Cancer Network Newsletter
2022: Issue 2

Bristol Cancer Research Network

Tessa Jowell Centre of Excellence status

The Bristol Network, which includes North Bristol NHS Trust (NBT), University Hospitals Bristol and Weston NHS Foundation Trust, Gloucestershire Hospitals NHS Foundation Trust, Royal United Hospitals Bath NHS Foundation Trust, has been recognised as a "Tessa Jowell Centre of Excellence" following rigorous expert-led assessments by the Tessa Jowell Brain Cancer Mission (TJBCM).

This award congratulates the six new brain tumour centres for excellence in treatment, research and care. This is an impressive achievement as despite the challenges of the COVID-19 pandemic, these centres have been able to transform their services to elevate their wrap-around patient care.

This initiative is part of TJBCM's national mission to ensure every patient has access to excellent care, no matter where they live. With the addition of six new centres, there are now 17 Centres of Excellence across the UK. In time, it is the Mission's aspiration that every brain

tumour centre in the UK becomes a Centre of Excellence. Due to the combined catchment area of these six centres, a further 14 million people now have access to excellent care should they need it, with the centres jointly treating more than 1,000 new brain tumour patients per year.

With 12,000 people diagnosed with a brain tumour every year in the UK, there has never been a more important time to recognise the efforts of NHS staff committed to developing and improving brain tumour treatment and care. The committee found the Bristol Network demonstrated excellent treatment and care across the network and Bristol was recognised for its commitment to service development, in particular the further development of its rehabilitation pathways.

In addition to the excellent patient support at all stages of their treatment, the committee commended Bristol for its neuropathology services. Bristol is a leading voice in the Tessa Jowell Academy and is spearheading the effort to widen access to genomic testing across the UK.

Image: Kathreena Kurian, Professor of Neuropathology and Honorary Consultant at NBT, Head of the Brain Tumour Research Centre at the University of Bristol and a member of the Bristol Network.

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University of BRISTOL
Elizabeth Blackwell Institute for Health Research

EVENTS

Festival of Enterprise
27 June 2022, 9.00 - 16.00, Wills Memorial Building, Queens Road, Bristol BS8 1QE

Exploring diagnosis of cancer as an emergency: Evidence and Insight from the UK and other countries
27 June 2022, 14.00 - 16.00, online

Living systematic reviews: Technical aspects and challenges when setting up and automating aspects of a living systematic review
28 June 2022, 13.00 - 14.00, Lena Schmidt and Francesca Spiga (University of Bristol), online

Bristol Poverty Institute Showcase event
30 June 2022, 13.30 - 18.00, The Bristol Hotel, Prince Street, Bristol BS1 4QF

BNSSG CCG Research Showcase Seminars
1 July 2022, 11.00 - 12.00, online

Cancer Research Network Early Career Researchers' symposium 2022
24 June 2022, 10.00 - 14.30, Life Sciences Building

This half-day event will comprise oral and poster presentations from ECRs as well as a **keynote** talk from **Prof Tim Frayling** (University of Exeter)

To join us, contact Catherine Brown ASAP

Enhancing Research Culture project showcase
1 July 2022, 13.30 - 16.30, MShed, Princes Wharf, Wapping Road, BS1 4RN

Cancer Genomics 2022 Conference
5 - 7 July 2022, Oxford Brookes University

What makes a good antibody target?
5 July 2022, 13.30 - 15.30, online

How to apply Public Involvement Effectively to your Research Application
6 July 2022, 13.30 - 14.45, online

Start Up Stories: Women's Health Technology
6 July 2022, 17.30 - 20.00, Engine Shed, Station Approach, Bristol BS1 6QH

An Immunological Lens For Cancer workshop
7 - 8 July 2022, Keynotes: Dr Jessica Strid (Imperial College London) and Prof Guido Kroemer (INSERM), Cancer Research UK Beatson Institute, Bearsden G61 1BD

SEE ALL EVENTS ON THE CANCER RESEARCH NETWORK WEBSITE

NEWS

New Network Clinical co-Lead

The Bristol Cancer Research Network is delighted to announce that Dr Helen Winter, Consultant Medical Oncologist at the Bristol Cancer Institute, University Hospitals Bristol and Weston NHS Foundation Trust; Honorary Senior Research Fellow, School of Cellular and Molecular Medicine, University of Bristol; and Clinical Director of the Somerset, Wiltshire, Avon and Gloucestershire (SWAG) Cancer Alliance, has taken on the role of Network Clinical co-Lead. Welcome, Helen!

Helen has a longstanding interest in the role and impact of companion animals in patients with advanced cancer and during their end of life care. She is developing an emerging research interest in the One Health approach to developing cancer research and has recently established a collaboration with Bristol Vet School. She has been committed to increasing access for clinical trials and novel approaches to improving outcomes for patients with cancer.

Thanks are extended to Dr Axel Walther for leading for over 8 years and steering the Network through a biomedical review, producing our research brochure, and instigating the MiniMD programme, which allows new PhD students and postdocs the opportunity to attend clinics to better understand the challenges facing cancer patients and health professionals which will feed into their own research.

Bristol Clinical Research Facility funding bid successful

Bristol Clinical Research Facility (CRF) is one of five new CRFs across the country to have been awarded funding by the National Institute for Health and Care Research (NIHR) in their latest round of funding. The bid was led by David Wynick, Director of Research of University Hospitals Bristol and Weston NHS Foundation Trust and North Bristol NHS Trust and was for £3.5 million. CRFs support the delivery of early translational and experimental medicine research, from first-in-human trials through to early safety and efficacy trials, and provide purpose-built facilities and expertise for their delivery. Starting from September 2022, the 5-year pump priming will be supported by commercial early phase trials income, thereby offering more cutting-edge research, driving forward innovation and helping to identify new treatments for patients.

The Bristol CRF will bring together early phase translational and experimental medicine research studies across Bristol under a single management and governance structure, covering research in a variety of areas that include cancer and immunity-based treatments, vaccine development and testing, cardiovascular medicine, neuroscience, and respiratory medicine.

New early detection projects

Cancer Research UK are collaborating with the Medical Research Council and the Engineering and Physical Sciences Research Council on an investment into new research projects taking on the challenge of cancer early detection and diagnosis. Four newly funded teams have been formed to develop cancer early detection approaches at a sandpit-style workshop held last year, with the aim of stimulating novel and innovative approaches to triaging primary care patients who may be at risk of receiving a cancer diagnosis.

The event united the cancer research community with researchers from outside biomedicine such as computational and data scientists, engineers, chemists and physicists. Over the course of the workshop, participants teamed up to develop pilot study proposals which they then pitched to receive funding for.

Each multidisciplinary team will receive up to £230,000 seed-funding to conduct feasibility work. They include:

Samplecam
Elena Cojocaru (Royal Marsden Hospital), **Sam Merriel** (University of Exeter & Honorary Research Fellow, Bristol Medical School: Population Health Sciences), Robert Kerrison (University of Surrey), Gerard Cummins (University of Birmingham), Heba Sailem (University of Oxford).
A multimodal electronic capsule for identification of visual and biological markers of early stage colorectal cancer.

Sens or pass
Paolo Bertoncello (Swansea University), Nicholas Turner (De Montfort University), **Sam Merriel** (University of Exeter & Honorary Research Fellow, Bristol Medical School: Population Health Sciences), **Paul Yousefi** (Research Fellow, Bristol Medical School: Population Health Sciences), **Zahraa Abdallah** (Lecturer, Department of Engineering Mathematics, University of Bristol), Stephen Mcgough (Newcastle University), Russell Harris (University of Leeds).
A sensor on a toothbrush that can recognise markers of cancer in gastrointestinal and upper respiratory tracts in saliva.

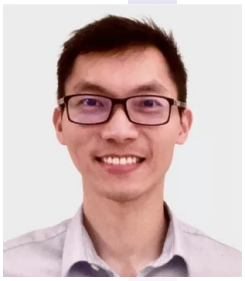
Epic dive
Maria Del Pilar Acedo Nuñez (University College London), Richard Luxton (University of the West of England), Joe Geraghty (Manchester Royal Infirmary (MRI), part of Manchester University NHS Foundation Trust), Robert Kerrison (University of Surrey), Amanda Winter (Newcastle Upon Tyne Hospitals NHS Foundation Trust), **Matthew Suderman** (Senior Lecturer in Epigenetic Epidemiology, Bristol Medical School: Population Health Sciences).
Early pancreatic cancer diagnosis in vivo evaluation. Aims to show that it is possible to capture and amplify ctDNA in circulating blood, thus increasing the chances of detecting ctDNA in a blood sample.

Maars
Julia Hippisley-Cox (University of Oxford), Jun Wang (Queen Mary, University of London), Konstantin Nikolic (University of West London), Tingting Zhu (University of Oxford), Robert Kerrison (University of Surrey), Joe Geraghty (Manchester Royal Infirmary (MRI), part of Manchester University NHS Foundation Trust).
Multimodal active adaptive risk stratification for gastrointestinal cancer.

Find out more about the funded teams

Bristol-Cardiff joint seed fund award

A joint event by the Universities of Bristol and Cardiff, held on 19 January 2022, comprised a series of short research presentations to foster closer collaborations between the two institutions and beyond. This third joint event, which received over 60 registrations, focussed on three areas: DNA repair, metastasis, and stem cells. Participants were eligible to apply for a £5,000 seed fund supported by the University Cancer Research Fund at Bristol and Cardiff's Development and Alumni Relations Department thanks to generous donations from graduates and members of the public.



We are delighted to announce that a project between Dr Siang Boon Koh (Lecturer in Cancer Biology, Cellular and Molecular Medicine, Bristol, left) and Andrea Brancale (Professor of Medicinal Chemistry, Pharmacy and Pharmaceutical Sciences, Cardiff, right) was successful. Entitled *Characterisation of RAS regulator interactome*, the collaboration will study the interactome of two clinically relevant RAS regulators (RASAL2 and RASGRF1) using a combined approach of proteomics and *in silico* modelling; this follows on from a recent discovery of a non-genetic deregulation of RAS signalling in primary human breast tissue. This effort will offer insights into the targetability of these proteins to disrupt chemoresistance.

Funding successes

Dr Hannah Sallis (Bristol Medical School and School of Psychological Science) was awarded £354,821 from **Cancer Research UK** for *Smoking and Vaping Transitions in Early Adulthood: investigating predictors with longitudinal data*, starting Feb '22 for two years.

The **Royal Society** awarded £19,715 to Dr Bethan Lloyd-Lewis (Vice Chancellor's Fellow, School of Cellular and Molecular Medicine [CMM]) a research grant for *Real time in vivo imaging of mammary epithelial cell fate decisions during pregnancy-induced tissue expansion and regression*. The scheme provides 'seed corn' funding for new projects of timeliness and promise. The project started in Feb '22 and will complete next year.

Repurposing inhibitors of epigenetics and autophagy for treatment of poor prognosis neuroblastoma has been supported by a £198,191 award from the **Children's Cancer and Leukaemia Group** to Prof Karim Malik (CMM), starting March '22 for two years.

Dr Siang Boon Koh (CMM) received £49,698 from the **Bristol Weston Hospitals Charity** to pursue *Predictive biomarkers of drug resistance and sensitivity in breast cancer patients*, starting May 2022 for three years.

Prof Eugenia Piddini (CMM) was awarded £1.68 million from **Wellcome** for *Ribosome mutant-induced Cell Competition: from mechanisms to identification of cancer vulnerabilities*, starting Sept '22 for 5 years.

A 5-year project starting April '22 led by Prof Marcus Munafò (Psychological Science) and funded by a £28,039 award from **Cancer Research UK** will look at *Targeting multiple levels of the smoking cessation system using novel scientific approaches*.

CRN West of England Research Awards

The winning nominees for the National Institute for Health and Care Research (NIHR) Clinical Research Network (CRN) West of England Research Awards were announced at the inaugural ceremony on 24 March 2022.

The Clinical Research Network (CRN) West of England, hosted at University Hospitals Bristol and Weston NHS Foundation Trust, facilitates research in NHS, Public Health and social care settings, supporting portfolio studies in 31 specialties in sites such as universities, schools, care homes, hospices, prisons and clinical settings.

Stephen McGlynn, Deputy Chief Operating Officer said: "A huge congratulations to our winners and short-listers alike. We really enjoyed having the opportunity to share and showcase some of the brilliant work that is happening across the West of England. We hope you all feel very proud of the contributions you have made and continue to make to research."

The full ceremony is available to watch on YouTube.

The winning nominees include:

CRSL of the Year

Helen Winter

The clinical research specialty lead (CRSL) of the year award went to Helen Winter, Medical Oncologist at the Bristol Cancer Institute, Clinical Director of the Somerset, Wiltshire, Avon and Gloucestershire (SWAG) Cancer Alliance, and one of our Network co-Leads.

Siblings and the genetics of disease

Genetic studies aim to find regions of the genome that associate with diseases or other outcomes. A new study has shown that for social traits these genetic effects are due to a mixture of direct effects (e.g. biological effects of DNA), and indirect effects (e.g. family or social environment). Whereas biological traits are mainly driven by direct effects.

An international group of 100 scientists studied 178,076 siblings to estimate the effects of genetics and environment on health and social outcomes. They found that the genetic factors on more social traits – like educational attainment, age of first child and depression – are strongly influenced by either the family or social environment. In contrast, the genetic influences on more biological traits – such as cholesterol and BMI – were found to be less socially influenced.

The findings suggest large-scale family datasets provide new opportunities to quantify direct effects of genetic variation on human traits and diseases. Looking at sociological questions and genetics together is a powerful tool for understanding why different health and social outcomes happen, providing better insight for potential interventions and treatments.

Howe L *et al*. (2022). Within-sibship GWAS improve estimates of direct genetic effects. *Nature Genetics*.

External engagements

Prof Anne Ridley (Cellular and Molecular Medicine) gave a seminar at University West of England entitled *Rho GTPases: signalling through time and space*.

Guillermo Legarda Herranz, a PhD student in swarm robotics based at IRIDIA, the Artificial Intelligence research laboratory of the Université Libre de Bruxelles, working alongside Drs Sabine Hauert and Simon Jones (both Engineering Mathematics), presented at the 22nd Institute of Electrical and Electronics Engineers (IEEE) International Conference on Autonomous Robot Systems and Competitions (ICARSC) held in Portugal, 29 - 30 April 2022. The talk was entitled *Decentralised Negotiation for Multi-Object Collective Transport with Robot Swarms*. Recent developments of robot swarms with richer capabilities for sensing and manipulation of the environment have opened the door to more complex applications of swarm robotics. They presented a method to control a swarm of robots to simultaneously transport multiple items that are too heavy or too large for a single robot to carry. We introduce a decentralised negotiation strategy based on inter-robot communication, which allows the robots to coordinate with subgroups of the swarm. We then use genetic programming to evolve behaviour tree controllers that generate the desired action of each robot, which is then fed to the negotiation strategy to produce the final output.

Excess weight almost doubles risk of womb cancer

The study from the University of Bristol is one of the first to find that for every five extra BMI units, a woman's risk of womb (endometrial) cancer is almost doubled (increase of 88%). This is higher than most previous studies have suggested and reflects lifelong weight status rather than a snapshot in time like most other studies. Five BMI units is the difference between the overweight category and the obese category, or of a 5'5 adult woman being two stones heavier.

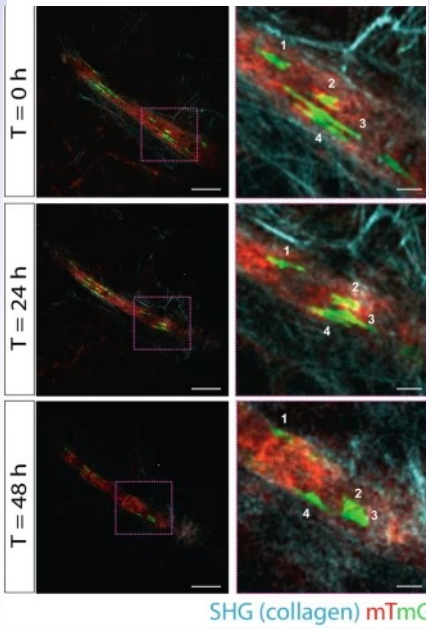
The team looked at genetic samples from around 120,000 women from Australia, Belgium, Germany, Poland, Sweden, the UK, and the USA of which around 13,000 had womb cancer. This large statistical analysis is one of the first studies of its kind to look at the effect of lifelong greater BMI on womb cancer risk.

They looked at markers of 14 traits which could link obesity and womb cancer. They uncovered two hormones - fasting insulin and testosterone – which increased the risk of being diagnosed with womb cancer. By pinpointing exactly how obesity increases the risk of cancer, such as through hormones, scientists in the future could use drugs to reduce or increase the level of these hormones in people already at a higher risk of cancer. For example, drugs like metformin used in diabetes treatment, can reduce the levels of hormones and research suggests this drug also affects cancer risk, though further study is ongoing.

Hazelwood E *et al*. (2022). Identifying molecular mediators of the relationship between body mass index and endometrial cancer risk: a Mendelian randomization analysis. *BMC Medicine.*

Fluorescence imaging of mammary gland development

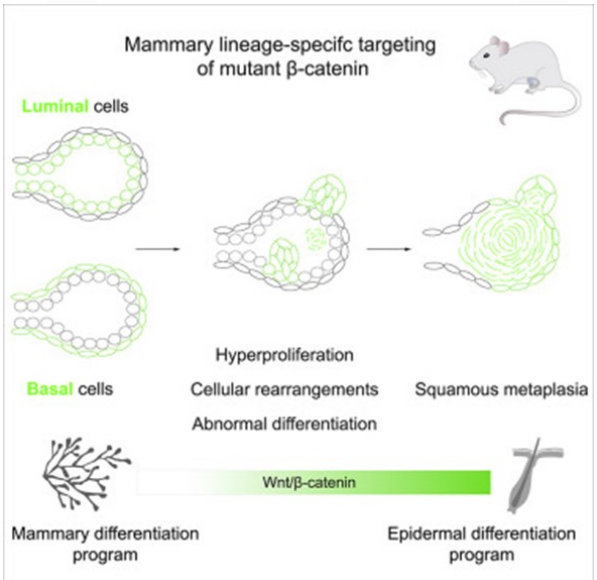
Multidimensional fluorescence imaging represents a powerful approach for studying the dynamic cellular processes underpinning the development, function, and maintenance of the mammary gland. Here, we describe key multidimensional imaging strategies that enable visualization of mammary branching morphogenesis and epithelial cell fate dynamics during postnatal and embryonic mammary gland development. These include 4-dimensional intravital microscopy and ex vivo imaging of embryonic mammary cultures, in addition to methods that facilitate 3-dimensional imaging of the ductal epithelium at single-cell resolution within its native stroma. Collectively, these approaches provide a window into mammary developmental dynamics, and the perturbations underlying tissue dysfunction and disease.



Carbaña C & Lloyd-Lewis B (2022). Multidimensional Fluorescence Imaging of Embryonic and Postnatal Mammary Gland Development. *Mammary Stem Cells*.

In vivo imaging of mammary epithelial cell dynamics

Real-time in vivo imaging provides an essential window into the spatiotemporal cellular events contributing to tissue development and pathology. By coupling longitudinal intravital imaging with genetic lineage tracing, here we capture the earliest cellular events arising in response to active Wnt/β-catenin signaling and the ensuing impact on the organization and differentiation of the mammary epithelium. This enables us to interrogate how Wnt/β-catenin regulates the dynamics of distinct subpopulations of mammary epithelial cells in vivo and in real time. We show that β-catenin stabilization, when targeted to either the mammary luminal or basal epithelial lineage, leads to cellular rearrangements that precipitate the formation of hyperplastic lesions that undergo squamous transdifferentiation. These results enhance our understanding of the earliest stages of hyperplastic lesion formation in vivo and reveal that, in mammary neoplastic development, β-catenin activation dictates a hair follicle/epidermal differentiation program independently of the targeted cell of origin.



Lloyd-Lewis B *et al*. (2022). *In vivo* imaging of mammary epithelial cell dynamics in response to lineage-biased Wnt/β-catenin activation. *Cell Reports*.

Accelerated biological ageing may cause bowel cancer

Epigenetic markers are changes to DNA which may alter the way in which our genes work and are known to vary as we age. DNA methylation, a type of epigenetic marker, is often used to measure age. DNA methylation patterns on the genome have been shown to relate closely with age and they can provide insights into 'biological ageing' – that is, how old our cells look compared to how old they are in years. Using Mendelian randomization, researchers mimicked a randomised trial evaluating the effectiveness of changes in epigenetic aging as a cancer prevention strategy.

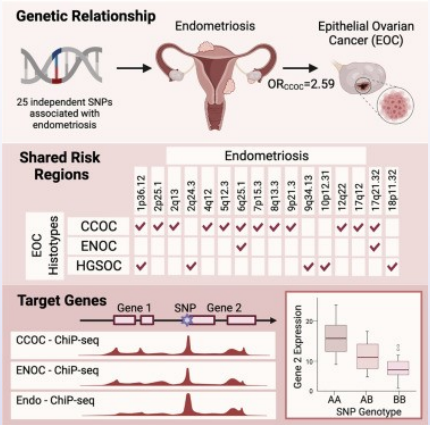
The team compared four established epigenetic clocks used to measure biological aging and their genetically predicted associations with a range of cancer types. Two were first-generation clocks which use patterns of DNA methylation strongly linked to chronological age. The others were second-generation clocks which use markers associated with increased risk of age-related diseases or death. They found limited evidence that accelerated epigenetic age is causally linked to breast, lung, ovarian or prostate cancer.

The most striking result was seen for bowel cancer, where the results measured by one of the second-generation clocks, called GrimAge, suggested a 12% increased risk of bowel cancer with every additional year of biological age (over chronological age). The results were corroborated by an association between biological age acceleration and parental history of bowel cancer.

Morales Bernstein F *et al.* (2022). Assessing the causal role of epigenetic clocks in the development of multiple cancers… *eLife*.

Relationship between endometriosis and ovarian cancer

Endometriosis is associated with increased risk of epithelial ovarian cancers (EOCs). Using data from large endometriosis and EOC genome-wide association meta-analyses, we estimate the genetic correlation and evaluate the causal relationship between genetic liability to endometriosis and EOC histotypes, and identify shared susceptibility loci. We estimate a significant genetic correlation (rg) between endometriosis and clear cell (rg = 0.71), endometrioid (rg = 0.48), and high-grade serous (rg = 0.19) ovarian cancer, associations supported by Mendelian randomization analyses. Bivariate meta-analysis identified 28 loci associated with both endometriosis and EOC, including 19 with evidence for a shared underlying association signal. Differences in the shared risk suggest different underlying pathways may contribute to the relationship between endometriosis and the different histotypes. Functional annotation using transcriptomic and epigenomic profiles of relevant tissues/cells highlights several target genes. This comprehensive analysis reveals profound genetic overlap between endometriosis and EOC histotypes with valuable genomic targets for understanding the biological mechanisms linking the diseases.



Ovarian Cancer Association Consortium, International Endometriosis Genetics Consortium (2022). A multi-level investigation of the genetic relationship between endometriosis and ovarian cancer histotypes. *Cell Reports Medicine*.

Mistletoe and breast cancer trial

A Cochrane review of mistletoe therapy concludes that there is some evidence that mistletoe extracts may offer benefits on measures of quality of life during chemotherapy for breast cancer, but these results need replication. The aim is to add to this evidence base by initially testing the feasibility of a UK pilot placebo-controlled, double-blind randomised controlled trial of mistletoe therapy in patients with breast cancer undergoing chemotherapy with or without radiotherapy.

This trial is the first of its kind in the UK. Currently, mistletoe therapy is mostly available

through private practice in the UK. Completion of this feasibility study will support applications for further funding for a fully powered randomised controlled trial which will measure effectiveness and cost-effectiveness of this herbal therapy.

Bryant S *et al*. (2022). A pilot study of the mistletoe and breast cancer (MAB) trial: a protocol for a randomised double-blind controlled trial. *Pilot and Feasibility Studies*.

Glycemic traits and colorectal cancer

Glycemic traits—such as hyperinsulinemia, hyperglycemia, and type 2 diabetes—have been associated with higher colorectal cancer risk in observational studies; however, causality of these associations is uncertain. The study used Mendelian randomization (MR) to estimate the causal effects of fasting insulin, 2-hour glucose, fasting glucose, glycated hemoglobin (HbA1c), and type 2 diabetes with colorectal cancer.

Genome-wide association study summary data were used to identify genetic variants associated with circulating levels of fasting insulin, 2-hour glucose, fasting glucose, HbA1c and type 2 diabetes. Using 2-sample MR, researchers examined these variants in relation to colorectal cancer risk.

In inverse-variance models, higher fasting insulin levels increased colorectal cancer risk. We found no evidence of any effect of 2-hour glucose or fasting glucose concentrations on colorectal cancer risk. Genetic liability to type 2 diabetes and higher HbA1c levels increased colorectal cancer risk, although these findings may have been biased by pleiotropy. Higher HbA1c concentrations increased rectal cancer risk in men, but not in women.

Results support a causal effect of higher fasting insulin, but not glucose traits or type 2 diabetes, on increased colorectal cancer risk. This suggests that pharmacological or lifestyle interventions that lower circulating insulin levels may be beneficial in preventing colorectal tumorigenesis.

Murphy N *et al*. (2022). Associations Between Glycemic Traits and Colorectal Cancer: A Mendelian Randomization Analysis. *Journal of the National Cancer Institute*.

Automation in systematic reviews

Dr Pau Erola (Bristol Medical School: Population Health Sciences) was awarded £198,699 from the World Cancer Research Fund for this project which started in March ' 22. forms part of the funder's Global Cancer Update Programme which analyses how diet, nutrition and physical activity affect cancer risk and survival. The programme has built up the largest global cancer prevention database in the world, housed at Imperial College, London. It's the only authoritative scientific resource of its kind, trusted by oncology experts, researchers and health professionals worldwide, and evaluated by an independent panel of leading cancer experts.

World Cancer Research Fund International

The study, on the automation of systematic reviews of cancer risk and survival, will use machine learning and natural language processing (NLP) to automate the processes in the Continuous Update Project (CUP) that synthesises global research to produce high quality and up-to-date systematic reviews of diet, nutrition, and physical activity and cancer. CUP currently employs more than 7 researchers to provide at least two high quality and up-to-date systematic reviews per year, who have to manually select and extract around 20,000 articles per search. A postdoctoral researcher has been recruited to focus on applying machine learning and automation to the processes of article screening, assessing article against inclusion/exclusion criteria, data extraction and assessment of risk of bias.

Body size and risk of cancers

It is unclear if body weight in early life affects cancer risk independently of adult body weight. To investigate this question for 6 obesity-related cancers, we performed univariable and multivariable analyses using 1) Mendelian randomization (MR) analysis and 2) longitudinal analyses in prospective cohorts.

Both the MR and longitudinal analyses indicated that larger early life body size was associated with higher risk of endometrial and kidney cancer. These associations were attenuated after accounting for adult body size in both the MR and cohort analyses. Early life body mass index (BMI) was not consistently associated with the other investigated cancers.

The lack of clear independent risk associations suggests that early life BMI influences endometrial and kidney cancer risk mainly through pathways that are common with adult BMI.

Mariosa D *et al*. (2022). Body Size at Different Ages and Risk of 6 Cancers: A Mendelian Randomization and Prospective Cohort Study. *Journal of the National Cancer Institute.*

E-reporting of adverse events for cancer patients

Cancer is treated using multiple modalities (e.g. surgery, radiotherapy and systemic therapies) and is frequently associated with adverse events that affect treatment delivery and quality of life. Regular adverse event reporting could improve care and safety through timely detection and management. Information technology provides a feasible monitoring model, but applied research is needed. This research programme developed and evaluated an electronic system, called eRAPID, for cancer patients to remotely self-report adverse events.

eRAPID was successfully developed and introduced across the treatments and centres. The systemic randomised controlled trial found no statistically significant effect of eRAPID on the primary end point at 18 weeks. There was a significant effect at 6 weeks and 12 weeks. No between-arm differences were found for admissions or calls/visits to acute oncology or chemotherapy delivery. Health economic analyses over 18 weeks indicated no statistically significant difference between the cost of the eRAPID information technology system and the cost of usual care.

Velikova G *et al*. (2022). Electronic self-reporting of adverse events for patients undergoing cancer treatment: the eRAPID research programme including two RCTs. *Programme Grants for Applied Research*.

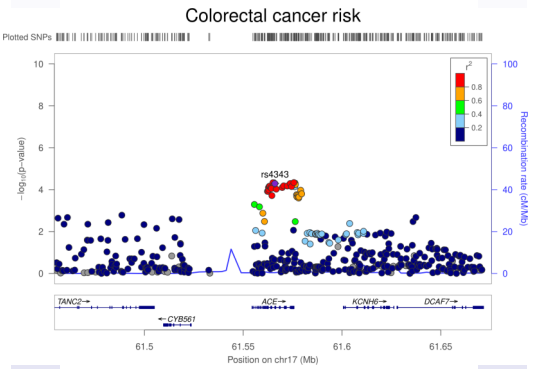
Antihypertensive drug targets and risk of common cancers

Angiotensin-converting enzyme (ACE) inhibitors, beta blockers, and thiazide diuretics are commonly prescribed antihypertensive medications. Some epidemiological studies have suggested that long-term use of these medications can increase cancer risk, though findings have been conflicting.

We used drug-target mendelian randomization to examine the association of genetically proxied inhibition of the drug targets of ACE inhibitors, beta blockers, and thiazide diuretics with risk of 4 of the most common adult cancers (breast, colorectal, lung, and prostate) in up to 289,612 cancer cases and 291,224 controls.

We found evidence that genetically proxied inhibition of the drug target for ACE inhibitors was associated with an increased risk of colorectal cancer.

There was little evidence that genetically proxied inhibition of the drug target for ACE inhibitors was associated with risk of the other cancers examined or evidence for an association of genetically proxied inhibition of drug targets for beta blockers and thiazide diuretics with risk of all 4 cancers examined.



Yarmolinksy J *et al*. (2022). Genetically proxied therapeutic inhibition of antihypertensive drug targets and risk of common cancers: A mendelian randomization analysis. *PLOS Medicine*.

Image: Regional Manhattan plot of associations of SNPs with colorectal cancer risk ±300 kb from the SNP used to proxy serum ACE concentrations (rs4343) in the ACE region.

ELIZABETH BLACKWELL FUNDING

Nurturing Research. Improving Health.

Research for Equality, Diversity & Inclusion in Health and Biomedicine

This includes projects that focus on the way in which research is conducted (careers and research community) as well in projects that focus on the equality, diversity and inclusion in the delivery of research or the analysis of data. Research projects should demonstrate clear pathways to deliverables and next steps, such as impact on practice or submission of applications for external research funding.

Closing date: 25 July 2022

Elizabeth Blackwell Institute support scheme for academic training 2022

This scheme is designed to provide support for attending or accessing externally-provided training courses, including training in research methods and techniques, in all areas of health research.

Closing date: 31 August 2022

Elizabeth Blackwell Institute academic bridging funding scheme 2022

We have funding available to provide bridging funding for salaries of academic staff in health-related research in all Faculties at the University of Bristol.

Closing date: 31 August 2022

Workshop support

We offer support for workshops in health and biomedical research to facilitate new interdisciplinary connections. Applications reviewed all year.

Returning Carers Scheme

The University of Bristol is running a Returning Carers Scheme (RCS) to support academic staff across all faculties in re-establishing their independent research careers. Applications reviewed all year.

FUNDING OPPORTUNITIES

Research Professional provides access to an extensive database of funding opportunities. You can set up individualised funding alerts based on keywords or areas of research . UoB staff and students have **FREE** online access to the database.

You can search for funding information by discipline, sponsor, database searches, by recent calls or by upcoming deadlines. Find out more about **Research Professional** on the RED website. Note that some calls may have an internal process; do always remember to check the major bids webpage here to see if there is an internal process.

The following listings represent a *brief selection* of available funding for the Cancer Research community. **Full listings of opportunities** are sent out via School Research Directors, and **are available on the Research Development website**.

Cancer Research UK

Prospective sample collection awards

Closing date: 21 July 2022 Award amount: unspecified

These provide support for the collection of samples within a clinical trial either where specific research questions cannot yet be generated, or where specific questions have been generated but the funding to carry out that work has been or will be obtained elsewhere. This may include sample collections within rare cancers or rare subtypes, those with associated distinct longitudinal data or collections in cancers of unmet need.

Medical Research Foundation

Child and adolescent cancer pain

Closing date: 27 July 2022 Award amount: £30,000

This supports projects to increase understanding of the mechanisms underpinning cancer pain and improving diagnosis, treatment and management.

National Cancer Institute, USA

Research opportunities in established cancer epidemiology cohort studies (U01 clinical trial not allowed)

Closing date: 29 July 2022 Award amount: unspecified

This supports research in established cancer epidemiology cohort studies, defined as studies that have achieved their initial planned recruitment goal. Applications must include hypothesis-based research using data from an established cohort study and are expected to include support for cohort maintenance, continued follow-up, and sharing of the existing resources in addition to addressing research questions across the cancer control continuum.

Horizon Europe: Missions
HORIZON-MISS-2022-CANCER-01 – implementation of the mission on cancer

Closing date: 7 September 2022 Award amount: €10 million

This supports proposals that assist with the implementation of the mission on cancer. The call includes the following topics:

- HORIZON-MISS-2022-CANCER-01-01 – improving and upscaling primary prevention of cancer through implementation research
- HORIZON-MISS-2022-CANCER-01-02 – strengthening research capacities of comprehensive cancer infrastructures
- HORIZON-MISS-2022-CANCER-01-03 – pragmatic clinical trials to optimise treatments for patients with refractory cancers
- HORIZON-MISS-2022-CANCER-01-04 – towards the creation of a European cancer patient digital centre
- HORIZON-MISS-2022-CANCER-01-05 – establishing of national cancer mission hubs and creation of network to support the mission on cancer

Cancer Research UK
Early detection and diagnosis primer award

Closing date: 8 September 2022 Award amount: £100,000

This enables researchers at all stages to develop early, novel and outside-the-box ideas and collaborations to build and make progress in the early detection field. The award provides seed funding to develop new relationships, ideas and lines of research, and the generation of pilot data, and encourages scientists at all career stages to engage with the early detection of cancer field.

Cancer Research UK
Prevention and population research programme awards

Closing date: 22 September 2022 Award amount: unspecified

These provide long-term support for broad, multidisciplinary research with transformative potential in prevention and population research.

Nuovo-Soldati Foundation for Cancer Research
Fellowships

Closing date: 22 September 2022 Award amount: unspecified

These support young doctors in pursuing a research project on cancer cells with the main aim being to support innovative techniques or novel therapeutic approaches. Medically qualified candidates or medical students at the end of their training who work in specialities such as pathology, oncology, radiotherapy or surgery, may apply. Preference is given to projects that take place outside the fellows country of origin or within centres of excellence with their home country.

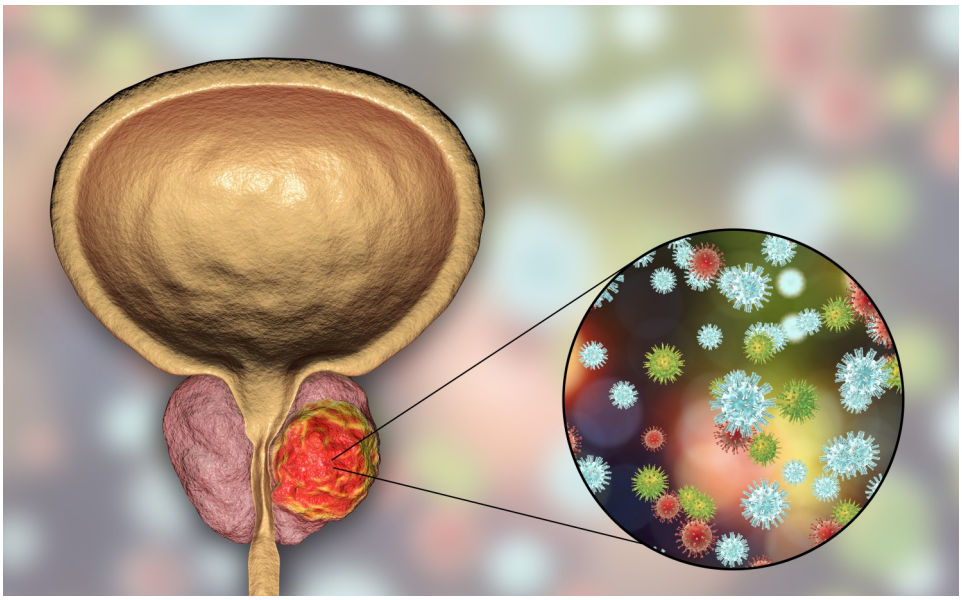
FEATURED PUBLICATION

Functional and quality of life outcomes of localised prostate cancer treatments (Prostate Testing for Cancer and Treatment [ProtecT] study)

Lane JA, Donovan JL, Young GJ, Davis M, Walsh EI, Avery KNL, Blazeby JM, Mason MD, Martin RM, Peters TJ *et al*. (2022). *British Journal of Urology International*.

Objective: To investigate the functional and quality of life (QoL) outcomes of treatments for localised prostate cancer and inform treatment decision-making.

Patients and Methods: Men aged 50–69 years diagnosed with localised prostate cancer by prostate-specific antigen testing and biopsies at nine UK centres in the Prostate Testing for Cancer and Treatment (ProtecT) trial were randomised to, or chose one of, three treatments. Of 2565 participants, 1135 men received active monitoring (AM), 750 a radical prostatectomy (RP), 603 external-beam radiotherapy (EBRT) with concurrent androgen-deprivation therapy (ADT) and 77 low-dose-rate brachytherapy (BT, not a randomised treatment). Patient-reported outcome measures (PROMs) completed annually for 6 years were analysed by initial treatment and censored for subsequent treatments. Mixed effects models were adjusted for baseline characteristics using propensity scores.



Results: Treatment-received analyses revealed different impacts of treatments over 6 years. Men remaining on AM experienced gradual declines in sexual and urinary function with age (e.g., increases in erectile dysfunction from 35% of men at baseline to 53% at 6 years and nocturia similarly from 20% to 38%). Radical treatment impacts were immediate and continued over 6 years. After RP, 95% of men reported erectile dysfunction persisting for 85% at 6 years, and after EBRT this was reported by 69% and 74%, respectively ($P < 0.001$ compared with AM). After RP, 36% of men reported urinary leakage requiring at least 1 pad/day, persisting for 20% at 6 years, compared with no change in men receiving EBRT or AM ($P < 0.001$). Worse bowel function and bother (e.g., bloody stools 6% at 6 years and faecal incontinence 10%) was experienced by men after EBRT than after RP or AM ($P < 0.001$) with lesser effects after BT. No treatment affected mental or physical QoL.

Conclusion: Treatment decision-making for localised prostate cancer can be informed by these 6-year functional and QoL outcomes.

Cancer Network

CONTACTS

The Cancer Research Network is led by a Steering Group:

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- Richard Martin, *Professor of Clinical Epidemiology*

Steering Group members:

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The content of this newsletter is not the intellectual property of the Network, but rather an amalgamation of information obtained through a variety of sources including our community members, research groups and University of Bristol school bulletins and press releases. Affiliations are stated wherever possible, however please note that omissions do happen and we apologise in advance for any you may come across. All information is merely for educational and informational purposes. We cannot offer medical advice and any queries regarding treatment for a specific medical condition or participation in a clinical trial should be addressed to your healthcare provider. While the information herein has been verified to the best of our abilities, we cannot guarantee that there are no mistakes or errors.

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