

ANNUAL REPORT

2022/23



The Centre for Trials Research (CTR) at Cardiff University is a UK Clinical Research Collaboration (UKCRC) registered clinical trials unit.



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Glossary

AML	Acute Myeloid Leukaemia	HTA	Health Technology Assessment
CARE	The Centre for Adult Social Care Research	NIHR	National Institute for Health Research
CI	Chief Investigator	PHR	Public Health Research
CRest	Cancer Research Strategy for Wales	PI&E	Public Involvement and Engagement
CTR	Centre for Trials Research	PPI	Patient and public involvement
CTU	Clinical trials unit	RCT	Randomised Controlled Trial
CU	Cardiff University	RfPPB	Research for Patient and Public Benefit Wales
EDI	Equality Diversity and Inclusion	UCL	University College London
HDR UK	Health Data Research UK		



Executive summary

Our report outlines key successes in generating the research evidence required to change practice and ultimately benefit the public.

Trials epitomise team-based science with multiple stakeholders, including patients and the public, needed to provide robust answers to the questions of most importance to service users. We show how we develop the research capacity to deliver such studies and this is reflected in new appointments to key leadership roles within our Centre and the large number of recent promotions. Similarly, the studies we feature reflect talent drawn from across Wales and beyond, as well as across all our Divisional and methodological teams. We describe initiatives that will continue to drive new collaborations and new studies. These include our partnership with the new adult social care research centre (CARE), participation in the newly re-funded HDR UK institute, the development of the Cancer Research Strategy for Wales (CRest), produced in partnership with Health and Care Research Wales and the Welsh cancer research community, and our new Treialon Cymru programme designed to increase connections between Wales-based health and care practitioners with the Centre.

We highlight the range of methods, populations and interventions across our four divisions. These span the internationally leading work of the AML team in the Cancer division, the PANORAMIC adaptive trial evaluating therapies for COVID-19 in the Infection, Inflammation and Immunity Division, the E-PaTS cluster Randomised Controlled Trial (RCT) of a supportive intervention for families of young children with learning disabilities in the Brain Health and Mental Wellbeing Division and the SONO-BREECH trial of handheld ultrasound for determining fetal presentation in late pregnancy in the Population Health and Social Care Division.

Our report includes a summary of the work of the Research Design and Conduct Service (RDCS) over the last three years. With the service no longer funded, research and development opportunities for Wales-based health and care practitioners will continue in different ways including through the Treialon Cymru programme.



The RDCS has supported 176 health and care practitioners to progress their own ideas through early stages of development through to submission and in 12 cases awarded funding. The less easily measured learning that has occurred along the way is as important and bodes well for the next generation of practitioner researchers from Wales.

As we move further beyond the pandemic phase, it is wonderful to see the extent and variety of high-quality research being undertaken in the Centre as reflected in the 112 peer reviewed publications last year. What is equally encouraging is the high number of new studies awarded to the Centre, with 46 new projects. This increased number of studies from last year represents £33m of new funding. While such figures should be expected to peak and trough across the years, it is especially pleasing to see the number of such studies being led by Welsh Chief Investigators (CIs) – at 28, nearly double that from last year. We have also seen a huge increase in the number of opportunities created for members of the public in working with us on studies. This undoubtedly reflects the collective impact of several initiatives driven from within the Centre itself through the Public Involvement and Engagement Hub and engagement projects such as Talking Trials, as well as networking with both School of Medicine and Health and Care Research Wales colleagues.

Thank you for taking the time to read about our work. We aim for our report to be of interest to as wide a group of stakeholders as possible. Please do contact us if you have any thoughts, questions or suggestions. We would like to acknowledge our funders, research partners, staff and collaborating investigators. Finally, we would like to thank all the patients, families and members of the public who have so generously given their time to take part in our studies. Our work is only possible with the collective contribution of all these people, and we thank you all.

Dr Rachel McNamara

Director, Brain Health and Mental Wellbeing Division

Professor Mike Robling

Director, Population Health and Social Care Division

Dr David Gillespie

Director, Infection, Inflammation and Immunity Division

Professor Richard Adams

Director, Cancer Division

Foreword

Mission and strategic aims

The Centre for Trials Research is a UKCRC registered clinical trials unit based in Cardiff University, Wales. The Centre is dedicated to tackling the big health and social concerns of our time. We work with investigators to produce research evidence for policy leaders, service commissioners and practitioners about treatments and services that may improve the health and wellbeing of the public.

Everyone, regardless of who they are, where they live, or what they do deserves the best health and care, and we will provide the evidence to make that happen.

Key programme partners and beneficiaries

The Centre receives infrastructure funding from Welsh Government through Health and Care Research Wales and Cancer Research UK, as well as from Cardiff University. This funding allows us to invest in core activities to support the design and oversight of high-quality studies and to win external funding to allow their conduct, analyses and publication. Most of our work involves external investigators undertaking applied research in health or social care (or both). The range of potential beneficiaries is broad, reflecting the diversity of studies and investigators we work in partnership with. These will include patients, social care service users, members of the public, health and social care service providers, health and social care policy makers. We also develop and utilise innovative methods and share these across the research community. These beneficiaries will be in Wales, the rest of the UK and in other countries outside of the UK. The Centre has a long-established record in promoting inclusive research and in producing evidence to support the care of traditionally underserved groups.

Who's who at The Centre

Our Director is Professor Kerry Hood. She is supported by a Directorial team including Dr Rachel McNamara (Brain Health and Mental Wellbeing Division), Professor Richard Adams (Cancer Division), Dr David Gillespie (Infection, Inflammation and Immunity Division), Professor Mike Robling (Population Health and Social Care Division) and Dr Rebecca Playle (Statistics).

How we work

Our researchers and professional staff work across our four divisions and within cross-cutting teams (including Statistics, Information Services and Technology Solutions, Quality Assurance and Regulatory Affairs, and Professional Services). Our current research portfolio includes evaluations of drugs and complex health and social care interventions, studies of mechanisms of disease and treatments, cohort studies and trials informing health and social care policy and practice. Activities embedded across these areas of work are public involvement and engagement, commercial/industry engagement and collaboration, NHS and social care professional engagement and collaboration, engagement with Welsh Government funded research infrastructure and communications, publicity and knowledge transfer.

Across everything we do we work to a clear set of values and principles.

Centre for Trials Research Values

1

Making a difference

Improving health, wellbeing and sustainability of society

2

Building trust and confidence

Growing together as partners

3

Aspiring and inspiring

Helping everyone to be their best and to do their best

4

Respecting individuality

Recognising different needs and aspirations of every individual in society

5

Innovating and researching

Empowered to be creative and questioning in everything we do

6

Leading and collaborating

Developing true partnerships (nobody wins unless everybody wins)

7

Protecting integrity and quality

Designing, delivering and publishing high impact research through academic and professional excellence

8

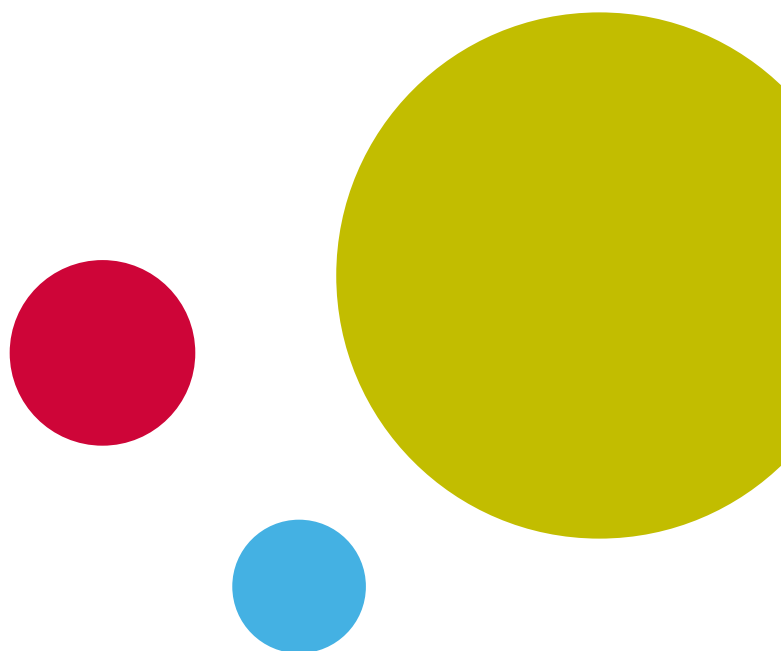
Recognising

Celebrating success, openness and transparency

Our work plan

We place continued emphasis on the development of working practices and expert staff to ensure we meet high standards for research across our portfolio. We design new studies and win the funding to make them happen in collaboration with researchers from other organisations across Wales and beyond. All our funded studies are conducted with high quality standards that produce outputs that will make a difference to the public and we strive to develop new ways to answer important clinical questions and sustain a dynamic and professional workforce.

Alongside this we support staff in the NHS and social care in Wales to develop their own research to address the important questions in the care of patients and the public. Here we showcase our work over the last year across all our divisions within the Centre for Trials Research. As this was the final year of the Research Design and Conduct Service we take a slightly longer look at what it has achieved over the last three years.



Centre for Trials Research Directors



Professor Kerry Hood,
Director Centre for Trials
Research



Professor Mike
Robling, Director
Population Health
and Social Care
Division



Dr Rachel McNamara,
Director Brain Health
and Mental Wellbeing
Division



Professor Richard
Adams, Director
Cancer Division



Dr Rebecca Playle,
Interim Director
Statistics



Dr David Gillespie,
Director Infection,
Inflammation and
Immunity Division

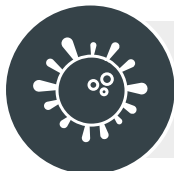
Centre for Trials Research Divisions



Brain Health and Mental Wellbeing



Cancer



Infection, Inflammation and Immunity



Population Health and Social Care



Centre for
Trials Research
Canolfan
Ymchwil Treialon



Research Design
& Conduct Service
South East Wales
Gwasanaeth Cynllun
a Chynnal Ymchwil
De-ddwyrain Cymru

Finding a Study Design That Fits Your Research Question

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Work packages







Health and Care Research Wales support three of our divisions whilst Cancer Research UK support the Cancer Division; both funders provide core funding to teams that work across all divisions. To report to Health and Care Research Wales we organise our work across six work packages (WP) in the following way.

<p>WORK PACKAGE 1: Managing our work</p>	<p>WORK PACKAGE 2: Working with other groups</p>
<p>WORK PACKAGE 3: Developing new studies</p>	<p>WORK PACKAGE 4: Overseeing funded studies</p>
<p>WORK PACKAGE 5: Ensuring methodological and professional development</p>	<p>WORK PACKAGE 6: RDCS and NHS</p>

Throughout this report, these graphics identify and introduce you to each section:

Cross-cutting themes

At the start of each work package throughout the report, you will see icons that represent our six cross-cutting themes below. This is to identify the ways in which our work has wider impact across the NHS, industry, social care, within Welsh Government and for the public. We hope you will find this a simple and easy way to navigate this report.

					
Public involvement and engagement	Social care	NHS engagement and collaboration	Commercial / industry engagement and collaboration	Engagement with Welsh Government funded research infrastructure	Communications, publicity and knowledge transfer

Core Metrics

Reporting period: 2022/2023

**Health and Care
Research Wales
Infrastructure
award to
the group**

Direct funding
awarded

£823,454



Jobs created
through direct
funding



Grants won during reporting period

Grants won	Led by group	Group collaborating
Number	17	33
Value	£16,129,103	£16,921,618
Funding to Wales	£8,219,473	£4,065,019
Funding to group	£7,860,959	£3,610,390
Additional jobs created for Wales	100.45	45.55
Additional jobs created for group	98.44	42.24



Number of publications



Number of public
engagement events



Number of public
involvement opportunities

Clinical Trials Unit metrics



46

Number of
studies awarded



28

Number of studies
led by Welsh Chief
Investigators



3,929

Total number
of participants
recruited



20.01

% participants
from Wales



WORK PACKAGE 1

Managing our work

Recruiting and supporting staff
and developing working practices
to make sure we meet high
standards for research



Our staff are at the heart of who we are and what we do. With 180 members in the CTR team, we value each individual and the unique skills and talents that each person brings to our work. We acknowledge the importance of a team structure that is supportive, optimising personal development and collective delivery, which are highlighted in our values.

During this year we have seen changes in our leadership team with Professor Monica Busse moving to be the inaugural Director of Faculty for Health and Care Research Wales and Professor Adrian Mander moving to work for GSK, replaced by Dr Rachel McNamara and Dr Rebecca Playle. We retain a strong working relationship with both Monica and Adrian in their new roles. Professor Kerry Hood decided to focus on Centre leadership and Dr David Gillespie took over the role of Director of the Infection, Inflammation and Immunity Division. Our Head of Quality Assurance and Regulatory Affairs, Claire Johnson, has moved to the Liverpool Clinical Trials Centre and been replaced by Kelly Gee. Since Claire also chaired our Equality, Diversity and Inclusion (EDI) committee, we appointed Martina Svobodova to provide leadership on EDI across the Centre supported by Rhys Denton, who focuses on embedding EDI within our business systems and processes.

This year we have seen a number of promotions in our team with

- James White promoted to Professor
- David Gillespie and Emma Thomas-Jones promoted to Principal Research Fellow
- Philip Pallmann and Victoria Shepherd promoted to Senior Research Fellow
- Joanne Euden, Nigel Kirby, Claire Nollett and Liz Randell promoted to Research Fellow

As part of building our international profile, Dr Claire Nollett went on sabbatical in Namibia working with our University of Namibia partners supporting the establishment of a trials unit for clinical research.

We have continued to be flexible in our working approaches, adapting and developing from what we have learnt during the COVID-19 enforced changes over recent years, which has allowed

us to increase our inclusive approach, with staff members from outside of the Cardiff region. The recent centre Advance HE Culture Survey evidenced strong engagement from staff within the CTR. With a response rate of 62%, and an excellent representation from academic and professional services staff, the results demonstrate that we can improve our working environment through considered and consistent action. 79% of CTR staff agreed that their contributions are valued by the Centre, 89% of staff agreed their line manager supports their career development and 86% agreed that the Centre leadership actively supports gender equality.

Adapting to the future we have developed a plan to streamline our database usage moving away from the MACRO IV database, which will no longer be supported by the manufacturer in future. We will expand our use of the RedCAP open-source database system, which we introduced last year, and feel this will maximise our ability to use the skills of our information systems team. We are working in partnership with CTUs in Bristol, Exeter and Swansea on how we can share knowledge and expertise in this system.

It is inspiring to look back at some of the things that have happened over the last year as we often forget to reflect and acknowledge the great work that is being done. Often it takes an outside voice looking in to highlight these achievements. As part of our work reaching out to others, we offer opportunities for undergraduates and masters students in the university to work with us over the summer period, completing intercalated research or simply work experience. One student kindly wrote a blog after her one-week work experience attachment as part of the “In2ScienceUK” initiative. She was surprised by the diversity of roles and jobs available in the CTR and was inspired to look for a future career engaged and involved in research and potentially in the CTR itself.

WORK PACKAGE 2

Working with other groups

Working in collaboration with researchers from other organisations across Wales and beyond



We will only be successful if we are effective in reaching out to key stakeholders and then working in partnership with them. Only by doing so can we develop research that will benefit the people of Wales and the broader international community. Our second work package focuses on the connections we make with networks and organisations in bringing forward new research.

In this year's report, we focus first on connections for one of our methodological streams and one of our subject matter themes and, second, our approaches toward involvement and partnership working.

Supporting administrative data research

Our Centre has considerable expertise in using administrative data in the design and conduct of trials and other well-designed studies. In the last 12 months we completed the COMORANT-UK study led by Dr Fiona Lugg-Widger (with Professor Matt Sydes, UCL, and Dr Marion Mafham, Oxford University), which identified research priorities in routine data use (funded by the National Institute for Health and Care Research (NIHR) Trials Methodology Research Partnership (TMRP)). This led directly to a second study (PRIMORANT, funded by HDR UK) and led by Professor Paula Williamson, Liverpool University, Professor Amanda Farrin, Leeds University and Dr Fiona Lugg-Widger, Centre for Trials Research. PRIMORANT developed modular training for promoting public trust when using administrative data in trials.

In the last year, the Centre for Trials Research became part of HDR UK, the national institute for health data science. HDR UK comprises over 1,500 researchers across 39 organisations and secured £72.3M for its new 5-year programme starting in April 2023. Our Centre's role is led by Professor Mike Robling in a work programme headed by Dr Marion Mafham and Professor Matt Sydes on 'Useable Data: Transforming data for trials'. This infrastructure and research funding (£3.1M) will advance methods for the use of administrative data in trials. The team will develop a route map for researchers designing, accessing, analysing and sharing healthcare systems data, supported by training and other resources such as case studies. The Cardiff team will lead on developing the range of training resources to support the work programme. Cardiff also joins the HDR UK Wales Consortium led by Professor Sinead Brophy in Swansea University.





Supporting adult social care research in Wales

Another major development in research infrastructure in Wales has been the funding of a new research centre for adult social care by Health and Care Research Wales. The new CARE Centre is under the interim leadership of Professor Jonathan Scourfield based in the CASCADE Centre at Cardiff University's School of Social Sciences. The Centre for Trials Research is the key methods partner in the new Centre and continues our successful partnership with CASCADE which has its primary focus on children's social care. Professor Scourfield and the new Centre's leadership team, including Professor Mike Robling, will oversee the set-up of the Centre including the appointment of a new Director, to be based in the School of Social Sciences.

A large number of investigators and collaborators drawn from across Cardiff University have begun sharing ideas and forming structures to catalyse ambitious grant development work. Key CTR-based investigators include Dr Rachel McNamara and Dr Victoria Shepherd who each hold impressive track records in research with adult social care populations and settings. Two new researchers appointed under the CARE Centre's initial 5-year programme will also be based in CTR.

Partnership working

In other parts of the report, we describe our new initiatives for working with research partners across Wales. Our 'Working with the Centre for Trials Research, Cardiff University - Collaborators Guide' is available on our website for investigators considering or currently collaborating with the CTR. It describes the main responsibilities assumed by both Centre staff and Chief Investigators, the methodological teams working within the Centre and key points of contact. This helps to establish expectations for collaborators and for our own staff about working in collaboration on new studies.

This year's launch of CReSt, the development of which was supported by members of the CTR team, has culminated in closer working relationships across the Cancer Research community in Wales. This has led to stronger working relationships with external groups with a cancer research interest, especially through the strategy's Cancer Clinical Trials theme. These relationships have included the Wales Cancer Research Centre, Wales Cancer Network, Wales Cancer Partnership, Wales Cancer Industries Forum and Welsh Health Board and Trust Research and Development teams, amongst others.



WORK PACKAGE 3

Developing new studies

Designing new studies and winning
the funding to make them happen



We are delighted this year to continue our collaborations with some of our longer-term partners but also to have new investigators on board with whom we have been successful in recent funding applications. Generally, this has meant a return to our more usual range of research after the dominance of COVID-19 research over the past few years. Notably many of our new projects include cross-division collaborations.



Brain Health and Mental Wellbeing Division

E-PATs

A Cluster Randomised Controlled Trial of Early Positive Approaches to Support for families of young children with intellectual disability.

Chief Investigator: Dr Nick Gore, University of Kent

Funder: NIHR Public Health Research (PHR) Programme

We want to test if a programme called Early Positive Approaches to Support (E-PATs) improves wellbeing for parents who have a child (18 months to 5 years) with Intellectual Disability (ID). We also want to test if E-PATs is good value for money.

Children with ID, often referred to as a learning disability in the UK, find learning and developing everyday skills hard. They can also have more psychological problems than other children. Problems for parents and children with ID are linked, and parents may need support to look after themselves and help their child. E-PATs is a group programme developed by parents and professionals. It helps parents to support their own wellbeing and support their child with ID.



This research project follows on from an earlier study run by the same team, where we showed that this approach is feasible and acceptable to families. We will recruit families across England, Wales, Scotland and Northern Ireland, with young children who have ID. Families will be randomised to one of two groups, an intervention group or a usual practice group. A group of parents have helped plan this research and will work with us to identify the best ways to engage families.



Cancer Division

SCC-After

Adjuvant radiotherapy in patients with high-risk primary cutaneous Squamous Cell Carcinoma AFTER surgery (SCC-AFTER): an open label, multicentre, two-arm phase III randomised trial.

Chief Investigator: Dr Agata Rembielak, The Christie NHS Foundation Trust

Funder: NIHR Health Technology Assessment (HTA) Programme

This phase III RCT will explore the challenges of optimising treatment for high risk locally advanced squamous cell carcinomas of the skin. There is a lack of high-level evidence to indicate whether, after surgical removal of the cancer, the addition of radiotherapy will reduce the risk of local and regional recurrence and to what extent any additional short- and long-term effects of the radiotherapy might have on an individual's quality of life. Within the study we have identified that there are a significant group of patients who are frailer and have cognitive difficulties, including early dementia.

It was agreed that these patients should not be excluded from the study but that their needs might be different from many other patients. We are fortunate in the CTR to have developed strong cross-division working and also to have expertise in both inclusivity and the challenges of consenting patients with cognitive impairment. Led by Victoria Shepherd, we brought together a group of carers of individuals with dementia to develop a "study within a trial" which will explore the specific requirements to support the entry of these patients to the trial and to evaluate the important outcomes for this group of individuals and their carers.



PICCOS

Pressurised IntraPeritoneal Aerosolised Chemotherapy (PIPAC) in the management of cancers of the colon, ovary and stomach: a randomised controlled phase II trial of efficacy in peritoneal metastases.

Chief Investigators: Professor Jared Torkington, Cardiff and Vale University Health Board, and Ms Sadie Jones, Cardiff University

Funder: NIHR Efficacy and Mechanism Evaluation (EME)

The PICCOS study has seen us working with a wide range of cancer specialists in ovarian, gastric and colorectal cancer, from surgeons in all three areas, through to specialist oncologists, radiologists and pre-clinical scientists from across the UK. This NIHR-funded study will efficiently deliver three trials in one, focusing on patients with cancer that has spread to the lining of the abdomen (the peritoneum), which carries a very poor prognosis in these three cancer types. In the trial we will explore the addition of aerosolised chemotherapy directly applied within the abdomen to maximise the chemotherapy delivered directly to the tumour whilst aiming to reduce the side effects and improve quality and quantity of life. This study is now in advanced stages of development and, despite its multi-disciplinary complexity, will hopefully open to recruitment in the second half of this year.



Infection, Inflammation and Immunity Division

PLACEMENT

Perineural Local Anaesthetic Catheter after Major Lower limb amputation Trial.

Chief Investigator: David Bosanquet, Aneurin Bevan University Health Board

Funder: NIHR HTA

Having a leg amputation is a life changing event. Around 5,000 leg amputations are performed in the UK every year. These are often very painful, both immediately following surgery and in the longer term. This pain may delay recovery times and may limit what people are able to do for the rest of their lives. Morphine is usually given to help relieve pain. However, morphine has major side effects, including sickness, confusion, and breathing problems. In the longer term, pain can be felt in the leg which is no longer there, called 'phantom pain'. This interferes with fitting and using an artificial leg.

The PLACEMENT trial will explore whether the use of a perineural catheter (PNC) with local anaesthetic infusion, placed at the time of major lower limb amputation (MLLA), impacts on pain and other patient-centred outcomes after surgery.

This is a randomised non-blinded pragmatic effectiveness study, which will recruit 650 adult patients undergoing Major Lower Limb Amputation for peripheral arterial disease and/or diabetes. They will be randomised to receive either the PNC with local anaesthetic infusion for the first 5 postoperative days, or not. Self-report pain will be measured twice daily for the first five days. We will also record longer-term outcomes, including pain, phantom limb pain and quality of life. The cost effectiveness and rate and timing of prosthetic fitting will also be evaluated.

PROTECT

Platform Randomised evaluation of clinical Outcomes using novel TECHNOLOGIES to optimise antimicrobial Therapy.

Chief Investigators: Professor Enitan Carrol, University of Liverpool, and Dr Philip Pallmann, Centre for Trials Research

Funder: NIHR HTA (Platform Trial Accelerator Award)

We have been awarded an accelerator award to develop a master protocol for a platform trial to assess the effectiveness, implementation, and efficiency of biomarker-guided antimicrobial stewardship interventions, to reduce unnecessary antibiotic usage by excluding severe bacterial infection in acutely unwell patients.

The overall aim of the trial will be to evaluate biomarker-guided interventions to optimise clinical decision-making within the first 72 hours of presentation, to improve speed of diagnosis, speed of starting or stopping antimicrobial therapy, and patient and carer experience for people with suspected bacterial infection. This will be achieved by: a) giving appropriate antibiotic therapy promptly, b) reducing inappropriate antibiotic use, c) reducing harm from adverse drug effects, and d) ensuring patients and carers are given the correct diagnosis.

The Acceleration Award will enable us to finalise the design and master protocol of the PROTECT platform trial, including a) building an inclusive research team, with PPI input into design and processes from the outset, b) defining clinical utility, and c) using implementation science to understand the policy and regulatory environment, peer pressure to implement the test, and structural and cultural characteristics of a healthcare organisation, internal communication networks and its capability and readiness for change.



Population Health and Social Care Division

OBS UK

Clinical and cost-effectiveness of a maternity quality improvement programme to reduce excess bleeding and need for transfusion after childbirth: the Obstetric Bleeding Study UK Stepped Wedge Cluster Randomised Trial.

Chief Investigators: Dr Sarah Bell, Cardiff and Vale University Health Board, and Professor Peter Collins, Cardiff University

Funder: NIHR Health and Social Care Delivery Research (HSDR)

Excess bleeding is the most common complication of childbirth. Every year about 50,000 women in the UK lose 1 litre (2 pints) of blood or more. Many women who need a blood transfusion may either be admitted to intensive care or develop post-traumatic stress disorder. A care bundle for managing bleeding after childbirth was developed in Wales, and rolled out as a quality improvement intervention called the 'Obstetric Bleeding Strategy' (OBS). Although outcomes were encouraging, we do not know whether the improved outcomes were due to the OBS intervention.

OBS UK will use routinely stored NHS maternity data on 189,000 women from 36 NHS maternity units over 30 months.

Maternity units will have an initial period during which standard care will be delivered and data collected. Units will then start to implement the care bundle using quality improvement methods over 9 months supported by training and feedback, followed by a further data collection period. Rates of blood transfusion before and after the care bundle is introduced will be compared, as will admission to intensive care, hysterectomy, and breastfeeding rates.

Embedded studies will look at the effect of the OBS intervention on the psychological wellbeing of women and birthing partners and how easily maternity units implement the care bundle, with special attention to the ethnicity and diversity in the maternity unit. To ensure effective and appropriate communication relating to ethnicity and diversity we will work with Equality Health. Equality are a community engagement agency working to improve health inequalities by increasing diversity in research.

The OBS Study is a collaboration with Oxford University, Liverpool University, Swansea University, Aberdeen University, Shrewsbury and Telford NHS Trust, Cardiff and Vale University Health Board and Equality Health.





SONO-BREECH

Diagnostic accuracy of handheld ultrasound at 36 weeks' gestation to determine fetal presentation.

Chief Investigators: Professor Christoph Lees, Imperial College London, and Dr Amar Bhide, St George's University Hospitals NHS Trust

Funder: NIHR HTA

Patient and Public Involvement was embedded throughout the development of this newly funded NIHR HTA trial (£2.2M). In working up this proposal, we engaged with a standing women's health community engagement group in West London. "The Bridge" includes 10 local core members with broad representation of reproductive experience, age, ethnicity, profession, and culture. We worked with The Bridge to run a focus group to consider this project at the outset. Eight people attended the focus group, six of whom have had babies, and one of whom had had a breech presentation in labour (ending in Caesarean). By chance, one attendee was a community midwife. The focus group attendees found the concept of midwives using a hand-held device and interpreting the results, as the project describes, to be good, as long as safety, training and effectiveness were addressed in the running of the project. There was a shared perspective that ultrasound scans present a desirable opportunity for women to see their baby. The idea that their midwife could facilitate this was appreciated in relation to strengthening the midwife-mother relationship and to save time.

The Solutions Trial

Solution Focused Brief Therapy (SFBT) in 10–17-year-olds presenting at police custody.

Chief Investigators: Professor Peter Langdon, University of Warwick, and Dr Sam Flynn, University of Warwick

Funder: Youth Endowment Fund

Children and young people who come into contact with the police often need help. Solution Focused Brief Therapy is a short-term therapy that helps people to change by focusing on building solutions rather than getting stuck thinking about problems. The aim of the Solutions trial is to evaluate the effectiveness of the therapy in reducing reoffending in children and young people who come in to contact with the police. The project was co-designed with the funder, the Youth Endowment Fund and Lancashire and South Cumbria NHS Trust, who are delivering the intervention. This project presents an exciting opportunity, having been the first project, fully coordinated by a trials unit, to be funded by the Youth Endowment Fund. Having opened at the start of 2023, the trial will recruit 448 children and young people.



WORK PACKAGE 4

Overseeing funded studies

Running studies to a high quality and producing outputs that will make a difference to the public





TRAK-MSK

A randomised controlled feasibility study of TRAK musculoskeletal digital self-management physiotherapy intervention for individuals with musculoskeletal pain.

Chief Investigator: Dr Kate Button, Cardiff University

Funder: Health and Care Research Wales Research for Patient and Public Benefit (RfPPB) Wales

In Wales approximately 1 in 3 people have a musculoskeletal (MSK) condition, with back pain and knee osteoarthritis being the most common. Treatments such as exercise and physiotherapy are recommended but have limited benefit in helping people manage their condition at home, as they often struggle to keep going with regular exercise. TRAK-MSK is a digital physiotherapy intervention for people with MSK pain, that helps people to manage their exercise and pain at home. Individuals can have up to five online consultations with a physiotherapist trained in self-management.

The combination of online consultations with a specially trained physiotherapist and access to the TRAK-MSK website will support individuals to practice and gain the skills to manage their condition themselves at home.

The aim of this study is to find out if it is feasible to deliver TRAK-MSK in this way, and if it is acceptable to patients. We are also interested in whether TRAK-MSK increases people's confidence to independently manage their pain and help them remain physically active. TRAK-MSK will be tested using a randomised study design across areas of Wales that represent a spread in wealth and population density. People who agree to take part will receive either the usual physiotherapy appointment (exercises and advice) or TRAK-MSK. A series of patient, public and clinician involvement workshops have informed the development of this project. Results are due to be published in May 2024.





Cancer Division

Our haematology portfolio has been particularly active in its outputs this year with oral presentations at global conferences of results from the international AML 18 and 19 phase III randomised controlled trials for patients with Acute Myeloid Leukaemia (AML), led by the CTR. We have presented at the American Society of Haematology (ASH) in December 2022 and will be presenting new data at the European Haematological Association 2023 annual conference in June.

AML19

A trial for younger adults with AML or high risk myelodysplastic syndrome (MDS).

Chief Investigators: Dr Mike Dennis, The Christie NHS Foundation Trust, and Professor Nigel Russell, Guy's and St Thomas' NHS Foundation Trust

Funder: Cancer Research UK

The National Cancer Research Institute (NCRI) AML19 trial, funded by Cancer Research UK, led by Professor Nigel Russell, Guy's and St Thomas' NHS Foundation Trust, aimed to determine the optimal induction regimen for younger patients with newly diagnosed AML. It randomised 1475 patients to FLAG-Ida plus Gemtuzumab Ozogamicin (GO) (either single or fractionated dose) with Daunorubicin, AraC (DA) plus GO in patients with newly diagnosed AML. No benefit was seen for fractionated GO, and there was no overall survival benefit for FLAG-Ida-GO, but there was an improvement in event-free survival. An oral presentation of results was given at ASH 2022 in New Orleans and the trial has been submitted for publication in the Journal of Clinical Oncology..

The NCRI AML19 Midotarg pilot trial, funded by Pfizer, led by Professor Nigel Russell, Guy's and St Thomas' NHS Foundation Trust, randomised 77 patients with newly diagnosed FLT3 mutated AML to receive DAGO1m: Daunorubicin (D), AraC (A) (DA) and a single dose of Gemtuzumab Ozogamicin (GO) plus midostaurin(m); or DAGO2m: DA plus two doses of GO (DAGO2) plus midostaurin. Results were similar for both DAGO1 and DAGO2 groups, and complete remission was achieved in 88% of patients, with good tolerability. Outputs include an oral presentation at the 2022 American Society of Haematology Annual Meeting, and a follow-up trial is planned.

FAKTION

A phase 1b/2 randomised placebo controlled trial of fulvestrant +/- AZD5363 in postmenopausal women with advanced breast cancer previously treated with a third generation aromatase inhibitor.

Chief Investigators: Professor Robert Jones, Cardiff University, and Dr Sacha Howell, The Christie NHS Foundation Trust

Funders: Cancer Research UK and AstraZeneca

An updated analysis of the FAKTION trial utilised next generation sequencing of tumour and blood samples in patients with advanced breast cancer. Overall survival was prolonged in patients treated with capivasertib compared to placebo, and planned subgroup analysis by AKT pathway mutational status showed this effect was mostly seen in patients harbouring mutations in this pathway. An oral presentation of results was given at the American Society of Clinical Oncology (ASCO) 2022 Annual Meeting in Chicago, and it has been published in Lancet Oncology. [https://doi.org/10.1016/S1470-2045\(22\)00284-4](https://doi.org/10.1016/S1470-2045(22)00284-4)

SCOPE 2

Chief Investigator: Dr Tom Crosby, Velindre University NHS Trust

Funder: Cancer Research UK

The SCOPE 2 trial is an ongoing trial comparing radiotherapy dose-escalation regimes in patients with oesophageal cancer. It included a substudy, led by Dr Somnath Mukherjee, Oxford University, evaluating the role of 18F-Fluorodeoxyglucose positron emission tomography (PET) scanning in the decision to switch chemotherapy regimens for patients with a metabolic response. The substudy was closed early as it was found that it was not prognostic and should not be used to switch treatment. An oral presentation was given at the European Society for Therapeutic Radiology and Oncology (ESTRO) in Vienna, and it has been submitted to eClinicalMedicine. A preprint is available https://papers.ssrn.com/sol3/papers.cfm?abstract_id=4380032



Infection, Inflammation and Immunity Division

PANORAMIC

Platform Adaptive trial of Novel antiVIRals for eARly treatMent of COVID-19 In the Community.

Chief Investigator: Professor Chris Butler, Oxford University

Funder: National Institute for Health Research

PANORAMIC, a major adaptive trial evaluating novel antiviral treatments for COVID-19 completed and published the evaluation of the first of these (Molnupiravir) showing no impact on hospitalisation, but some reduction in duration of symptoms. Ongoing analysis is exploring longer-term outcomes and economics of this drug. The trial continues to recruit to evaluate a second antiviral, Paxlovid.

MISSOURI

A self-controlled case series study of the effect of urinary tract infections (UTIs) on subsequent cardiovascular events.

Chief Investigator: Dr Harry Ahmed, Cardiff University

Funder: British Heart Foundation

MISSOURI has had its preliminary findings presented at an international infections meeting, the General Practitioners' Research in Infections Network (GRIN). This study uses electronic health record data in Wales, in partnership with the SAIL Databank (<https://saildatabank.com>), to investigate whether there may be a causal link between a UTI diagnosis and myocardial infarction or stroke and thus informing intervention targets for cardiovascular disease prevention.

Evaluation of the sore throat test and treat service delivered through Community Pharmacies

Chief Investigator: Dr Efi Mantzourani, Cardiff University and Digital Health And Care Wales

Funder: The Welsh Value in Health Centre and Digital Health And Care Wales

We provide statistical leadership to the evaluation of the sore throat test and treat service delivered through community pharmacies across Wales. This innovative service has been presented at several international meetings, including GRIN, and has resulted in high-quality publications of scientific, clinical, and policy interest – and was awarded the Diagnostic Stewardship Award at this year's annual [Antibiotic Guardian Awards](#).

- <https://academic.oup.com/jac/article/78/1/8w4/6770011>
- <https://ijpds.org/article/view/1999>

DO-PrEP and UPrEP

Development of an intervention to optimise use of pre-exposure prophylaxis (PrEP) to prevent HIV-acquisition in at-risk individuals living in Wales (DO-PrEP).

Chief Investigator: Dr David Gillespie, Centre for Trials Research

Funder: Health and Care Research Wales

The DO-PrEP and UPrEP projects on HIV pre-exposure prophylaxis in Wales are nearing completion. Over the last year there have been research outputs in the form of publications and conference presentations at the British HIV Association Spring conference, British Association of Sexual Health and HIV Annual Conference, AIDS 2022 World Congress, Fast Track Cities 2022 Meeting, and International Society for Medication Adherence annual conference.

- <https://link.springer.com/article/10.1007/s10461-022-03890-4>
- <https://link.springer.com/article/10.1007/s10461-022-03967-0>
- <https://bmcpublichealth.biomedcentral.com/articles/10.1186/s12889-022-14645-0>



Population Health and Social Care Division



STEADFAST

Chief Investigators: Dr Rob French, Cardiff University, and Lucie Burgess, Diabetes UK

Funder: HDR UK DARE sprint exemplar funding

Type 1 diabetes is a common long-term health condition affecting 40,000 children and young people in the UK, requiring daily management. The four UK home nations have legal commitments to support young people with medical conditions in their education. However, there are significant challenges in providing evidence to support interventions. Wide public understanding and strong support are critical for the use of sensitive data in research, such as health and education data. Young people are particularly challenging to engage in such conversations.

The STEADFAST project has explored the best ways to inform, engage and involve young people, their families and the wider public in important issues around the use of their sensitive data for research. The aim of the project was to recruit 50% of participants from under-represented groups. We used trusted branding working with Diabetes UK and Equality Health, an agency which links community networks with researchers. The team created a short video featuring a young sportsperson with type 1 diabetes who described his experience through poetry and music. The video subsequently won a 'Silver' award for diversity and inclusion in communications at the [PM Society Awards](#).



WORK PACKAGE 5

Ensuring methodological and professional development

Developing new ways to
answer important clinical questions
and sustaining a dynamic
and professional workforce



Methodology is about how we do the research rather than the outcome of the research. Improvements in methodology can bring direct benefits to our portfolio of trials and to how others undertake research.

We work across four areas:

1. Novel Trial Design & Analysis

2. Maximising the Use of Existing Data

3. Trial efficiency

4. Inclusivity

Optimisation and feasibility of Triple P parenting programme for remote delivery

Chief Investigator: Dr Jeremy Segrott, Centre for Trials Research

Funder: Nuffield Foundation

One area of methodological innovation accelerated by the COVID-19 pandemic was that of remote intervention delivery. The newly awarded feasibility trial of the Group Triple P parenting programme provides a good example of this.

The pandemic lockdown drove a rapid shift in the delivery of group-based parenting programmes from face-to-face to remote delivery (e.g. via Zoom, Teams). Whilst initially undertaken as an emergency response, there remains significant interest in understanding the potential benefits of remote delivery (such as reaching typically underserved groups) and what adaptations may be needed for long-term implementation. Our research addresses these important questions by fully optimising an adapted group-based face-to-face parenting intervention – Group Triple P, for remote delivery via videoconferencing. By undertaking this study, the researchers will determine whether remote delivery can increase parent engagement and participation in the programme and how well it can reach traditionally underserved groups. The study will lay the foundation for a definitive trial to establish whether remote training can replicate the effectiveness of face-to-face delivery.

Implementing the INCLUDE Framework for People with Impaired Capacity

Chief Investigator: Dr Victoria Shepherd, Centre for Trials Research

Funder: Innovation for All

One underserved group is people who have cognitive impairment and are unable to provide consent to take part in a trial. This may be due to a condition such as dementia, an acute illness such as a stroke, or a learning disability. Our previous research found that researchers struggle to design and conduct trials involving people with a cognitive impairment due a lack of knowledge and support. Researchers identified a need for more guidance.

Building on the work of the NIHR INCLUDE project we have developed the INCLUDE Impaired Capacity to Consent Framework. We worked with organisations who design and conduct trials to develop a toolkit to help researchers to implement the framework in their work and so design more inclusive trials in the future. The toolkit includes multi-media resources such as videos and infographics to raise awareness with researchers (and lay research partners) about the issues around inclusivity and the purpose of the framework, and more focused workshop materials to give concrete pointers on how research teams can work through the framework and address any barriers to the inclusion of people with impaired capacity. It will also include the development of ‘easy read’ materials to ensure that the framework is accessible to research partners with additional communication needs.





Development and prototype testing of a method to quantify the carbon footprint of current clinical trials to inform future lower carbon clinical trial design

Chief Investigators: Professor Paula Williamson, University of Liverpool, and Dr Lisa Fox, Institute for Cancer Research

Funder: NIHR

In 2007, the Sustainable Clinical Trials group concluded clinical trials contribute substantially to greenhouse gas emissions, but there has been little progress subsequently in reducing their carbon footprint. This project aims to investigate how to run clinical trials with a lower carbon footprint, without compromising quality and integrity. The first step is to develop the method for estimating the carbon footprint of a trial.

Clinical trial carbon footprints are being investigated through the full clinical trial lifecycle from set-up and conduct through to analysis and reporting. A sample of trials will be selected, and using emission factors for each activity, will then provide a base for testing the method alongside interpretation. We have been part of the partnership developing this approach and an Intercalated BSc student, Elis Midha, has been carbon footprinting two of our trials (PRONTO and Stand Together) to explore how we can use it across our portfolio.

WORK PACKAGE 6

RDCS and NHS

Supporting staff in the NHS and social care in Wales to develop their own research to address the important questions in the care of patients and the public



With the creation of the new Faculty, Health and Care Research Wales are looking at other ways of supporting researcher development and will no longer be funding the RDCS from April 2023. Here we reflect on the work we have done in this last three-year funding period.

The Research Design and Conduct Service (RDCS)

The Research Design and Conduct Service (RDCS) South East Wales supports staff working within the National Health Service and social care to develop high-quality research funding proposals.



Service provided by RDCS consultants from the Centre for Trials Research, the largest group of academic clinical trials staff in Wales.

12

successful submissions



176
proposals



Funding

£11,662,466



44
submissions



176

clients from

20

NHS and social care organisations



We have worked with clients from 20 different organisations, ranging from large Health Boards to small charities: Each of the 176 clients will have taken away something different, be it enthusiasm for their research, new design ideas, guidance on public involvement or the ever-popular sample-size calculation, through to those who achieve a fully worked up grant application. Success looks very different for each of those clients: There were 12 whose research has been funded, bringing in awards totalling over £11 million.

For others the success might be less immediately tangible, such as connecting with others with similar research interests or learning about funding opportunities they can apply for; these clients will have a longer arc to success but are a fundamental part of the organic process of creating the network needed to develop high quality research.

RDCS and COVID-19

As for everyone, the pandemic changed the work of the RDCS in 2020: We adapted the service to offer methodological support to our NHS partners in service evaluations and academic colleagues in developing urgent COVID-related research and applying for funding. Examples of this include an application for the LISTEN trial, funded by NIHR and now recruiting people living with long COVID from across Wales; and the PEACH study which also received funding from NIHR and included several hundred participants from Wales. An ongoing programme of Virtual Reality research in Cwm Taf Morgannwg University Health Board (CTUHB) started at the height of the pandemic: It began with a brief evaluation of DR.VR Frontline with staff from CTUHB to help reduce stress and anxiety of frontline workers.



RDCS and CTR Chief Investigator project

An important part of our remit was to increase research capacity in Wales. This included supporting NHS and social care researchers new to leading research projects, a role described as Chief Investigator (CI). It can be a big step up from being part of a research team to leading the study and so we wanted to find out what support new CIs need. The report from this project, based on interviews with CIs at different stages in their career, will form the foundation for building a stronger support system via the Treialon Cymru initiative.



Events

The team switched to hosting virtual research funding application events in 2021 and made the most of the move online by creating a virtual library of recorded presentations that people can access when they are developing their research ideas. We celebrated the move back to in-person events in 2022 with an “early ideas” event for staff interested in learning more about how to turn a vague idea into a research study, with a view to applying for grant funding.

One of the Centre’s strategic goals is to increase the number of new CIs in Wales from allied health professional backgrounds, so our last event was open to delegates registered with the Health and Care Professions Council (HCPC), the regulatory body for 15 different professional groups in health and social care. The two-day event, attended by 21 HCPC registered professionals from across Wales, was not just about the research ideas but also focused on the researcher themselves. We hope to see these practitioners developing their research ideas further through the opportunities opening up in the Centre, via the Treialon Cymru Associate Members Programme, and also through the Health and Care Research Wales Faculty.





Conclusion

Our annual report captures well the Centre's vision and the challenges we have set for ourselves as a trials unit. Our new studies draw broadly across the clinical and care spectrum, working with national and internationally leading investigators. Some of our new studies such as OBS UK represent long-standing collaborations and programmes of work that grow over time. Often this is the progression of an innovation from early development through to feasibility and then to definitive evaluation stage, the E-PAtS study being an example of such progression. Increasingly how we make the best use of existing research and service data has become a priority to reduce burden on patients and professionals and to make efficient use of existing resource. Our Centre's early investment in promoting routine data use continues to produce benefits in terms of new studies such as PRIMORANT, our new HDR UK funding and increased instances of trial data sharing.

Further innovation in how we design studies and interventions is evidenced strongly; for example, the PROTECT study which is developing a master protocol for a platform trial, and the study of the remotely delivered Triple P parenting programme. The latter arose as a necessity of pandemic-driven remote working practices but the move to increasingly decentralised trials has gathered pace over a much longer period.

Designing trials that bring treatments and interventions closer to all patients and service users and make capturing outcome data easier are already essential: methods and systems to facilitate this will increasingly evolve. We want our Centre to be at the heart of that. This means that studies are designed and adopted by the Centre with essential input from the public and to promote inclusion. The SCC-AFTER study exemplifies how to innovate and apply approaches that will do just that.

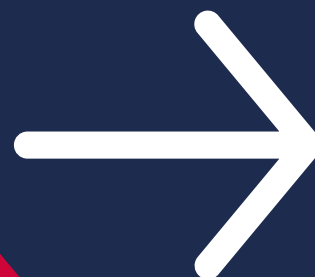
We aim in this report to show how our team-based, multidisciplinary approach creates opportunities for our investigators to deliver practice-changing evidence. Ultimately a Centre is the sum of its parts; these parts are our staff and as such we hope this report reflects their expertise and commitment well. This includes the RDCS team who completed their work this year with an impressive record of support to new investigators in Wales. The statistical record of their work – numbers of successes and amount of funding – only captures part of their value to their clients. The much larger number of proposals received, submissions made and clients supported represents a significant investment in research capacity which will continue to pay dividends in the form of new research ideas, new submissions, greater confidence and skills.

Looking forward

We have much to look forward to with new collaborations and new strategies. In particular, we are delighted to have brought our skills to bear and to have gained a key role in some major initiatives which we are grabbing with both hands.

These include:

- The Joint Research Office has been established which brings together clinical research oversight and expertise across Cardiff University and Cardiff and Vale University Health Board and is establishing a synergistic approach to support efficient trial development and delivery.
- The first national cancer research strategy for Wales (CReSt) was launched in 2022. The goal is to build on the best of the research being done already to increase the depth and critical mass of cancer research activity in Wales. Clinical Trials are a key part of this, and CReSt offers an opportunity for greater integration with the Welsh cancer research community and NHS cancer trials delivery.
- We are phasing out our Cancer Research UK core funding over the next two years, which will present us with new opportunities. Cancer Research UK have adopted a new strategy which does not fully complement our own approach within the cancer division or the CTR as a whole. This will give us greater freedom to develop our research portfolio in a truly integrative fashion.
- The Centre for Adult Social Care Research (CARE) is funded by Health and Care Research Wales as a five-year investment and will be led from Cardiff University's School for Social Sciences. CTR will be a methodological partner in the new Centre, drawing together social care research expertise from across our Divisions.
- The 'Useable Data' initiative involves an Oxford-led team working with Cardiff, University College London and Dundee to optimise approaches to working with routine healthcare-systems data. The Cardiff team will be responsible for developing a range of training packages for UK trialists.
- Treialon Cymru is an exciting initiative funded by Health and Care Research Wales, which aims to provide opportunities across the whole of Wales for people to engage in trials. Initially funded for a two-year period, it is underpinned by three key elements:
 - A **Research Development Programme**, which aims to increase the number of large-scale studies led from Wales
 - An **Associate Membership Programme**, which offers CTU mentoring and professional development to people interested in trials across Wales
 - A **Stakeholder Engagement Programme**, which aims to reach as many people as possible across Wales to raise awareness of trials, CTUs, and the schemes offered through Treialon Cymru



Thank you

The Centre for Trials Research wishes to thank all the members of the public and study participants who give their time to take part in our studies, freely and with great generosity to help improve health outcomes for future generations. It is our vision to produce a more evidence-based culture, so we know what works and what does not. This is impossible without their contribution and support.

Thank you to all our Research Partners who give their time to take part in study management groups, steering committees, and are both involved in delivering and participating in research. You inform research questions, study design, planning, management and reporting, ensure study materials are helpful for the public – and ultimately help all our studies to progress to successful completion and publication.

In preparing this report we thank our Public Involvement and Engagement (PI&E) Hub representatives Sue Campbell and Sarah Peddle.



Sue Campbell



Sarah Peddle

Contact us

The Centre for Trials Research is willing to consider any well-designed study or trial idea, even those outside its current areas of research. For more information about collaborating with our research team or to keep up to date with news and events:

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