcitabine to select a gemcitabine resistant (GR) phenotype. The GR cells were characterized for chemoresistance using cellular proliferation and colony forming assays in the presence of gemcitabine. Metabolomic analysis of the overlying media from the PANC1 WT and GR cells was performed using 1H- nuclear magnetic resonance (1H-NMR) spectroscopy. Global proteomic analysis was performed on the protein lysates from PANC1 WT and GR cells using data independent proteomic technique. Statistical analysis was performed to identify differentially regulated metabolites and proteins in PANC1 GR cells compared to WT cells. Ingenuity Pathway Analysis (IPA) was performed on the proteomic data.

There was a markedly and significantly higher IC50 for gemcitabine in PANC1 GR compared to WT cells in both cellular proliferation (WT: 0.1 μM, GR: 450 μM) and colony formation (WT 6 nM, GR: 14 μM) assays, demonstrating selection of a chemoresistant phenotype. Analysis of metabolites in cellular media demonstrated significantly reduced levels of glucose in GR cells compared WT, indicating a potential increase in cellular uptake of this essential nutrient. Furthermore, there was an increase in the levels of by-products of cellular respiration (pyruvate, lactate and fumarate) in GR cells, indicating heightened cellular energy metabolism. Proteomic analysis identified that the most downregulated protein in GR cells was deoxycytidine kinase (39.4-fold lower), a vital protein required for the phosphorylation and intracellular activation of gemcitabine. The most upregulated protein was tumour protein D52 ligand 1 (>28-fold higher), which is involved in cell cycle control and proliferation and might thus infer a more aggressive phenotype in GR cells. Pathway analysis identified several important upstream regulatory pathways that could be responsible to the chemoresistant phenotype. Of note, AMPK-dependent energy homeostasis pathway was shown to be increased in GR cells.

These findings identify specific metabolic and proteomic signature in gemcitabine resistant PDAC cells. This indicates an altered energy metabolism that could be responsible for the development PDAC chemoresistance.

Quantitative proteomics reveals cancer cell genotype can drive matrisomal changes associated with aggressive disease in pancreatic ductal adenocarcinoma (PDAC)

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Pancreatic ductal adenocarcinoma (PDAC) is highly lethal, with a five-year survival rate of ~9%. PDAC is characterised by robust stromal activation, leading to pro-tumourigenic extracellular matrix (ECM) deposition. Recently, we have shown that targeting this desmoplastic reaction improves chemotherapy efficacy and impairs metastasis in pre- clinical PDAC models [1-2].

To use quantitative proteomics to dissect the matrisomal signatures of murine pancreatic tumours that are highly metastatic (KPC; Pdx1-Cre; LSL-K-rasG12D/+; LSL-p53R172H/+) or poorly metastatic (KPflC; Pdx1-Cre; LSL-K- rasG12D/+; LSL-p53fl/+). We hypothesised that these tumours would have distinct matrisomes, with these changes revealing novel pro-metastatic matrisomal proteins involved in PDAC.

Pancreatic tissue from wildtype, KPC, and KPflC mice were collected at early (6wks), mid (10wks) and end-stage disease (+12wks). To enrich for matrisomal proteins, specimens underwent a decellularisation protocol prior to proteomic analysis. Data-independent acquisition (DIA) liquid-chromatography tandem mass spectrometry (LC- MS/MS) was used to identify differentially abundant proteins.

LC-MS/MS demonstrated an increased abundance of Nidogen 2 (NID2) in KPC tumours at mid stage disease compared to KPflC. NID2 is a 200 kDa basement membrane glycoprotein that closely interacts with laminins, type IV collagen and perlecan to promote the assembly of ternary complexes. Interrogation of single cell-RNASeq KPC and human PDAC datasets revealed that NID2 is overexpressed in PDAC compared to normal pancreatic tissue, with this expression associated with stromal cells such as cancer-associated fibroblasts (CAFs) and perivascular cells. Strikingly, NID2 expression was enhanced in mid stage human PDAC, mirroring our proteomics results.

NID2 was assessed in cancer cells (CC) and CAFs derived from the KPC and KPflC tumours. Immunofluorescence, western blotting, and qPCR show that NID2 was predominantly expressed by CAFs, with this expression significantly enhanced in mt-e-CAFs. To assess the functional properties of NID2, CRISPR interference (CRISPRi) was employed to reduce the expression of NID2 in KPC CAFs. 3D organotypic collagen matrices seeded with NID2-lo CAFs had significantly decreased desmoplasia, shown via second harmonic generation (SHG) imaging and Picrosirius Red staining. In addition, 3D invasion assays revealed that depletion of CAF-derived NID2 impeded invasion of KPC and KPflC CCs in the presence of standard- of-care Gemcitabine/Abraxane chemotherapy, when compared to control. Ongoing work includes subcutaneous and orthotopic co-seeding experiments using CRISPR-edited NID2 KO KPC CAFs in combination with KPC CCs to assess the role of CAF-derived NID2 in metastasis and chemoresistance in vivo.

Overall, NID2 is a promising stromal target in PDAC, with in vitro experimentation revealing its effect on desmoplasia and tumour cell invasion. With further work, we will assess the role of NID2 in tumour progression, invasion, metastasis and chemoresistance.

Mapping the extracellular matrix through breast tumour progression

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Mammary tumour development is a complex process regulated by interactions between tumour cells and the surrounding microenvironment, particularly stromal cells and the extracellular matrix (ECM). The ECM exerts a great degree of cell-extrinsic regulation over cellular phenotype, providing cells with context-specific cues that guide cell and tissue programs. However, throughout breast cancer the ECM is spatio-temporally remodelled, creating a spatial heterogeneity that provides tumour cells with the essential cues for malignant progression.

We hypothesized that stage- and regional-dependant perturbations in the ECM facilitate progression in mammary cancer tumourigenesis.

To map the ECM through tumour development we used the Polyoma Middle-T (PyMT) mammary mouse tumour model, consisting of staged tumours (early, mid, and late) and age-matched healthy mammary tissue. Tumour histology ranged from benign hyperplasia to advanced metastatic carcinoma. Label-free quantitative liquid chromatography tandem mass spectrometry (LC-MS/MS) was utilised in order to profile proteins within the evolving ECM system, or 'matrisome'. Differentially expressed proteins were cross-referenced to expression and survival data in the 'The Cancer Genome Atlas' (TCGA) and 'Gene Expression Omnibus' human breast cancer cohorts to reveal potential targets in breast cancer. Matrisomal proteins were then correlated to known drivers of progression within the matrix (i.e. collagen I) via histological staining and multi-photon microscopy. Single-cell RNA sequencing was used to delineate stromal cell expression of matrisomal proteins, and key proteins were validated and targeted for functional investigation in in vitro and vivo models of tumour progression.

Our data identify 113 differentially regulated matrisomal proteins clustering into 4 distinct temporal profiles. We have identified a subset of matrisomal proteins demonstrating paralleled increased expression in the human setting, with protein expression negatively correlating with progression free survival. Systematic targeting of specific matrisomal proteins in stromal and cancer cell compartments has allowed us to dissect their functional role in tumour development.

This comprehensive analysis of the evolving matrisome in breast cancer progression is facilitating the development of new potential stromal therapies to improve patient outcomes in breast cancer.

Extracellular matrix remodelling defines aggressive non-small cell lung cancer

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Non-small cell lung cancer (NSCLC) is the leading cause of cancer death worldwide and the 5th most common cancer in Australia. The extracellular matrix (ECM) is highly dysregulated in lung cancer. Chronic obstructive pulmonary disorder, a degenerative disease characterised by hyperactivated ECM remodelling is also associated with an increased risk of lung cancer progression, supporting a role for ECM remodelling in lung tumourigenesis. However, the importance of ECM remodelling in regulating tumour aggressiveness, response to therapy and metastatic dissemination remains poorly characterised. We hypothesise that ECM remodelling in early stage lung cancer primes for more aggressive and chemotherapy-resistant tumours.

To define the extracellular landscape in NSCLC and its role in promoting tumour aggressiveness.

Through interrogation of the transcriptome of human NSCLC tumours we have defined a tumour-promoting NSCLC ECM landscape that predicts for with recurrence, which has been validated in second cohorts. Single harmonic generation imaging and picrosirius red staining coupled with ECM-specific imaging analyses of early stage human NSCLC tumour specimens from multiple cohorts including the Enrich substudy, have further refined a collagen remodelling signature associated with patient outcome. Functional studies using novel organotypic lung ECM- derived co-culture models of fibroblasts and cancer cells are defining the mechanisms by which ECM remodelling drives the proliferative and invasive capacity of NSCLC cells and reduces chemotherapy efficacy.

Transcriptomic analysis of human NSCLC has identified that the ECM of these tumours is highly dysregulated and these changes occur early in tumour development. These changes overlap with ECM remodelling in chronic lung diseases that predispose patients to developing lung cancer, suggesting an important role for ECM remodelling in accelerating NSCLC tumourigenesis. The ECM landscape within NSCLC tumours defines distinct molecular subtypes with differential prognosis and may constitute a "field of cancerization" that primes aggressive, metastatic NSCLC. Poor prognosis NSCLC patients have specific fibrotic ECM -remodelled tumours that our analysis indicates would be effectively targeted by anti-fibrotic agents. Advanced ECM-specific imaging is defining the association of collagen- centred ECM remodelling with patient outcome in early stage lung cancer.

The ECM landscape in NSCLC defines an actionable subset of poor prognosis patients at high risk of recurrence. Translational Impact: ECM remodelling may be used as a prognostic biomarker to define the subset of early stage NSCLC patients at high risk of recurrence and to identify a personalised medicine approach that co-targets this ECM remodelling to inhibit metastasis and improve patient outcome.

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Genomic and clinical profiles of patients with innate resistance to anti- PD-1- Based immunotherapies in melanoma

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While immune checkpoint inhibitors targeting the cytotoxic T-lymphocyte-associated protein 4 (CTLA-4) and programmed cell death protein 1 (PD-1) receptors have significantly improved the outcomes of many patients with metastatic melanoma, approximately 50% of patients demonstrate no benefit. Understanding the underlying clinical, pathologic and genetic factors associated with failed response to immunotherapies is key to identifying therapeutic strategies to overcome resistance.

This study sought to investigate the baseline tumour characteristics of poor prognosis patients treated with anti-PD-1-based immunotherapies.

Targeted-RNA sequencing using a custom panel of 500 genes was performed on pre-treatment formalin-fixed paraffin-embedded (FFPE) metastatic melanoma specimens from 37 non-responders (progressive disease or stable disease ≤ 6 months) to anti-PD-1+/-anti-CTLA-4 therapy. Patients were divided into three groups (high, intermediate and low) based on the levels of tumour-infiltrating lymphocytes (TILs) evaluated on haematoxylin and eosin-stained FFPE sections. Clinical characteristics, including LDH, tumour burden and number/sites of metastases, were compared between non-responders based on their time to progression, level of TILs, and gene expression data.

Patients clustered into two groups based on their gene expression profiles, with one group (n=19) expressing genes associated with interferon signalling and exhaustion (STAT1, TIGIT, TBX21, HAVCR2, and FASLG), and the second group (n=18) expressing genes associated with antigen presentation and angiogenesis (HLA-A, TAPBP, ANGPT1, and WARS). A significantly higher proportion of patients in the second cluster presented with brain metastases compared to those patients in the first cluster (P = 0.03). There were no other significant differences in clinical characteristics between these two groups (P > 0.05). Patients with rapid progression (progression-free survival < 2 months) had significantly lower TILs compared to other non-responders (P = 0.04), and this subset of patients also displayed a lower overall immune-related gene expression profile. Furthermore, a trend towards a higher tumour burden was observed in rapid progressors (P = 0.06).

These findings demonstrate the inter-patient heterogeneity within non-responders, and highlight the need for a multilayer, personalised research approach in order to achieve precision immunotherapy.

Gut microbiota predicts response and adverse events during anti-PD1/anti- CTLA4 neoadjuvant immunotherapy

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Immunotherapies targeting PD-1/PD-L1 and CTLA-4 have revolutionised the treatment of metastatic melanoma. Whilst combining strategies is associated with improved response rates, this is accompanied by increased incidence of severe immune related adverse events (irAEs). There is an urgent need to identify biomarkers predicting irAE development. The intestinal microbiota modulates immune processes throughout the body. It therefore likely also influences both anti-tumour immune responses and the development of irAEs during immunotherapy.

We sought to examine the relationship between the intestinal microbiota, response and irAE development during combined anti-PD-1/anti-CTLA-4 immunotherapy. Specifically, we aimed: 1. To define the microbial composition associated with response and toxicities 2. To determine whether dietary features are associated with microbial composition and clinical outcome in melanoma patients.

Pre-treatment faecal microbiomes of Australian and Dutch stage III melanoma patients (n=103) enrolled in clinical trials of neoadjuvant anti-PD-1/anti-CTLA-4 immunotherapy were analysed using 16S rRNA gene sequencing. Microbial metabolic gene abundance and short chain fatty acid (SCFA) levels were assessed by metagenomic sequencing and NMR respectively, and nutritional input was estimated from dietary surveys of food intake. Machine learning was utilised to test the ability of microbial data to predict response and irAE development.

Pre-treatment loads of Ruminococcaceae and methanogenic archaea, and greater relative abundance of butyrate production pathways were associated with better immunotherapy responses and less frequent irAEs. Patients who both failed to respond and developed severe irAE had low microbial diversity before treatment. These features were associated with reduced dietary consumption of fibre and omega-3 consumption. Geographical variance in biomarkers of clinical outcomes was observed, however, this was found to be linked to differences in enterotype (microbial community type) distribution between countries reflecting dietary differences. Machine learning confirmed unique microbial signatures of response and irAE development according to enterotype leading to improved prediction accuracy of models.

Together the data suggests that fibre and omega-3 rich diets are associated with diverse gut ecosystems, enriched with beneficial microbial functions including fibre-metabolism to produce butyrate. We observe that these features, which are known to support intestinal homeostasis, are associated with improved responses to immunotherapy and reduced irAEs. Our findings will inform the design of therapeutic dietary interventions to enhance the beneficial microbial balance and could lead to personalised predictions of patient outcomes.

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Tumour specific, tumour resident CD8 T cells are associated with reduced recurrence in adjuvant PD-1 treated melanoma

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Adjuvant anti-PD-1 therapy significantly prolongs recurrence-free survival in high-risk resected melanoma. However, patients can recur following therapy and reliable predictive biomarkers for response are lacking.

This study investigated intratumoural CD8+ T cell populations in stage III patients treated with adjuvant PD-1 therapy.

The study consisted of a discovery (n=40) and a validation cohort (n=50), and further divided into recurrence and recurrence-free patients, with a median follow up of 14 months (range 5-37 months). Intratumoural CD8+ T cells were quantified in pre-treatment melanoma biopsies using multiplex fluorescent immunohistochemistry.

CD8+ T cells were phenotyped based the expression of CD103 (tumour resident), CD39 (tumour antigen specificity) and PD-1. CD8+ T cell density was higher in recurrence-free patients. A further 8 T cell phenotypes were quantified, finding two populations which were significantly different in both the discovery and validation cohorts. Tumour resident and antigen-specific (CD103+CD39+PD-1+ CD8+) T cells comprised a higher proportion of CD8+ T cells in recurrence-free (6.2% vs 16.4% total CD8+ T cells, p=0.0042), while tumour naïve (CD103-CD39-PD-1- CD8+) T cells were higher in recurrence patients (26.7% vs 16.9% CD8+ T cells, p=0.0464). Spatial analysis also revealed that CD103+CD39+PD-1+CD8+ T cells localise within close proximity to melanoma cells in comparison to CD103-CD39-PD- 1-CD8+ T cells, suggesting differing functional roles for these populations.

These data suggest that the presence of baseline CD103+CD39+PD-1+ CD8+ T cells may be associated with a lower risk of melanoma recurrence in patients treated with adjuvant anti-PD-1.

Inhibition of the NPY signalling axis as a novel therapeutic option in pancreatic cancer

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Due to surgically unresectable, locally advanced or metastatic disease being present at the time of clinical diagnosis, pancreatic cancer (PC) is one of the most lethal forms of human cancer, with >90% of patient deaths occurring within 1 year of diagnosis. Consequently, the development of more effective strategies to overcome these limitations and efficiently treat PC is required. Exciting new research from the Garvan Institute has previously identified that Neuropeptide Y (NPY), normally produced by sympathetic neurons and endocrine cells, has a strong cancer- promoting ability in mouse models of Lewis Lung Carcinoma and B16F10 Melanoma. Excitingly, we found that 16.16% of PC patients from the Australian Pancreatic Cancer Genome Initiative (APGI) exhibit an amplification of NPY signalling components. This evidence led us to investigate the role NPY plays in PC using genetic and pharmacological manipulation of the NPY signalling axis.

Therefore, the overall aim of this project is to investigate the efficacy of using NPY signalling inhibition in combination with current standard-of-care chemotherapy as a novel therapeutic option in PC

We have state-of-the-art tools at our disposal to effectively answer and fine-tune our approach to this question, including: i) An invasive and metastatic PC mouse model (KPC) that closely mimics the human disease ii) NPY/ Y1 receptor knock-out mice that have been crossed to the KPC mouse model for genetic manipulation of NPY signalling, iii) Two different pharmacological inhibitors, a small molecule Y1 receptor antagonist BIBO3304 and a monoclonal NPY blocking antibody (for which we also have a humanised version), iv) Access to Patient-Derived Cell Lines (PDCLs) and Patient-Derived Xenografts (PDXs) of PC exhibiting different NPY/Y1 signatures with associated Tissue Microarrays (TMAs), genomic and transcriptomic profiling and clinicopathological outcome data.

We show that NPY is overexpressed in tumours and metastases from the KPC mouse model relative to wildtype pancreas. Interestingly, NPY is upregulated in KPC cancer cells, while its counterpart Y1 receptor is upregulated in the cancer-associated fibroblasts, suggesting a paracrine interaction between cancer and stromal cells. Moreover, inhibition of the NPY signalling axis in combination with standard-of-care gemcitabine in vivo significantly reduces PC tumour growth and metastatic burden within the liver. Finally, in an orthotopic model NPY inhibition alone significantly improved survival.

NPY is a novel tumour promoting pathway in PC and inhibition of this signalling axis could represent an exciting new therapeutic option in this devastating disease. Importantly, having access to a humanized version of the NPY- blocking antibody highlights this projects ability for rapid translation into the clinic and the potential to directly benefit patient prognosis in PC.

Procoagulant platelets as a diagnostic predictor of thrombosis in lung cancer patients

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Thrombotic events are a major cause of morbidity and mortality in patients with malignant disease (cancer- associated thrombosis). Unfortunately, the pathophysiology of cancer-associated thrombosis remains largely unknown. Recently, a specialized subpopulation of blood platelets, the procoagulant platelets, were identified to be responsible for blood clotting. Here, we hypothesize that procoagulant platelet levels in cancer could have prognostic significance, guiding clinical decisions and minimising thrombotic events. Using serial, citrated blood samples from a prospective cohort of patients with lung cancer enrolled in the EnRICH (Embedding Research (and Evidence) In Cancer Healthcare) Program, a flagship program of Sydney Catalyst and University of Sydney, this is the first clinical study of this measure in a cancer setting.

To investigate a potential role for procoagulant platelets in lung cancer and evaluate the prognostic value of procoagulant platelets to identify lung cancer patients that are at increased risk for thrombosis.

Human studies were approved by Royal Prince Alfred Hospital and University of Sydney ethics committees and conducted according to the Declaration of Helsinki. All participants gave written informed consent. Whole blood was collected in 3.2% citrate and stimulated with platelet agonists (thrombin and collagen) for ten minutes to reveal procoagulant platelets. Samples were labelled and analysed by flow cytometry.

Preliminary analyses revealed that lung cancer patients (n=88) have significantly higher levels of procoagulant platelets at time of diagnosis relative to healthy volunteers (n=55), and cancer patients reached peak procoagulant platelet levels at 6 months after diagnosis of lung cancer. Procoagulant platelet formation correlated with neutrophil and monocyte count, but not with lymphocyte count, pointing to a link with the innate immune system. Significant associations were found between procoagulant platelets and thrombotic events during follow-up and with a cancer- associated thrombotic risk score (as per Khorana score). Conversely, procoagulant platelet levels were comparable in patients with or without a history of thrombosis, suggesting that procoagulant platelet levels increased around the time of cancer development. In addition, trends were observed correlating the formation of procoagulant platelets with disease progression and overall survival.

Collectively, our data suggest that procoagulant platelets correlate with cancer-associated thrombosis and a poor prognosis. The increased procoagulant platelet capacity of lung cancer patients may therefore provide novel insights into the risk of thrombotic events in cancer patients. Further collection of data will help to characterise the pathophysiology of thrombosis in cancer.

LOX family inhibition improves response to standard of care therapy in desmoplastic pancreatic cancer

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Pancreatic ductal adenocarcinoma (PDAC) is a highly aggressive and metastatic tumour with poor prognosis. It is estimated to become the second most prevalent cancer by 2030 representing a significant burden of disease and complex therapeutic challenge. PDAC is characterised by extensive extracellular matrix (ECM) remodelling leading to significant changes in both the biochemical and biomechanical properties of the tissue. In particular, PDAC typically presents with excessive deposition of fibrillar collagens in and around the tumour. This fibrosis contributes in part to the poor penetration of stand-of-care chemotherapies leading to the emergence of chemoresistance. The lysyl oxidases (LOX) family of 5 enzymes are absolutely essential for the synthesis of collagen fibres. The LOX family are typically dysregulated in fibrotic diseases and cancers. To date, a functional role for lysyl oxidases has been reported in almost all solid tumours. High LOX family expression signatures are particularly associated with PDAC and represent a critical mediator of the desmoplastic response in these tumours. Therefore therapeutic targeting the LOX family is an exciting and emerging area of research.

1. Assess the clinical potential of PXS-5505 mediated LOX inhibition in vitro. 2. Determine PXS-5505 stromal targeting in the spontaneous autochthonous KPC genetic model of pancreatic cancer.

Pancreatic cancer cells and cancer associated fibroblasts (CAFs) derived from the KPC autochthonous model (Pdx1- Cre; LSL-KrasG12D+;LSL-p53R172H/+) were used to recapitulate the microenvironment of PDAC tumours. Using our in house developed 3D organotypic co-culture assay the interplay between the matrix, cancer associated fibroblasts and cancer cells in response to treatment with PXS-5505 was determined. The spontaneous KPC genetically engineered model was used to administer PXS-5505 in combination with standard-of-care chemotherapy. Once established, KPC tumours closely mirror pancreatic cancer development in patients.

We have recently completed the pre-clinical evaluation of a novel pan-LOX family inhibitor, PXS-5505 that specifically targets the LOX family of enzymes. We show PXS-5505 inhibits LOX family activity in our PDAC in vitro and in vivo models. Specifically, PXS-5505 results in fewer collagen cross-links in our models. In our in vivo genetically engineered mouse models of pancreatic cancer, PXS-5505 extends survival when used in combination with standard- of-care chemotherapy versus chemotherapy alone.

Overall, we show our anti-stromal targeting strategy is able to increase efficacy of standard-of-care chemotherapy by targeting the underlying mechanism of tumour fibrosis.

Epithelial versus stromal targeting of FAK in pancreatic cancer: deconstructing treatment regimens according to Merlin status for improved outcome in personalized medicine

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Pancreatic cancer is characterized by its aggressive metastatic nature and its resistance to common chemotherapy treatment with a dense, desmoplastic extracellular matrix (ECM) that can both promote and prevent PDAC progression. The multifunctional protein Focal Adhesion Kinase (FAK) acts at the intersection of various signalling pathways often hijacked in cancer progression and metastasis and is a known regulator of ECM stiffness and mechano-signalling in both stromal and epithelial compartments.

Here, we aim to deconstruct stromal versus epithelial targeting in a stratified subset of human pancreatic cancer patients to determine which patients will best benefit from FAK inhibition prior to chemotherapy.

Utilising intravital imaging in live tumours we are able to visualise fine-tuned epithelial and stromal manipulation via FAK priming. Live imaging of the FUCCI cell cycle reporter, in parallel with target validation via FRET imaging of FAK and Second Harmonic Generation imaging of ECM manipulation was used to guide optimised treatment response at both primary and secondary sites. Lastly, orthotopic stratification of PDAC patient samples allowed us to deconstruct the potential of FAK priming regimes in a personalised manner.

Analysis of ECM ultrastructure revealed that FAK priming reduced collagen crosslinking, and ECM stiffness of fibroblast-remodelled matrices, resulting in altered mechano-reciprocity and tumour-stroma feedback. This softer matrix stalled cancer cells during cell cycle progression rendering them increasingly vulnerable to Gemcitabine/Abraxane chemotherapy at both primary and secondary sites. Critically, fluid flow-induced shear-stress enabled us to deconstruct the benefits of FAK priming regimes in reducing PC spread. Lastly, stratified patient samples revealed a subset of patients who may benefit from FAK priming prior chemotherapy.

Our short-term stromal manipulation and epithelial FAK inhibition prior to chemotherapy may improve patient outcome and reduce drug toxicity often associated with chronic combination therapy in PDAC.

A Src-FRET biosensor mouse to predict cancer spread and response to anti-invasive therapies: Insights from intravital imaging

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E-cadherin-mediated cell-cell junctions play a prominent role in maintaining epithelial architecture. Their dysregulation in cancer can lead to the collapse of tumour epithelia and subsequent invasion and metastasis. Recent evidence suggests that, apart from modulating E-cadherin expression, cells are able to mobilise E-cadherin within their cell-cell junctions upon migration and invasion, which can be impaired using Src kinase inhibitors.

Here, we have developed new tools to assess and target: (i): The spatiotemporal dynamics of epithelial tumour cell- cell junctions (E-cadherin biosensor mouse) and (ii): Pro-invasive Src activity in migratory cancer cells (Src biosensor mouse).

Utilizing a next-generation E-cadherin-GFP knock-in mouse, we have established Fluorescence Anisotropy Imaging Microscopy (FAIM) to quantify the dynamics of E-cadherin clustering. This enables real-time, in-vivo assessment of E- cadherin-based cell-cell junction strength and integrity during cancer progression and upon response to treatment. Furthermore, we have generated a Src-FRET biosensor mouse to track changes in Src activity, a known driver of cancer invasion and metastasis.

Using subcellular imaging we show that: (1) E-cadherin mobility and clustering become de-regulated in invasive and metastatic cancers compared to healthy tissues. (2) These subcellular aberrations in E-cadherin dynamics can be targeted using anti-invasive treatment to re-stabilise cell-cell junctions. (3) Using our Src biosensor mouse, we demonstrate that fluctuations in Src activity can be quantified in any tissue of interest in physiological and pathological contexts and that the biosensor mouse, as well as primary cell lines isolated from the mouse, can serve as a platform from which to rapidly assess the efficacy of anti-invasive treatments.

We show that our biosensor mouse models can be used as novel tools to fundamentally expand our understanding of cell-cell junction dynamics and cancer invasiveness in vivo in native microenvironments. Using these mice, we can image treatment response using both E-cadherin dynamics and Src activity as a surrogate readout of the efficacy of ant-invasive therapies in real time in the native tumour microenvironment. These models can therefore be used as novel pre-clinical drug-screening platforms to predict the spread of cancer cells and estimate the efficacy of anti- invasive treatment in vivo.

YB-1 knockdown inhibits the proliferation of mesothelioma cells through multiple mechanisms

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Malignant pleural mesothelioma (MPM) is an aggressive, asbestos-related disease. The low survival rate of MPM patients (5-year survival >10%) is largely attributed to limited effective treatment options. Finding new therapeutic targets is therefore of top priority. Y-box binding protein-1 (YB-1) is a multifunctional oncoprotein that has been shown to regulate proliferation, invasion and metastasis in a variety of cancer types. We previously demonstrated that YB-1 is overexpressed in mesothelioma cells and its knockdown significantly reduces tumour cell proliferation, migration, and invasion, suggesting that targeting it may have therapeutic significance. However, the mechanisms driving these effects are unclear and a study investigating the effect of YB-1 knockdown on global gene expression changes is yet to be done in cancer cells.

To determine the underlying mechanism of YB-1 siRNA-mediated proliferation inhibition in MPM cells.

RNA sequencing (RNA-seq) with poly(A) selection, TALI apoptosis, propidium iodide cell viability flow cytometry and live-cell imaging with fate map analysis assays were conducted after transfection with control or YB 1 specific siRNA.

We utilised an unbiased RNA-seq approach to characterise the changes to gene expression caused by loss of YB 1 knockdown in three mesothelioma cell lines (MSTO-211H, VMC23 and REN cells). Bioinformatic analysis showed that YB-1 knockdown regulated 150 common genes that were enriched for regulators of mitosis, integrins and extracellular matrix organisation. However, each cell line also displayed unique gene expression signatures, that were differentially enriched for cell death or cell cycle control. Interestingly, deregulation of STAT3 and p53- pathways were a key differential between each cell line. Using flow cytometry, apoptosis assays and single-cell time- lapse imaging, we confirmed that MSTO-211H, VMC23 and REN cells underwent either increased cell death, G1 arrest or aberrant mitotic division, respectively.

This data indicates that YB-1 knockdown affects a core set of genes in mesothelioma cells. Loss of YB-1 causes a cascade of events that leads to reduced mesothelioma proliferation, dependent on the underlying functionality of the STAT3/p53 pathways and the genetic landscape of the cell. This project therefore sets the foundations to further investigate the interaction between YB-1 and the STAT3/p53 pathway in MPM. Furthermore, these findings contribute towards understanding which biological contexts YB-1 may be targeted in MPM tumours down the line.

Examination of small nerve fibre neuropathy in chemotherapy-treated patients using sudomotor function testing

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Chemotherapy-induced peripheral neuropathy (CIPN) is a side effect of neurotoxic chemotherapy treatment that can produce nerve damage to sensory, motor or autonomic nerve fibres. Small nerve fibre and autonomic neuropathy can produce significant symptoms such as sweating abnormalities and dizziness but are difficult to objectively measure. Since sweat glands are innervated by these fibres, sudomotor function testing (via SUDOSCAN) is suggested as a method to quantify small nerve fibre and autonomic neuropathy in CIPN.

This study aimed to examine sudomotor function abnormalities in upper and lower-limbs, and identify associations between SUDOSCAN results with clinical factors, CIPN severity and autonomic neuropathy questionnaires.

We assessed participants cross-sectionally who completed taxane, platinum-based or bortezomib chemotherapy treatment 3-24 months prior. Participants completed a SUDOSCAN test twice (averaged data), to assess electrical skin conductance (ESC) in the upper and lower-limbs which was compared to SUDOSCAN reference ranges. Neuropathy severity was graded using clinical grading scales (NCI-CTCAE), objective neurological assessment (Total Neuropathy Score-clinical (TNS-c)) and sural and tibial nerve conduction studies. Participants completed the FACT/GOG-Ntx-13, EORTC-QLQ-CIPN20, Pain Numerical Rating Scale (PNRS) and Survey of Autonomic Symptoms (SAS) questionnaires. The associations between ESC with overall questionnaire scores, individual autonomic questions and clinical characteristics (age, BMI and waist-to-hip ratio) were calculated using Pearson's correlation.

134 participants (23% Grade-1 CIPN; 48.5% Grade-2+ CIPN) consented (69% female, 56.3±13.0 years old, 9.3±7.9 months post-treatment). 33.5% displayed moderate-severe ESC upper-limb dysfunction, while 25% displayed moderate-severe ESC lower-limb dysfunction. Lower ESC was associated with older age (hands: r=-0.24, feet: r=- 0.27), higher BMI (feet: r=-0.20) and higher waist-to-hip ratio (feet: r=-0.19) (all p<0.05). Both upper and/or lower- limb ESC was correlated with CIPN severity on multiple measures (EORTC-QLQ-CIPN20, TNSc, NCI-CTCAE and FACT/GOG-Ntx-13 (all p<0.05), but not with pain or autonomic function measures (PNRS or SAS). However, upper- limb ESC correlated with individual autonomic questionnaire items including tinnitus (r=0.194) (via FACT/GOG-Ntx- 13) and dizziness (r=-0.238) and blurred vision (r=-0.220) (all p<0.05) (via EORTC-QLQ-CIPN20), but no items from the SAS (all p>0.05).

Some cancer survivors treated with neurotoxic chemotherapies demonstrated upper and lower-limb sudomotor dysfunction using the SUDOSCAN. CIPN severity correlated with sudomotor function, however there were no correlations between sudomotor function and specific small fibre autonomic neuropathy questionnaires. The translational/clinical significance of SUDOSCAN in assessing CIPN in these patients remains limited. Future methods of assessing small fibre and autonomic nerve function are required to quantify deficits.

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Unravelling the role of immune cells targeted by immunotherapy

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Immunotherapy has had a huge impact in patients with end stage cancer. However, not all patients respond to currently available immunotherapies. In order to improve the efficacy of immunotherapy a greater range of targets need to be identified, in particular for patients that develop resistance. Checkpoint blockade therapy (CBT) is the most common immunotherapy. CBT employs monoclonal antibodies (mAbs) to block negative signalling on both tumour and immune cells, aiming to restore anti-tumour immune effector functions. Combination anti-PD-1 and Anti-CTLA-4 is the most effective currently employed immunotherapy for melanoma with up to 40% response rates in patients. We hypothesise that response rates to CBT can be improved by identifying and utilizing more diverse immune targets.

To elucidate the specific role of immune cells targeted by immunotherapy in melanoma.

High-dimensional Flow Cytometry and quantitative Multiplex Immunohistochemistry were used to assess protein expression on immune cells in melanoma metastases. Cytokine Bead Arrays were employed to determine the functional capacity of T cells and macrophages through measurement of their cytokine production in response to stimuli.

We focused on V-domain Ig Suppressor of T cell activation (VISTA) molecule, a PD-1 homolog showing promising pre-clinical data in cancer patients not responding or developing resistance to current treatments. We found the expression of VISTA and its ligands CD28-H and VSIG-8 on both lymphocytes and myeloid cells, although the expression of VISTA was higher on myeloid populations. Interestingly, we found CD4 T-helper cell subsets to show the highest levels of positivity for VISTA, CD28-H and VSIG-8 amongst lymphocytes, suggesting that they could be a critical target population for anti-VISTA antibodies. Preliminary work also shows different functional properties between VISTA+ and VISTA- CD4+ helper T cells. Similarly, VISTA+ macrophages also produced distinct effector molecules when compared to VISTA- macrophages.

Here we show that immunotherapy targeting VISTA molecules are likely to impact both lymphocytes and myeloid cells. Our data suggests that VISTA+ immune cells could have a distinct function within the TME. Understanding the role of VISTA+ immune cells may provide insight into how immunotherapy targeting these molecules are likely to work.

nanoP³ – A new class of nanocarriers for the treatment of breast cancer

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Breast cancer is the most common cancer in women in Australia, yet despite improvements in survival rates over the past decades, it continues to be the second greatest cause of cancer related death in women. Cancer patients frequently rely on non-targeted systemically delivered chemotherapy agents, resulting in significant side effects for the patient. The application of nanotechnology in cancer has emerged as a way to enhance tumour targeting and controlled release of therapeutic agents, whilst minimizing toxicity. The number of nanoparticle platforms for delivery of anti-cancer therapies has increased vastly in recent decades, however previous platforms have yielded little translational success due to complex manufacturing protocols, poor drug binding efficiencies and limited biodistribution.

This work describes a new class of cost-effective, and highly stable carbon nanoparticles (nanoP3), for the treatment of breast cancer. This novel nanoP3 platform demonstrates extraordinary drug-binding capacities and an exceptional biodistribution profile *in vivo*.

nanoP3 were functionalized with siRNA-VEGF and standard-of-care chemotherapy paclitaxel and tested for their efficiency, using the in vitro tubulogensis assay and in vitro cytotoxicity studies in breast cancer cells. An orthotopic breast cancer model was used to demonstrate the *in vivo* potential of the nanoP3 platform in inhibiting primary tumour growth.

nanoP3 were effective at delivering siRNA-VEGF to primary endothelial cells, resulting in a significant knockdown of VEGF expression and consequent inhibition of tubule formation *in vitro*. Similarly, paclitaxel was shown to retain its cytotoxic potency when delivered on the nanoP3 surface. *In vivo*, local delivery of our multifunctional nanoP3 resulted in a 24% reduction in tumour burden after one week of therapy, whilst tumours of saline treated mice increased in size by 78%.

This work is the first to demonstrate the *in vivo* potential of our nanoP3 platform, representing an exciting new option for the treatment of breast cancer.

ABSTRACTS T2T3

'The tyranny of distance': facilitators and barriers to early diagnosis and treatment of head and neck cancer

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In NSW, targets for timely diagnosis and treatment of head and neck cancer (HNC) are not yet being met, particularly for patients in regional areas. Our previous work found that depending on remoteness of residence and place of treatment, commencement of primary or adjuvant treatment within the recommended guidelines of four and six weeks respectively varied between 14% and 56%. These delays may result in disease progression and significant distress for patients and carers.

The study aim was to investigate patient and carer perceptions of facilitators and barriers to early diagnosis and treatment of HNC in NSW.

Patients with HNC and their carers were purposively sampled from participants in a prospective cohort study investigating times to diagnosis and treatment of HNC. Interviews were conducted between April 2019-March 2020, transcribed verbatim, and analysed using content analysis. Data collection and analysis were underpinned by the Model of Pathways to Treatment.

Forty-four semi-structured interviews were conducted among 39 patients and 17 carers until data saturation. Help-seeking was mediated by the nature of symptoms, with bodily changes that were 'not right' prompting more urgent help-seeking compared to those that patients had previously experienced (eg gingivitis, neck lumps). Facilitators of timely diagnosis and treatment included a sense of urgency imparted on patients by health care professionals (HCPs), advocacy by the HCP or carer on the patients' behalf, and leveraging 'social capital' by consulting friends or relatives who were HCPs. Distance to services, financial costs, and a perceived lack of emotional investment by HCPs acted as barriers to timely diagnosis and treatment. Participants often qualified their experiences of delays into 'good' and 'bad', which were acceptable and not-acceptable, respectively. Reasons for 'good' delays included complex surgical planning and difficult diagnoses, whereas 'bad' delays resulted from HCP or patient inaction in response to symptoms.

Reflecting on their experience of the HNC diagnosis and treatment pathway, participants were able to identify perceived 'good' and 'bad' delays, accepting the need for delays when the complexity of their care was acknowledged. The findings provide insight into the interacting nature of factors that facilitate and impede early HNC diagnosis and treatment, which may be used for patient and HCP awareness campaigns to improve adherence to optimal care guidelines.

Qualitative exploration of intention to change behaviour in patients undertaking genome sequencing

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In order for genomic testing to reach its full promise in helping cancer patients prevent future disease, it is important that they act on the results that they receive. We designed this study to investigate behavioural intentions of participants undertaking genome sequencing.

To explore the factors that participants perceived would impact behavioural intentions following receipt of genomic sequencing results.

Individual semi-structured interviews were conducted with a purposive sub-sample of 24 adults with a cancer of likely genetic aetiology who undertook genomic sequencing as part of a larger genetic study (the RiSC study).
Participants were interviewed at 12 months following their consent to a longitudinal psychosocial sub-study of RiSC (the PiGeOn study), before receipt of results. Data were analysed using thematic analysis and data saturation was reached.

Analysis revealed three main themes: facilitators, barriers and motivators to behaviour change. The primary goal for behavioural change was to be healthy for oneself and one's family. Future receipt of actionable genomic sequencing results was seen as a powerful driver of behaviour change. Past experience of cancer facilitated positive modifications to lifestyle, such as increased exercise and healthy diet, higher prioritisation of mental health and well-being, and having regular health check-ups and tests; however, maintaining these changes was difficult for some due to daily commitments and lack of emotional control. Limited knowledge and the inevitability of developing cancer due to genetic predisposition were seen as barriers to making lifestyle changes.

Understanding the barriers and facilitators to behaviour change in the context of genomic sequencing can guide healthcare professionals in offering tailored care, support and therapy to patients and to manage patients' expectations.

Short-term quality of life outcomes following robotic-assisted surgery

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Several surgical specialties have adopted use of the robotic-assisted surgery (RAS), including urology, gynaecology, cardiothoracic and colorectal. Emerging evidence shows that the RAS has advantages with regard to length of stay, complications, and pathological outcomes, compared to conventional or laparoscopic surgery. With the debate over high costs associated with current robotic system , it is essential that the quality of life aspects for patients are properly evaluated. Currently, evidence on improvement in quality of life of patients undergoing the RAS is limited. Using health-related quality of life of urinary, sexual and bowel functions, studies found mixed results on the difference in quality of life outcomes across treatment types for localised prostate cancer.5, 6 Assessment on changes in physical and mental health over time for patients undergoing the RAS will provide evidence for the decision making of patients and healthcare providers.

The aim of the study is to describe the short-term quality of life trajectories following robotic-assisted surgical (RAS) within an Australian public hospital.

This is a cohort study of prospectively collected data of all patients who underwent RAS at Royal Prince Alfred Hospital from August 2016 – July 2020, including those from Cardiothoracic (Coronary Artery Bypass surgery, Mitral Valve replacement/repair and Lung resection, Urology (Prostatectomy and Partial Nephrectomy), Gynaecology (Endometrioses and Hysterectomy) and Colorectal (Rectal Resection). All patients completed quality of life questionnaires (SF-36v2) before surgery, 6 weeks and 6 months after surgery. Physical (PCS) and mental (MCS) health component scores were calculated and compared amongst these time points, with higher scores indicating better quality of life outcomes.

A total of 382 patients underwent RAS, 62 (16%) Cardiothoracic, 220 (58%) Urology, 74 (19%) Gynaecology and 26 (7%) Colorectal. Most of these patients were male (70%) presenting a mean age of 59 years. The PCS decreased at 6 weeks and returned to baseline levels at 6 months postoperatively in patients undergoing Urological and Gynaecological procedures. No significant changes in PCS was observed in patients undergoing Cardiothoracic and Colorectal procedures. The MCS significantly increased from baseline to 6 months postoperatively in patients undergoing Colorectal and Gynaecological procedures. MCS in patients undergoing Urological procedures decreased at 6 weeks and returned to baseline levels at 6 months postoperatively. In patients undergoing Cardiothoracic procedures, no changes in MCS was observed during the study period.

For patients undergoing RAS the PCS returned to baseline levels within 6 months postoperatively, whereas the MCS maintained or improved beyond baseline levels within 6 months after surgery. RAS can be performed with acceptable quality of life outcomes even at short-term follow-up.

Adaptation and evaluation of a smoking cessation clinical pathway implemented within cancer services

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The detrimental impact of smoking tobacco can be mitigated when people diagnosed with cancer quit smoking. Assessment of patient smoking status and referral to smoking cessation services are not consistently implemented within cancer services.

This study aimed to adapt, implement and evaluate a Queensland Health smoking cessation clinical pathway (the 'checklist') into NSW oncology services.

A mixed-method study design was employed using surveys and semi-structured interviews with health professionals from three hospital services. The checklist adaptation process involved smoking cessation training, mapping the clinical pathway and identifying clinical champions. Two services implemented the checklist without adaptations, while the third site incorporated the checklist within their existing medical record assessment.

1446 checklists were completed with about 10% of patients identified as smoking tobacco. Of the identified smokers, 25% accepted referral to smoking cessation services. Pre-implementation collaboration with health professionals and IT facilitated implementation. Checklist implementation within cancer services was generally accepted by health professionals and readily adopted into clinical practice. Adaptation was driven by clinical champions, including the integration of the checklist within existing workflow. Evaluation was based on survey (n=17) and interview data (n=11) with health professionals, who reported that a sense of responsibility and their capacity to carry out the checklist were the most important factors influencing uptake. Differences between sites in relation to access to resources, checklist modality (hard-copy or electronic), and whether the checklist was physician or nurse-led has provided insightful lessons for further refinement of the checklist and future implementation in cancer services.

This study in three NSW cancer services suggests that implementing an existing smoking cessation clinical pathway is feasible and acceptable to health professionals. Further research is required to identify how best to adapt the checklist into the existing workflows.

A cross-sectional investigation into quality of life and survival after resection for pancreatic cancer

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Pancreatic cancer is the fifth leading cause of cancer death in Australia. The five-year survival for pancreatic cancer is one of the lowest worldwide at about 8.7%. There are many challenges in the treatment of pancreatic cancer and limited treatment options, with resection the only potentially curative option. Given the limited treatment options and survival, an insight into the quality of life (QOL) of pancreatic cancer patients after surgery is of interest and has the potential to inform patients, clinicians and policy makers.

To investigate QOL trajectories and overall survival following pancreatic resection for malignant and premalignant disease.

Consecutive patients undergoing pancreatic cancer resection between April-2014 and April-2019 at six major hospitals in Sydney, Australia were included. The main outcome was QOL assessed with the Short Form 36 (SF-36v2) and expressed as mental (MCS) and physical component scores (PCS) (/100, 0 worst QOL) and the Functional Assessment of Cancer Therapy – Hepatobiliary (FACT-Hep) (/180, 0 worst QOL). Time from surgery was categorised into 3-11, 12-23, 24-35, and 36-62 months post-surgery for analysis of QOL outcomes. The survival of these patients was analysed using Kaplan-Meier and Log-rank tests.

A total of 226 patients underwent surgery. Mean (SD) age was 66.4 (12.3) years and 53% (n=119) were female. Pancreaticoduodenectomy was the most common procedure (n=142, 63%). 158 patients were eligible and invited to participate in the QOL study, of which 100 (44%) responded. No difference in the PCS was observed during the studied period. A significant improvement in the MCS was observed between 3-11 months and 12-23 months (MD: 12.7; 95%CI: 5.9, 19.6), 24-35 months (MD: 9.9; 95%CI: 3.2, 16.6) and 36-62 months postoperatively (MD: 11.7; 95%CI: 4.9, 18.6). A significant improvement in total FACT-Hep was observed between 3-11 months and 12-23 months postoperatively (MD: 14.8; 95%CI: 0.41, 29.1). The median overall survival was 43.9 months (95%CI: 40.2, 47.5). A significant difference in median overall survival curves was observed according to cancer type; adenocarcinoma 36.2 months (95%CI: 31.3, 41.1), pancreatic neuroendocrine tumour 51.5 months (95%CI: 45.5, 57.6), premalignant 54.3 months (95%CI: 47.5, 61.0), other malignancy 38.7 months (95%CI: 30.0, 47.4).

MCS improved significantly between 3-11 months and the other timepoints (12-23, 24-35 and 36-62 months). The total FACT-Hep score improved significantly between 3-11 months and 12-23 months. with no further significant changes in QOL outcomes observed. A significant difference in median survival curves was observed for cancer type.

A thematic synthesis of qualitative research in colorectal cancer survivorship

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Colorectal cancer (CRC) is the third most common cancer worldwide. Five-year survival rates for CRC are approximately 70%. Clinicians need to understand the psychosocial outcomes of CRC survivorship to provide optimal care. Qualitative research allows for deep insight into cancer survivors' psychosocial experiences, yet synthesis of qualitative research into CRC survivorship is limited.

This paper aims to fill this gap through a systematic review (PROSPERO CRD42019131576) and thematic synthesis of qualitative research into the experiences of colorectal cancer survivorship.

CINAHL, Embase, MEDLINE, PsycINFO, and PubMed were searched for qualitative CRC survivorship papers. Titles, abstracts, and full texts were screened by two raters. Included articles underwent data extraction, CASP qualitative bias ratings, and thematic synthesis by two raters. Disagreements were discussed until a consensus was reached, or a third rater was consulted.

81 articles were included in the final review. CASP quality ratings ranged 5-10 out of 10 (mean = 8.7). Most studies (n=40) included patients treated with curative intent, versus for advanced cancers (stage IV, Dukes' D, recurrent, or metastatic) (n=11), and 30 had mixed or unclear staging. Specific treatments were poorly reported, with 35 articles not reporting treatment or included mixed combinations. Other studies recruited patients who: had surgery alone (with or without stomas) (n=4), underwent surgery with adjuvant treatment not reported (n=27), had adjuvant treatments with or without surgery (n=15). Most studies (n=42) explored experiences within two years post- treatment, 12 at least 5 years post-treatment, and 27 with mixed or unknown time since treatment, ranging from 1 week to 35 years. Thematic synthesis revealed that bowel dysfunction caused functional limitations and negative quality of life (QoL), while stomas posed threats to body image and confidence. Physical symptoms made return to work challenging, which increased financial burdens. Survivors' unmet needs included desires for: information provision regarding symptom expectations and management, and ongoing support throughout follow-up and recovery. Advanced and early-stage survivors shared similar experiences, however advanced survivors reported struggling more with fear of cancer recurrence/progression and feelings of powerlessness. Functional limitations, financial impacts, and sexuality in advanced survivors were under-explored areas.

CRC and its treatments impact survivors' QoL in all areas. A co-ordinated supportive care response is required to address survivors' unmet needs. Future qualitative studies should explore advanced CRC subpopulations, treatment- specific impacts on QoL, and long-term (>5 years) impacts on CRC survivors.

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Surgical outcomes and survival of local and remote patients undergoing pelvic exenteration

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Pelvic exenteration (PE) is a highly radical and morbid procedure used to treat patients with locally advanced or recurrent cancer of the pelvis. Little is known about the effects of geographical location on surgical outcomes and overall survival of patients who undergo PE.

This study aims to compare patient characteristics, surgical outcomes, and survival between local and remote patients undergoing PE.

The study population consisted of adults (aged ≥18 years) who underwent PE surgery for a locally advanced or recurrent pelvic cancer at the Royal Prince Alfred Hospital between September 1994 and July 2020. Patients were divided into two groups (Local and Remote) based on their place of residency. Patients living outside metropolitan Sydney area were defined as remote based on the New South Wales Health districts classification. The main outcomes of interest included surgical margin, postoperative complications, length of hospital stay and overall survival. Difference in outcomes between local and remote patients were assessed using either chi-square test, independent t test or Kaplan-Meier estimates. For all analysis a p value <0.05 was considered statistically significant.

Of 773 patients included in the study, 314 (40.6%) were local and 459 (59.4%) were remote patients. Sex was evenly distributed in both groups; males made up 48.7% and 56.5% of the local and remote patients, respectively. The average age across both cohorts was 59.3 years. Overall, more than three-quarters of the patients had R0 surgical margins, no difference between local (73.9%) and remote patients (78.1%) was observed (p=0.17). Similarly, no difference in postoperative complications (83.1% versus 85.6%, p=0.34), and length of hospital stay (26.9 days versus 27.3 days, p=0.80), between local and remote patients, respectively. The median overall survival was 57 months, with no significant difference observed between local (median survival: 50 months; 95%CI: 36.4 to 63.6) and remote patients (median survival: 63 months; 95%CI: 52.7 to 73.3; p=0.284).

Remote patients undergoing treatment in a central referral unit for patients with locally advanced or recurrent cancer within the pelvis have similar surgical outcomes and overall survival estimates when compared to local patients.

Information needs of children with cancer and their parents for managing cancer-related symptoms: Preliminary findings of a systematic review

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Communication between healthcare providers, parents and children with cancer is critically important throughout cancer trajectory for the delivery of high-quality patient- and family-centred care. However, managing information- sharing in childhood cancer care is a complex process in triadic encounters (Coyne et al. 2016; Bahrami et al. 2017). Furthermore, informational needs of many children with cancer and some of their parent-carers about physical and emotional impact of cancer and its treatment have been found to be unmet by oncologists (Levine et al. 2019).

The aims of this systematic review are to (1) identify and synthesise available evidence regarding the information needs of children with cancer and their parents to manage cancer-related symptoms and (2) provide practical recommendations on meeting needs of children with cancer and their parents for information about managing cancer-related symptoms.

A systematic literature search was conducted using CINAHL, EMBASE, MEDLINE, PsycINFO and Web of Science. Overall, 13,042 relevant articles were screened independently by two reviewers. Eligible articles included empirical research on information needs related to cancer-related symptoms as well as late effects of cancer treatment in general reported by children aged ≤19 years and/or their parents/guardians' during and after curative treatment of paediatric cancer.

Ten studies included in this review, of which two used mixed methods design, one used a qualitative methodology, and seven utilised a quantitative methodology. Four studies assessed information needs about late effects, physical/emotional impact of cancer treatment, and/or symptoms management. One study investigated parents' usage and desires on mobile technology, while the remaining studies focused on explored experiences of cancer- related symptoms. The majority of the included studies focused on parents' needs for information only. Three studies assessed information needs of both children and their parents, and one of these studies reported separate results for children's needs for information about symptoms management. Similarly, few studies explored children with cancer and their parents' preferences for information presentation.

This review revealed a dearth of studies on information needs of children with cancer and their parents for managing cancer-related symptoms. This review will suggest the recommendations for developing educational resources and programs to address children with cancer and their parents' needs for information about symptoms management.

Cancer patient experience of uncertainty while waiting for genome sequencing results

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The translation of genomics into practice provides hope for improvements in cancer risk management, morbidity and mortality. However, there is limited knowledge about cancer patients' experience of uncertainty during genome sequencing (GS) and whether uncertainty contributes to psychological factors such as anxiety and fear of cancer recurrence (FCR) in this context.

We aimed to investigate uncertainty in patients with a cancer of likely genetic origin waiting for GS results.

Participants completed questionnaires at baseline (within one month of agreeing to GS; N=381, response rate 92%), and at three (N=332, response rate 83%) and 12 months (N=282, response rate 79%) follow ups. A subset of patients (N=20 at baseline, N=23 at three months, N=24 at 12 months) participated in semi-structured interviews. Interview recruitment continued until data saturation was reached. Transcripts underwent thematic analysis. All data were collected prior to patients receiving results.

Participants had negative attitudes towards uncertainty (M=4.02, SD 0.70) at baseline. Uncertainty about GS did not change significantly from 3 months (M=8.24, SD 7.36) to 12 months (M=7.97, SD 7.57) follow up (t(205)=.579, p=0.563). Greater uncertainty at three months significantly predicted greater FCR at three months, b=0.38 [0.18, 0.58], p=0.000, and at 12 months, b=.31 [.04, .58], p=0.024. Greater uncertainty at 3 months significantly predicted greater worry about GS at three months, b=0.59 [0.40, 0.77], p=0.000. Greater uncertainty at three months b=0.42 [0.15, 0.69], p=0.002, and at 12 months b=0.40 [0.09, 0.70], p=0.010 significantly predicted greater worry about GS at 12 months. Semi-structured interviews revealed that while participants were motivated to pursue GS as a strategy to reduce illness uncertainty, GS generated additional practical, scientific and personal uncertainties. Some uncertainties were consistently present over the 12 months, while others emerged over time.

This study demonstrated the complexity of uncertainty generated by GS for cancer patients and provides further support that uncertainty impacts anxiety and FCR. Thus, addressing uncertainty may ameliorate psychological morbidity.

Clinical strategies to building health literacy in adolescents and young adults with cancer and their families

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Health literacy has been identified as an essential asset required for adolescents and young adults with cancer (AYAs) to become empowered in their healthcare. However, best-practice guidelines do not currently address clinical approaches to build health literacy in this group.

We aimed to investigate clinician approaches to building health literacy in AYAs and their families using a qualitative methodology.

Clinicians working with AYAs aged 15-25 years old participated in a semi-structured qualitative interview. Primary recruitment took place at the 3rd Global Adolescent and Young Adult Cancer Congress and subsequent snowball sampling was used. Interviews were recorded and transcribed, and analysed using Framework Analysis.

Thirty clinicians across Oncology, Nursing, Clinical Psychology, Social Work and other Allied Health were interviewed (mean interview length= 40 minutes). Clinical approaches for supporting the acquisition and use of health literacy in AYAs were identified throughout the provider-, team- and service-level of healthcare services. Approaches included clinical strategies to i) prioritise rapport with AYAs; ii) engage in clinician reflective practice to consider the unique cancer experience from the AYA perspective, iii) tailor communication by providing appropriate educational material; iv) teach transferrable skills to empower AYAs; v) prioritise family engagement; and vi) work collaboratively as a multidisciplinary team. A model of care that prioritised family involvement and survivorship care was considered essential for supporting the development of health literacy in AYA-family-clinician networks.

Clinicians use a number of different strategies that target the AYA and their family as well as building rapport and a cohesive relationship with the wider multidisciplinary team. This research represents the first step to devising best-practice guidelines for supporting the acquisition of health literacy in AYAs and their family systems. We suggest that recognising the systems that surround AYA cancer care can promote shared, coordinated and effective care across AYA, family and clinician triads.

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Treating (or monitoring?) low-risk ductal carcinoma in situ: focus groups about women's views

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Organised breast screening has greatly increased DCIS incidence. Recognition that some DCIS lesions might remain indolent for many years has led to concern about overtreatment, and international clinical trials are currently assessing the safety of active monitoring for low-risk DCIS. Women may not be aware of what DCIS is and the dilemmas around its optimal management.

We aimed to explore women's understanding and views about DCIS and current and potential future management options.

A community-based sample, recruited by telephone, of 56 women aged 50-74 with no personal history of breast cancer/ DCIS participated in six age-stratified focus groups around Sydney, Australia. Sessions incorporated a purpose-designed presentation explaining the nature of DCIS, current standard management, uncertainty around progression, and ongoing clinical trials of monitoring for low-risk DCIS. Throughout the sessions, participants shared their thoughts, feelings and questions in response to the information presented. Discussions were audio-recorded, transcribed and analysed thematically.

Very few participants had heard of DCIS. Many women showed interest in being monitored if diagnosed with low- risk DCIS; others expressed a stronger preference for immediate treatment. Although women mostly supported clinical trials of monitoring (and just over half would join if invited), they also had important concerns and misconceptions about such trials. Some participants struggled to understand the need for randomisation. Many would be reluctant to leave their management to chance, including some who felt strongly against surgery if monitoring were considered viable.

Public awareness of DCIS is very limited. Most focus group participants gained a reasonable understanding of the issues during the session, and we found substantial interest in monitoring for low-risk DCIS. If clinical trials are to generate much-needed high-quality evidence about new management approaches, effective communication is essential to facilitate informed decisions about screening, treatment and trial participation, and to implement future changes in practice. Translational significance: Findings of this study enhance our understanding of public responses to and concerns about a conservative approach to management for low-risk DCIS, which could be translated into the development of evidence-based strategies and tools to communicate more effectively in clinical practice and support high-quality, well-informed and shared decision making.

Prevalence and severity of scanxiety in people with advanced cancers: Final results of a multicentre survey

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Scan-associated anxiety ('scanxiety') is common, but underreported, for people with advanced cancer. Scanxiety may be higher in this population due to profound implications on treatment and prognosis.

To determine the prevalence, severity and associations of scanxiety in adults with advanced cancers.

Eligible participants had advanced solid cancers and a computed tomography (CT) scan within the previous four months. Participating sites were metropolitan (Concord & Campbelltown) and rural (Dubbo) cancer centres and the Breast Cancer Network Australia (BCNA) Review & Survey Group. Participants completed an online or paper survey consisting of 100-items including self-rated presence (yes/no) and severity (distress thermometer, 0-10) of scanxiety, state anxiety (STAI-6), clinical anxiety depression (HADS), and fear of progression (FOP-Q-SF). Associations with scanxiety were evaluated.

222 surveys were returned (Concord: 96, Campbelltown: 69, Dubbo: 21, BCNA: 34). Participant characteristics: mean age 64 years (range 26 to 91 years); female (61%); at least secondary education (77%); breast (37%), lung (19%), or bowel (16%) cancer; and, had a CT scan within the last month (62%). Over half (55%) of participants experienced scanxiety. Scanxiety was more prevalent in participants who: were younger (mean age: 62 years with scanxiety v 66 years without scanxiety, p=0.01); were female (v male, odds ratio 2.9, p=0.0002); had breast cancer (v other, odds ratio 2.5, p=0.002); and had higher mean scores for STAI-6 (p<0.002), HADS-A (p<0.0001) and FOP-Q-SF (p<0.0001). Among participants with scanxiety, the median severity score was 6 (range, 1 to 10). More severe scanxiety occurred in people with higher mean scores for STAI-6 (p=0.001), HADS-A (p<0.001) and FOP-Q-SF (p<0.001). Participants valued practical factors (e.g. experienced staff for cannulation, convenient scan location, receiving a management plan) and psychosocial factors (e.g. relationship with staff) to improve the scan experience.

Scanxiety is common and often severe. A prospective, longitudinal scanxiety study to better inform the timing of interventions to reduce scanxiety is underway.

Patterns and predictors of exercise following surgery for breast cancer

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Exercise is an effective strategy for women with breast cancer to manage treatment-related side effects. However, exercise levels typically decline during treatment.

This study describes exercise behaviour in the 18 months following breast cancer surgery and examine predictors of behaviour.

Women (n=203) aged 58.4 (SD 10.5) years enrolled prior to breast cancer surgery. Eighty percent received radiotherapy and 47% chemotherapy. Women completed weekly diaries reporting exercise were categorised as completing aerobic or resistance exercise, or not, at 6, 12 and 18 months. Relationships between exercise and clinical, demographic, anthropometric and baseline activity variables were assessed using chi-square and significant variables (p£0.2) examined with a multivariate model.

Prior to surgery, 95% reported aerobic exercise, dropping to 13%, 23% and 38% at 6, 12 and 18 months, respectively. Post-surgery resistance training levels were minimal at 6 (0%), 12 (1%) and 18 months (1.5%). In adjusted analysis, factors associated with aerobic exercise at 18 months were baseline activity ≥50min/wk of moderate-vigorous physical activity (MVPA; vs. <50min/wk; AOR: 2.3, p=0.03) and ≥105 mins/wk of walking (vs. <105min/wk; AOR: 3.1, p<0.01), and working (vs. not working; AOR: 2.7, p<0.01).

Aerobic and resistance exercise levels among breast cancer patients following surgery are low. Women who worked and had higher levels of MVPA and walking prior to surgery were more likely to engage in aerobic activity at 18 months, with clinical and medical variables playing a limited role. Given the benefits of exercise, support from healthcare professionals is essential to encourage exercise during breast cancer treatment, particularly those previously inactive.

The effect of aerobic exercise on tumour blood delivery: a systematic review of preclinical and clinical studies

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Tumours are structurally and functionally abnormal. Tumour blood vessels are unevenly distributed and poorly developed, resulting in areas of hypoxia and heterogenous blood supply. Aerobic exercise may modulate tumour blood flow and normalise the tumour microenvironment to reduce hypoxia and improve chemotherapy delivery.

This systematic review aims to evaluate the effects of aerobic exercise on tumour hypoxia, vascularisation and blood flow.

We searched Medline, EMBASE, Scopus and CINAHL through July 2020. Preclinical and clinical randomised controlled trials examining the effects of aerobic exercise (≥ 2 repeated bouts) on markers of hypoxia, vascularisation or blood flow in solid tumours were included (PROSPERO: Protocol number CRD42020159201). Two independent reviewers performed screening and data extraction.

Fifteen preclinical studies and one clinical study met criteria. Nine studies assessed hypoxia, 15 studies assessed vascularisation and seven evaluated blood flow. There was large variability in the range of measures, cancer type and exercise interventions. Hypoxia showed little consistency with three studies demonstrating a decrease in hypoxia, five studies demonstrating no change and one study demonstrating an increase. Similarly, the effect on vascularisation was heterogenous with three studies demonstrating a decrease in vessel density, eight studies demonstrating no change and four studies demonstrating an increase. However, blood flow demonstrated a mostly positive effect across all the studies.

Most evidence of aerobic exercise effects on tumour blood flow is in animal models, with very limited evidence in humans. Despite wide variability in methodology, these findings suggest exercise has a positive effect on blood flow to solid tumours. However, evidence in inconsistent regarding effect on hypoxia and vascularisation. Further research is needed to extend this work in clinical trials and to investigate the potential for translation to intravenous chemotherapy delivery.

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Minimal clinically important differences in patient reported outcome measures used in chemotherapy-induced peripheral neuropathy

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Patient reported outcome measures (PROMa) are increasingly used to measure chemotherapy-induced peripheral neuropathy (CIPN) in both research and clinical settings. However, the minimal clinically important differences (MCID) suggesting significant clinical symptom deterioration and subsequent impact on treatment modification remain ill-defined. Clinician judgements on dose modification currently rely on the NCI-CTCAE grade.

This study aims to determine the MCID for PROMs using the NCI-CTCAE grade as an anchor.

342 patients (mean age=55.5±12.6) were prospectively assessed prior to receiving neurotoxic treatment (taxanes, platinums, vincristine, bortezomib, thalidomide), mid-treatment, end-of-treatment and at follow-up (mean=6.1±3.0months), each time completing FACT/GOG-NTX13, EORTC CIPN18 and NCI-CTCAE. Anchor-based approaches were used to identify MID for PROMs using clinical change groups (0=no change in NCI grade; 1=minimal deterioration- one NCI grade change; 2=above minimal deterioration- NCI grade change>1). Mean change and linear regression methods of calculating MCID were utilised with effect sizes (ES) of 0.2-0.8 considered appropriate.

PRO scores were moderately correlated to NCI grades at each timepoint (r=0.4-0.7), demonstrating the NCI grade as an appropriate anchor. The MCID score from baseline to mid-treatment was 3.7-4.5 for the FACT (ES=0.75) and 3.2-3.6 for the CIPN18 (ES=0.69). Score changes of 10.7 and 9.9 for the FACT and CIPN18 were associated with above minimal deterioration. From mid-treatment to end-of-treatment, the MCID for the FACT was 5.6-6.8 (ES=0.64) and 4.5-5.9 for the CIPN18 (ES=0.71), with above minimal deterioration leading to score changes of 8.4 and 8.2. Patients at follow-up with grade≥2 CIPN demonstrated mean score changes of 5.2 for the FACT and 4.5 for CIPN18 by mid- treatment, and 11.7 and 10.4 by end-of-treatment compared to baseline.

This study demonstrates the changes evident on common PROMs when patients experience minimal neuropathy symptom deterioration, as well as the change associated with more significant symptom change. Further, we identified PROM score differences associated with long-term clinically significant CIPN.

The role of cognitive biases in the context of cancer: A systematic review and meta-analysis

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Fear of cancer recurrence/progression (FCR/P) is amongst the most commonly reported long-term survivorship issues. However, much less is known about the cognitive processes involved in the development and maintenance of FCR/P.

This systematic review aimed to (1) synthesize the literature on cognitive biases (attention, interpretation or memory) in cancer survivors and their caregivers; and (2) assess if these biases are associated with indicators of psychological distress.

Studies were identified through a systematic search in PsycINFO, Medline, Scopus, CINAHL, Web of Science and Embase databases. We included studies that examined cognitive biases using an accepted experimental paradigm in the context of cancer.

Of 4105 papers identified, 25 met inclusion criteria. Cancer survivors had a greater attentional bias towards salient stimuli (cancer/negative stimuli) as compared to controls (Hedge's g= 0.82). Importantly, survivors who were more distressed had greater attentional biases (Hedge's g= 0.27). It was unclear whether the nature of stimuli was important in driving these effects (e.g. cancer-specific versus negative). Similar biases were identified in caregivers, although this data could not be meta-analysed. Of only two studies assessing interpretation biases, both found evidence for interpretation biases amongst cancer survivors. Of only two studies assessing memory bias, neither found evidence of a memory bias.

These results demonstrate that cancer survivors have a bias towards cancer-related or negative stimuli, and that bias is greater for those with high levels of distress. The literature should adopt consistent use of paradigms and stimuli, and use more direct measures of cognitive bias, where possible. More studies of interpretation and memory bias are needed.

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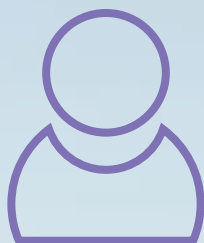
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