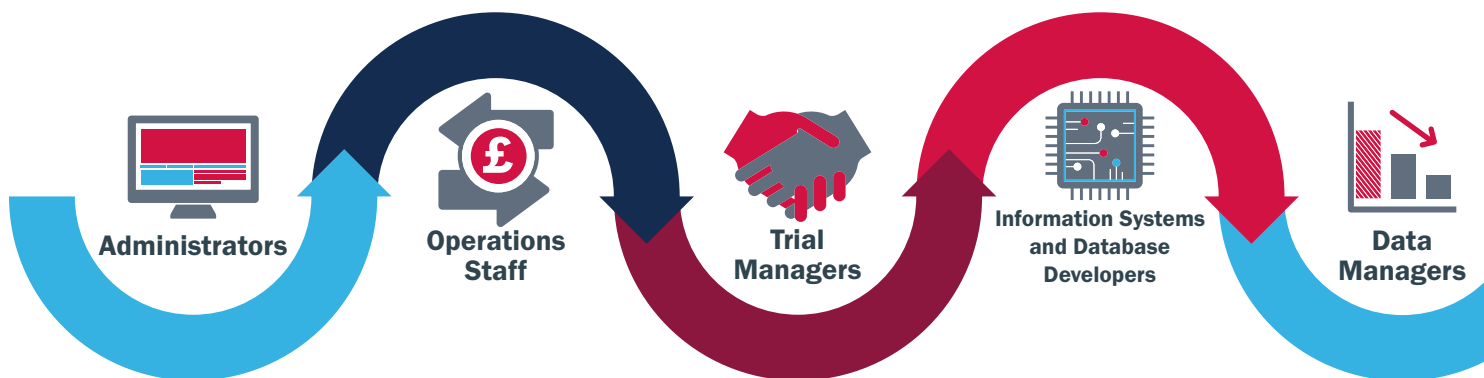




ANNUAL REPORT 2019/20

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



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Images on front cover:

1. Professor Monica Busse: Cardiff University researchers are part of a global consortium who have published the first clinical guidance for the management of Huntington's disease through physiotherapy.
2. Chief investigator (CI) Professor Nick Francis. He was co-CI on the OSTRICH study, which was published in the Lancet.
3. On Saturday 28th September 2019, staff from Cancer Research UK funded clinical trials units in Birmingham, Cardiff and Southampton joined together to raise funds for life-saving research and raise awareness of clinical trials and the vital role they play in developing cancer treatments.
4. Lay representatives at PACE dissemination event. Dissemination and feeding back to the public, participants and patients is important for ensuring the transparency of trial results.
5. Professor Chris Butler, co-CI of PACE study and OSTRICH, meeting members of the public at the dissemination day event.
6. Delegate at PACE dissemination event.



Executive summary

Over the last year April 2019 to March 2020, we have maintained our international reputation in the design and conduct of trials across our areas of thematic interest.

Our now established divisional structure sees our innovative methods applied across trials and other well-designed studies in the fields of Cancer, Infections, Inflammation and Immunity, Population Health and Mind, Brain and Neuroscience.

We have continued to ensure that public involvement is appropriately embedded in all our research and have continued to build successful partnerships with other parts of the Health and Care Research Wales funded infrastructure, the NHS and Social Care across SE Wales and beyond.

We have developed specific expertise to support the use of routine data in trials and have developed the processes and systems to ensure that data and samples collected through prospective studies are made available for future research. Alongside this we have continued to support innovation from the NHS through our Research Design and Conduct Service, which supported 117 research ideas and 25 NHS and Social Care grant submissions in Wales.

Our strategic planning and development of policies and strategies governing all Centre for Trials Research activities has continued this year. We have continued to see great success with collaborative grant winning with investigators working in the NHS, social care, Health and Care Research Wales infrastructure and industry across Wales, the rest of the UK and internationally.

Infrastructure funding has facilitated our ability to continue to ensure all staff are appropriately trained to deliver research to Good Clinical Practice (GCP) standards and have equal accessible opportunities for development and training. Our effective resource management and success in retaining and developing our 161 skilled research and professional staff has helped us to secure £9,855,375 in funding from national and international funders (a total of 30 major awards in the Health and Care Research Wales and Cancer Research UK strategic thematic areas over the current period of funding).

Our high-quality research is reflected by more than 138 peer reviewed publications over the past year, including high impact papers in the Lancet, British Medical Journal (BMJ), and New England Journal of Medicine. Our programme of research has been underpinned by the inclusion of the public in the design, conduct and dissemination of research (20 engagement events and 1,159 public involvement opportunities in this period).

We would like to acknowledge our funders, research partners, staff and, above all, the participants in our research studies without whom none of this work would be possible. Thank you for taking the time to read about our work.

Professor Monica Busse

Director, Mind, Brain and Neuroscience Division

Professor Mike Robling

Director, Population Health Division

Professor Kerry Hood

Director, Infections, 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, that is dedicated to tackling the big diseases and health 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 well-being of the public.

Key programme partners and beneficiaries

The Centre receives infrastructure funding from Health and Care Research Wales and Cancer Research UK. This funding allows us to invest in core activities that are inherent requirements for 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 primary research in health or social care (or both). The potential beneficiaries are broad, reflecting the range 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. These beneficiaries will be in Wales, the rest of the UK and in other countries outside of the UK.

Who's who

The CTR Director (and Director of Division of Infections, Inflammation and Immunity) is Professor Kerry Hood. She is supported by a senior management team including Professor Mike Robling (Population Health Division), Professor Monica Busse (Mind, Brain, Neuroscience Division), Professor Richard Adams (Cancer Division), Professor Adrian Mander (Statistics) and Dr Sue Channon (Research Design and Conduct Service).

How we work

Our 161 researchers and professional staff work across our four divisions and within cross-cutting teams (including Information Services, Quality Assurance and Regulatory Affairs and Professional Services). Our current research portfolio includes evaluations of drugs and complex healthcare 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, social care aspects, commercial / industry engagement and collaboration, NHS service professional engagement and collaboration, engagement with Welsh Government funded research infrastructure and communications, publicity and knowledge transfer.

Our work plan

We place continued emphasis on development of working practices and expert staff to make sure 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.



Centre for Trials Research Directors



Professor Kerry Hood, Director
Centre for Trials Research and
Infections, Inflammation and
Immunity Division



Dr Sue Channon,
Director Research Design
and Conduct Service
(RDCS) SE Wales



Professor Mike Robling,
Director Population
Health Division



Professor Monica Busse,
Director Mind, Brain and
Neuroscience Division



Professor Richard Adams,
Director Cancer Division



Professor Adrian Mander,
Director Medical Statistics

Centre for Trials Research Divisions



Infections, inflammation and immunity



Mind, brain and neuroscience



Cancer



Population health

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 cross-cutting 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. Throughout this report, these graphics identify and introduce you to each section:

WORK PACKAGE 1:

Managing our work

WORK PACKAGE 2:

Working with other groups

WORK PACKAGE 3:

Developing new studies

WORK PACKAGE 4:

Overseeing funded studies

WORK PACKAGE 5:

Ensuring methodological and professional development

WORK PACKAGE 6:

Supporting innovation from NHS and social care practice

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

Our year in numbers...

April 2019 to March 2020

We are a registered clinical trials unit and the largest group of academic clinical trials staff in Wales.

Increasing research capacity in Wales

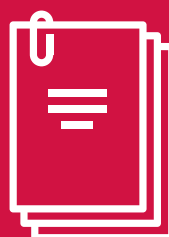
The Centre for Trials Research is publicly-funded by Welsh Government through Health and Care Research Wales and Cancer Research UK to enable applied research that informs policy in health and social care, and is currently running studies across Wales, the UK and internationally. Over the past year, we have continued to support and grow research capacity, particularly in Wales.

Here we highlight some of our achievements and impact during the past 12 months.



161

Centre for Trials Research staff



138

papers published



2,121
event attendees



30
new grant awards



1,159
public involvement opportunities

20

engagement and dissemination activities



Total funding awarded

£9,855,375

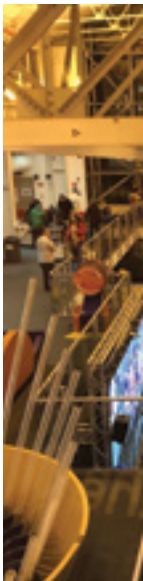


WORK PACKAGE 1:

Managing our work

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





Cardiff University Celebrating Excellence Awards 2019

Centre for Trials Research Health and Wellbeing Group was nominated for a Celebrating Excellence Award in the category of “Excellence in Voluntary Contribution”. This is a group of staff who are involved in furthering positive wellbeing throughout the Centre – and this nomination is all down to their hard work.

Executive Committee Away Day

The executive committee awayday at the end of January 2020 was a chance to reflect on what had worked well in the previous funding period - and what changes might be needed to take the Centre forward as we continue to grow and evolve (161 staff at the time of writing this annual report). We focused the discussion around three areas highlighted within the staff survey (internal communication, workload and learning and development). This resulted in a set of actions and plans which we shared with the whole staff group across workload, communication and line management.

Each action has a lead within the Executive Group and a timeframe for exploration and/or implementation over the next year.

Task and Finish Groups

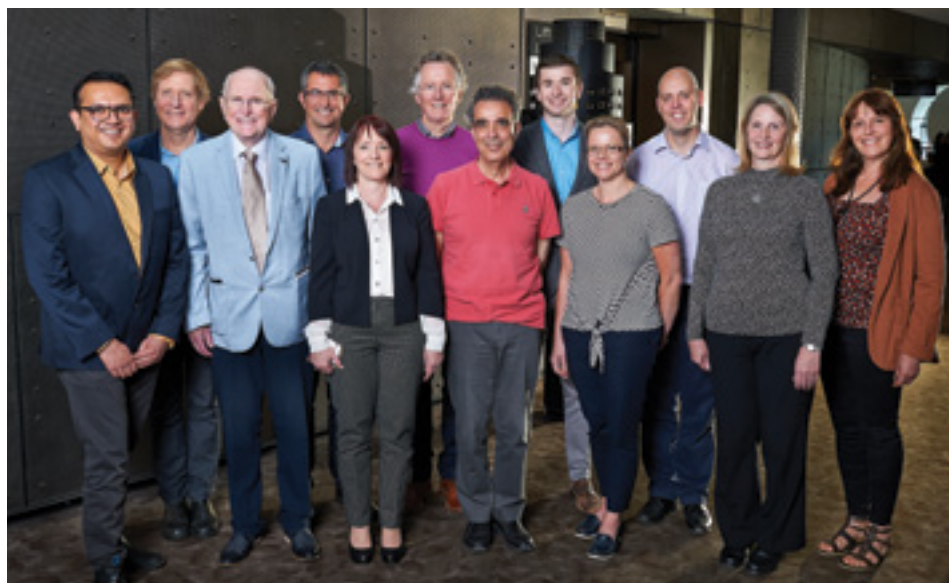
A Task and Finish group is a group set up as a sub group of larger project group, that specifically looks at one item that needs to be delivered.

Trial Set-up Task and Finish Group

The trial set-up task and finish group made recommendations to the Executive Group to take more of a risk based approach to Quality Assurance reviews of trial documentation. These recommendations have been endorsed and the task and finish group is currently overseeing completion of various actions to implement this.

Medical Devices Task and Finish Group

The medical devices task and finish group made recommendations which were endorsed by the Executive Group at the last meeting. The group identified that there is only currently a small number of CTR staff who have some experience in setting device trials and with the changes and regulations and broad spectrum of trial possibilities under the medical devices banner it is sensible to share knowledge and grow expertise in this field.



SOP Training Task and Finish Group

The need to improve our processes for delivering Standard Operating Procedures (SOP) training has been identified via audit recently. The Executive Group requested that a task and finish group makes recommendations for this and report back.

Successful NHS Digital Audit

We have been successfully externally audited by NHS Digital, a principal supplier of routine clinical data to a number of CTR studies. This was a routine audit of the Data Sharing Agreement for the Building Blocks 2 study and involved not only CTR but also the Secure Anonymised Information Linkage (SAIL) databank at Swansea University who provide the safe haven for the study data. This is the first time CTR have been audited by NHS Digital and the audit provided moderate assurance. CTR and SAIL have finalised an action plan and are currently managing the Corrective And Preventive Actions (CAPA) which were raised to address the auditor's findings and observations. We are satisfied with the outcome of the audit, which has been a useful developmental experience for the Cardiff team. This has built upon work undertaken by a working group in CTR who have been developing systems to work with routine data (for example, working with the new Data Security and Protection Toolkit).

Information Systems and Database Development

The Centre Executive has approved a scoping exercise to identify the technologies and roles & responsibilities needed to allow the Information Systems and Database Development (IS&DD) team to better support future trials and studies. This will take a long-term view of the next 5 to 10 years and will consider new clinical software and the best tools to collect fitness and activity data for research.

The IS&DD Team has also recruited a Technology Solutions Manager who will be our main link with University IT and will also focus on how technology can better support our research. This is particularly timely with the rapid move of staff to home working at the onset of the COVID-19 pandemic.

Human Tissue Authority (HTA) Inspection

In collaboration with the Cardiff University Wales Cancer Bank we have undergone an official inspection by the HTA to review processes in relation to samples collected from patients in our studies. These samples form a rich source of information when linked to data collected on individuals and help to optimise the research opportunities as well as external collaborations, bringing the best science in to play. The inspection has allowed us to develop and fine tune our processes for future work.

Public Involvement and Engagement

The Centre for Trials Research Public Involvement and Engagement (PI&E) Hub finalised the new Centre Policy which now incorporates the UK Standards for Public Involvement. In tandem with this, a new template for public involvement planning has been drawn up for piloting with study teams. It is intended that this will support teams to develop their own explicit plans for public involvement and engagement. The hub itself and its new policy will be formally launched with CTR early in the autumn.

Our hub lay representatives (Sarah Peddle, Susan Campbell) have been actively involved in contributing to the new Centre Annual Report, working closely with our Senior Communications Officer. As importantly, both have helped us in the preparation of our re-commissioning bid to Health and Care Research Wales. The hub collectively informed the statements included in the submission, including the strategic plans for the next five years for PI&E. We were also very grateful to Sarah who joined with other members of the applicant team at the interview stage in June.

Cardiff investigators in the PARC collaboration co-hosted a patient and public involvement (PPI) workshop in London (attended by charity stakeholders and patient representatives) as part of the final stages of the programme development grant activities that are funded by National Institute for Health Research (NIHR) Programme Grants for Applied Research (PGfAR). This has led to the submission of a stage 1 programme grant application to NIHR PfgAR in partnership with University College London.

The DOMINO-HD team held a PPI hub meeting in Amsterdam with representatives from Norway, Switzerland, Poland, Spain and Germany. DOMINO-HD have implemented a PPI model which will involve the hub members liaising with stakeholders in their relevant countries. The PPI hub is supported through the European Huntington Association.

Chief Investigator Brochure

To support more transparent models of working with external investigators we have recently finalised a new Centre brochure for chief investigators, which is available on our website. This describes the role and constitution of the Centre and how it aims to work with investigators. It lays out typical responsibilities of both Centre and Investigators in the design, conduct and reporting of studies. This will be made available on our web site and for use in discussion with investigators at the outset of new funding applications. This is part of strategy to support the development of new Wales-based investigators. We also created novel animated videos as a way to engage with the public and to explain what we are doing.



WORK PACKAGE 2:

Working with other groups

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



BRAIN Unit

As part of CTR collaboration with the BRAIN unit (through the delivery of the TRIDENT trial and a range of other invasive therapy trials), representatives attended the launch meeting of the European Huntington's Disease Network Advanced Therapies working group in Barcelona in September. This is a working group that brings together a diverse group of contributors, including neurologists, neurosurgeons, healthcare workers and providers, scientists, and other interested parties from academia and industry to address the complex, wide-ranging and multi-component challenges in delivery of substances and cells to the brain for therapeutic purposes. We have representation on the executive committee of SC4HD (Stem Cells for HD) which is a global initiative whose mission is to define and publish guidelines for preclinical testing and clinical development of cell therapies to be transplanted in the brain for treatment of Huntington's Disease.

TRIDENT

Trident (which is delivered in partnership with the Wales BRAIN unit) provides a unique example of the multiple methodological and operational challenges faced in trials of a highly specialised, emergent area of direct brain delivery. Our design involves the use of a trial within a cohort that has been developed to address many of the constraints inherent in such early phase activities. Over the past year we have progressed to achieving all the regulatory approvals for opening all phases of the TRIDENT trial. The first surgery was scheduled for 17th March 2020. We also completed 5 of the 12-month assessments with those recruited to the observational cohort. Unfortunately, this was not able to be completed due to COVID-19; however, all aspects are in place for the team to complete the surgery as soon as possible.

Working with Other Clinical Trials Units (CTUs)

It has always been an important part of our structure to work with a range of clinical trials units from around the UK and by doing so, we believe we optimise the development and delivery of academic studies and clinical trials. We have additional specific affiliations with our sister CTUs in Wales funded through Health and Care Research Wales and those in the UK funded through Cancer Research UK. As a part of this collaborative work we have: shared database expertise (AML trials) and collaborated on trial development with successful funding; shared our high quality standard operating procedures; and, in September 2019, we led on an 80 mile bikeathon with sister Cancer Research UK CTUs in Southampton and Birmingham to raise awareness of clinical trials and raise funds for Cancer Research UK.



Cancer Research UK Sponsored Bike Ride with colleagues from other clinical trials units.

UN Office of Drugs and Crime

Dr Jeremy Segrott was part of an informal consultation meeting at the UN Office of Drugs and Crime discussing their new handbook for policymakers on engaging young people in substance misuse prevention. This was an opportunity to learn from an international group of young people about its importance for them and ways of working.



COVID-19 Response

Staff at the Centre for Trials Research are collaborating with researchers across the UK to develop a better understanding of the impact of COVID-19 on pregnancy and the public attitudes and experiences of lockdown.

Temporarily, our Cancer Division, led by Professor Richard Adams, has had to pause recruitment to a number of cancer trials for the safety of patients and medical staff. We are working to get these activities rapidly restarted and are developing studies to better understand the impact of this pandemic on cancer diagnoses and cancer patients.

Staff from across the Centre have also been working with Health and Care Research Wales to support the roll out of the UK wide prioritised trials in COVID-19, including the Oxford Vaccine Trial which opened in Aneurin Bevan University Health Board in May 2020.

Much of this activity has come at the end of the 2019-2020 reporting period, and we look forward to sharing regular updates with you on Twitter, in blogs, via press releases and published news features on our website – as well as in the 2020-2021 annual report.

WORK PACKAGE 3:

Developing new studies

Designing new studies and winning
the funding to make them happen





Cancer Division

We have established a number of new collaborations with CIs from Manchester, Oxford, Imperial, and The Royal Marsden Hospital and scientists within imaging (Cardiff University Brain Research Imaging Centre (CUBRIC)) and biomarker development of enzyme-linked immunosorbent assay (ELISA) testing (Manchester) with ongoing development of trials in myeloma, cervix, ovarian, brain, sarcoma and pancreatic cancers. We have supported funding applications using our expertise and knowledge from other CTUs including Leeds, Oxford and Birmingham.

We supported the multi-disciplinary development of the Oelixir programme (led by Cambridge) in oesophageal cancer with clinical trials input and are continuing to develop a trial originally associated with this bid, which scored very highly in feedback.

CONSCOP2

Randomised controlled trial of contrast enhanced colonoscopy in the reduction of right sided bowel cancer.

Chief Investigator: Dr Sunil Dolwani

Funder: NIHR Health Technology Assessment Programme

Funded £2.1M colonoscopic bowel cancer screening Randomised Controlled Trial (RCT). This study has been a natural evolution of the successful CONSCOP feasibility study and brings together a broad range of researchers working within and outside the NHS. The trial is aiming to open in 2020. We have already submitted for funding additional research concepts within this study linking in industrial partners and Artificial Intelligence.

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: Dr Robert Jones and Dr Sacha Howell

Funders: Cancer Research UK and AstraZeneca

The data from this study has been shared with Astra Zeneca to inform the development of a new phase III trial which will be industry led.

TIC-TOC

Targeted Intensive Community-based campaign To Optimise Cancer awareness.

Chief Investigator: Dr Grace McCutchan

Funder: Cancer Research Wales

Funded feasibility of a symptom awareness campaign to support the Multidisciplinary/ Rapid Diagnostic Centre referral pathway in a socioeconomically deprived area optimising the strengths of the new collaborative CTU bringing in the strengths of the population health division and the cancer division of the CTR.

TIC-TOC has been awarded 26 months of funding by Cancer Research Wales. The study is evaluating a targeted intensive community based campaign to optimise cancer symptom awareness. This work is intended to support the work of multidisciplinary / Rapid Diagnostic Centre (M/RDC) referral pathways being introduced to expedite assessment of patients with vague cancer symptoms.

VALTIVE 1

An integrated biomarker feasibility study with mixed methods.

Chief Investigator: Professor Gordon Jayson

Funder: Cancer Research UK

This £1.1M collaboration with the University of Manchester, funded by Cancer Research UK will assess the feasibility and assist in the validation of the novel biomarker TIE2 which is designed as a predictive marker for anti-cancer drugs that impact upon the blood supply of tumours such as bevacizumab. The study will collate serial blood samples from patients with ovarian cancer and will lead to a randomised discontinuation study if successful. Key to the study is a qualitative piece of work to assess the understanding and acceptability of such a strategy in patients receiving palliative chemotherapy.



Infections, Inflammation and Immunity Division

PRONTO

PROcalcitonin and NEWS evaluation for Timely identification of sepsis and Optimal use of antibiotics in the Emergency Department.

Chief Investigator: Professor Neil French

Funder: NIHR Health Technology Assessment Programme

The Centre for Trials Research is to coordinate a trial looking at use of antibiotics in sepsis.

Sepsis is a potentially life-threatening complication of an infection and it is estimated that 52,000 people in the UK die every year as a result of it.

Optimal treatment includes early recognition, prompt antibiotics and fluids.



The PRONTO study team

The £2 million trial will look at emergency assessment of sepsis and whether antibiotics are being overprescribed, which experts cite as a significant factor leading to increasing antimicrobial resistance.



Mind, Brain and Neuroscience Division

STORM

STanding up fOR Myself.

Chief Investigator: Katrina Scior

Funder: NIHR Health Technology Assessment Programme

The STORM psychosocial group intervention for young people and adults with intellectual disabilities. This work contributes to our expanding portfolio of intellectual disability research (NIHR PHR, £624,000).

TAPERS

Treating Anxiety to PrevEnt Relapse in pSychosis.

Chief Investigators: Professors Jeremy Hall and James Walters (Cardiff University)

Funder: Health and Care Research Wales Research for Patient and Public Benefit Scheme (RfPPB: £229,865)

The main aim of the TAPERS feasibility trial is to establish whether adding antidepressant medication to treatment as usual in early psychosis is feasible and acceptable to patients.

In the longer term (i.e. in a later, larger trial if this proves feasible) we will also look at whether this decreased relapse rates.

ZIPPY'S Friends

Chief Investigator: Dr Biza Stenfert-Kroese

Funder: NIHR Health Technology Assessment Programme

Zippy's Friends is a programme for children providing support for social and emotional difficulties used widely (and shown to be effective) in mainstream schools. The programme has now been adapted for children (aged 9-11 years) in Special Educational Needs and Disability (SEND) schools. The aim of this study is to determine the feasibility of conducting a future controlled trial to establish the impact of the adapted programme on mental health, behaviour, emotional and social functioning and quality of life, and its cost- effectiveness (economic evaluation). Conducted in partnership with the Centre for Trials Research (NIHR PHR, £553,071).



Population Health Division

SaFE

A sexual health and healthy relationships intervention for Further Education.

Chief Investigator: Honor Young

Optimisation, feasibility testing and a pilot randomised trial of SaFE. January 2020 – April 2022. NIHR PHR, £510,815. The Chief Investigator is a first time Principal Investigator mentored by Dr James White. The study will be run in partnership with DECIPHer.



WORK PACKAGE 4:

Overseeing funded studies

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





Cancer Division

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: Dr Robert Jones and Dr Sacha Howell

Funders: Cancer Research UK and AstraZeneca

FAKTION was published in Lancet Oncology. Data from the trial is being licensed for a U.S. Food and Drug Administration (FDA) submission for licensing.

This study has had significant impact with data being licensed to Astra Zeneca to support FDA licensing of AZD5363. The results were accepted as an oral presentation at American Society of Clinical Oncology (ASCO) in the Breast Cancer symposium and has received significant media coverage and likely to be licensed in this indication.

Millions of patients with incurable breast cancer could benefit from Welsh-led research presented at the ASCO Annual Meeting in Chicago on 4 June 2019.



Centre for Trials Research Cancer Division and Chief Investigators presented FAKTION at the American Society of Clinical Oncology (ASCO) Annual Meeting in Chicago on 4 June 2019.

FAKTION research shows that, by combining investigational therapy with a standard treatment, patients may expect that their cancer will be controlled for twice as long.

Involving 140 patients from 19 hospitals across the UK, FAKTION is sponsored by Velindre University NHS Trust. It is jointly led by Dr Rob Jones from the Velindre Cancer Centre and Cardiff University and Dr Sacha Howell from the Christie NHS Foundation Trust and University of Manchester.

ABACUS 3

Chief Investigator: Professor Kate Brain

Funder: Yorkshire Cancer Research

Analyses of ABACUS 3 has been completed and is to be presented to Yorkshire Cancer Research as part of the ABACUS 4 implementation proposal. ABACUS 3 was a cancer prevention study, designed to increase awareness of cancer symptoms in older people from socio-economically deprived areas and encourage early presentation.

ROCS

Radiotherapy after Oesophageal Cancer Stenting.

Chief Investigators: Dr Douglas Adamson and Dr Anthony Byrne

Funder: NIHR Health Technology Assessment Programme

The ROCS report has been submitted and has potential for practice changing impact to reduce additional burden of planned palliative radiotherapy after oesophageal stent insertion. ROCS has demonstrated the lack of significant benefit from the addition of radiotherapy to the oesophagus for patients with incurable oesophageal cancer that has undergone stenting.



Infections, Inflammation and Immunity Division

PACE

General Practitioner (GP) use of a C-Reactive Protein (CRP) Point of Care Test (POCT) to help target antibiotic prescribing to patients with Acute Exacerbations of Chronic Obstructive Pulmonary Disease (AECOPD) who are most likely to benefit.

Chief Investigators: Professor Christopher Butler and Professor Nicholas Francis

Funder: NIHR Health Technology Assessment Programme

A key publication is that of PACE which was published in the New England Journal of Medicine. PACE investigated the use of a point of care test in the management of COPD patients presenting to primary care with an exacerbation. The study concluded that CRP guided antibiotic prescribing for COPD exacerbations in primary care clinics reduced patient reported antibiotic use and clinician antibiotic prescribing without evidence for harm. The PACE team held a dissemination event in June at the Wales Millennium Centre, which was attended by Welsh Government and UK policy makers, clinical, industrial and patient representative stakeholder groups.

A simple finger-prick blood test could help prevent unnecessary prescribing of antibiotics for people with the lung condition chronic obstructive pulmonary disease (COPD).

With funding from the National Institute for Health Research (NIHR), the team demonstrated that using a CRP finger-prick blood test resulted in 20% fewer people using antibiotics for COPD flare-ups. Importantly, this reduction in antibiotic use did not have a negative effect on patients' recovery over the first two weeks after their consultation at their GP surgery, or on their well-being or use of health care services over the following six months.

Safely reducing the use of antibiotics in this way may help in the battle against antibiotic resistance.



"Working with the Centre for Trials Research has enabled me to deliver world-leading trials, including being published in both the Lancet and the New England Journal of Medicine. A team of experts in a Clinical Trials Unit facilitates running trials to a very high standard and means every aspect of a study should be robustly managed, compliant and follows best practice. To have the diverse group of experts needed to deliver high-quality trials all in the one place means studies are much more likely to be done efficiently, timely, and to the highest international standards."

Professor Chris Butler, University of Oxford

Seal or Varnish

Chief Investigator: Professor Ivor Chestnutt

Funder: NIHR Health Technology Assessment Programme

Professor Ivor Chestnutt, from the School of Dentistry, Cardiff University won a 2019 International Association of Dental Research (IADR) award for best paper published in the Journal of Dental Research.

He was awarded the prestigious William J. Gies Award in the clinical research category for the 'Seal or Varnish?' study.



Pictured is Professor Chestnutt (third left) receiving the award from Professor Rena D'Souza, President of the International Association for Dental Research, Prof William Giannobile, Editor of the Journal of Dental Research, and Professor Maria E. Ryan, President of the American Association for Dental Research.

The study, in collaboration with Cardiff and Vale University Health Board Community Dental Service, treated over 800 children with either fissure sealants or fluoride varnish to discover which treatment is most effective and offers the best value for money for children aged 6-7 years.

The team found that applying fluoride varnish to children's teeth is just as effective at preventing tooth decay as the alternative method of sealing teeth and could save the NHS money.

BATHE study wins Research Paper of the Year 2019 Award

Our record in producing high quality outputs was recognised as the team that won Research Paper of the Year at Royal College of General Practitioners (RCGP) Annual Conference 2019. This was awarded to Professor Miriam Santer from the University of Southampton for a BMJ paper on the BATHE study, which found that pouring emollient additives into the bath do not add any benefit over standard management.

The study was funded by the National Institute for Health Research (NIHR) Health Technology Assessment Programme and was conducted with the Centre for Academic Primary Care's Dr Matthew Ridd, in partnership with the Centre for Trials Research and the University of Nottingham.

AZTEC

The Azithromycin therapy for Chronic Lung Disease of Prematurity (AZTEC) study is a national clinical trial investigating if the antibiotic azithromycin can improve the lung outcomes of premature babies who are born at less than 30 weeks of gestational age.

Chief Investigator: Professor Sailesh Kotecha

Funder: NIHR Health Technology Assessment Programme

AZTEC is a multi-centre, randomised controlled trial of azithromycin for the prevention of chronic lung disease of prematurity in preterm infants, aiming to recruit 800 babies across the UK. The first participants are to be recruited to AZTEC to investigate if the antibiotic azithromycin can improve lung outcomes of premature babies who are born at less than 30 weeks of gestational age.



Mind, Brain and Neuroscience Division



RAPID

Chief Investigator: Professor Jonathan Bisson

Funder: NIHR Health Technology Assessment Programme

Pragmatic RANdomised controlled trial of a Trauma-Focused Guided Self Help Programme versus InDIVidual Trauma-Focused Cognitive Behavioural Therapy for Post-Traumatic Stress Disorder.

The aim of this research is to determine if trauma-focused guided self help (GSH) using a web-based programme provides a faster and cheaper treatment for Post-Traumatic Stress Disorder (PTSD) than individual trauma-focused cognitive behavioural therapy (current NICE recommended treatment), whilst being equally effective. We have successfully recruited 196 participants across the UK (Wales, England, Scotland) to the study, and are now in the process of collecting follow-up outcome data (response rates are currently above 80% post-treatment). Professor Jonathan Bisson is the Chief Investigator for the study, which is due to report in April 2021 (NIHR HTA, £1, 135,331).



First clinical guidance for the management of Huntington's disease through physiotherapy

Cardiff University researchers are part of a global consortium who have published the first clinical guidance for the management of Huntington's disease through physiotherapy.

It follows more than a decade of ground-breaking collaborative research led by the Cardiff team (and coordinated from within CTR) into how to manage the devastating and life-limiting neurodegenerative condition.

There is no treatment to halt or reverse Huntington's, which damages nerve cells in the brain affecting movement, memory and behaviour and affects 6-13 people in every 100,000.

This means physiotherapy is one of the few routes to offer a better quality of life for those with the inherited disease.

A joint review by researchers at Cardiff, Columbia, Ohio State and Wayne State universities looked at previous research in this area, analysing data from 26 separate studies.

The review found physiotherapy was critical to improve motor impairments, such as dystonia or chorea (uncontrollable movements), rigidity, gait or balance issues in people with the disease.

LEAP-MS

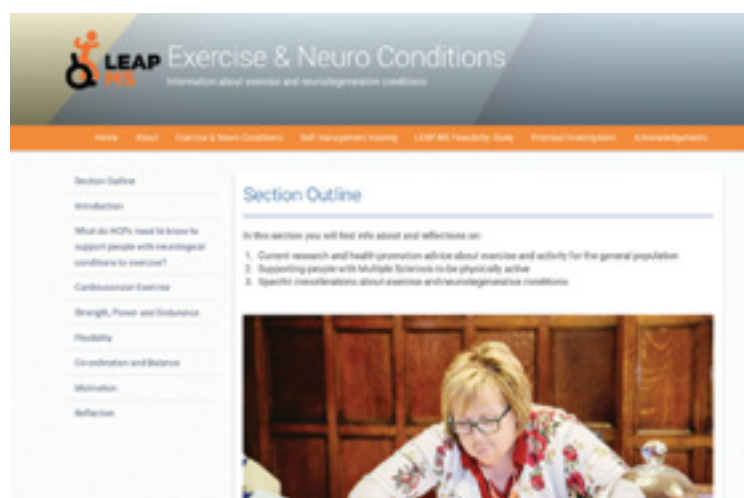
Chief Investigator: Professor Monica Busse

Study Manager: Dr Julie Latchem-Hastings

We know that physical activity and exercise are important for people with Multiple Sclerosis (MS) and can help to manage MS symptoms such as fatigue. People with MS, particularly those with mobility issues, can however find it hard to start and maintain activity. This project is developing new ways of helping them to be as physically active as possible. In the previous year we have used the information gathered in Phase 1 to co-produce (with the involvement of People with Progressive MS (PwPMS) patients and physiotherapists/ healthcare professionals) a personalised intervention; 'Life-style, Exercise and Activity Package for people living with progressive Multiple Sclerosis (LEAP-MS) to facilitate on-going physical activity for people with PwPMS.

The activity suite is made up of appropriate freely available material online – such as that provided by the MS Society, videos of activities created by members of the research team for related projects and newly developed material to fill gaps in materials available. The major element of new material that the team have produced is a series of high-quality seated aerobics/dancercise with a company called 'MojoMoves'. The new series of 'Mojo Moves for MS' combines popular music, dance actions, aerobics and comedy to make exercise fun – and to make it possible for those people with MS unable to attend and participate in conventional aerobics classes. The sessions were filmed with members of the Bath and District MS Society and the LEAP-MS PPI group have reviewed them. The response to the Mojo Moves for MS sessions has been overwhelmingly positive.

We are now in a position to test and evaluate the intervention. We aim to recruit 21 people with progressive MS to look at whether the LEAP-MS intervention is feasible and acceptable to them: this will at this point only be delivered online due to constraints of COVID-19. PwPMS will be told about the study via their local MS branch and via MS Society endorsed communication channels. Anyone who is interested in taking part will be able to self-refer to the study via the LEAP-MS study website.





Population Health Division

Evaluation of Family Nurse Partnership: methods and process of evaluation

Chief Investigator: Professor Mike Robling

This paper presents the methods of using routinely collected health, education and social care data to evaluate the Family Nurse Partnership (FNP) in Scotland using a natural experiment methodology.

Read the full paper here:

www.gov.scot/publications/evaluation-family-nurse-partnership-scotland-methods-paper-process-success-linkages

FRANK friends

Chief Investigator: Dr James White

Funder: NIHR Health Technology Assessment Programme

The FRANK friends study will be the largest evaluation of a drug prevention ever conducted in the UK, with over 5,000 secondary school students taking part. In FRANK friends we trained 25 Public Health Wales (NHS) staff across Wales to deliver the intervention.



WORK PACKAGE 5:

Ensuring methodological and professional development

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





Tim Pickles at the GW4 Crucible. Tim now has a successful NIHR Doctoral Fellowship application.

NIHR Doctoral Fellowship

Tim Pickles has been awarded an NIHR Doctoral Fellowship. This is a 3-year full-time Fellowship supported by a National Institute of Health Research (NIHR) Doctoral Fellowship, funded by the Welsh Government through Health and Care Research Wales. The Fellowship will focus on validating items from Patient Reported Outcome Measures (PROMs) for Rheumatoid Arthritis (RA) Symptom Severity using Rasch measurement theory, with the end goal to develop a computer adaptive test.

Post-Doctoral Research Awards

Researcher: Dr Julie Latchem-Hastings

Award: Social Care Postdoctoral Fellowship

Research title: Feeding, Eating and Drinking in Neurological Care: Sharing Practice to Transform Care (FEAST)

Researcher: Dr Heather Strange

Award: Research Funding Scheme: Health Grant

Research title: NIPT (Non-Invasive prenatal testing) WALES: Understanding and Improving the New Landscape of Prenatal Screening

Successful doctoral graduates

Our two recently successful doctoral candidates were:

Dr Vicky Shepherd. Vicky studied the topic of involving people who lack capacity to consent to research, which raises ethical, legal, and practical challenges. There has been a recent focus on under-represented populations in research, including adults who lack capacity, and calls for the development of innovations to address these research inequalities. During her NIHR Fellowship she explored these challenges, and developed a novel complex intervention to support family members making decisions about research participation on behalf of someone who lacks capacity.

Dr Gwen Moody. Gwen is a part-time member of CTR staff working as a Trial Manager and Research Associate. Gwen explored the factors that may predict child maltreatment through secondary analysis of a trial data set. This also involved an exploration of how routine data may be used to understand and answer questions about maltreatment, including lay and professional opinions as well as governance considerations within a UK context. Gwen is one of several CTR staff who have pursued part-time doctoral studies alongside their 'day job'.

South West Research Hub Event Meeting

The 2nd South West Research Hub meeting was hosted by the Centre for Trials Research on Thursday 5th September 2019 in Cardiff University's Glamorgan Building. This year's theme was Trial Methodology. There were around 60 delegates from across the South West region and G4 partnership, including The Centre for Trials Research, Bristol Randomised Trials Collaboration (BRTC), Clinical Trials and Evaluation Unit (CTEU) Bristol, Peninsula Clinical Trials Unit (PenCTU) Plymouth, Swansea Trials Unit and Exeter Clinical Trials Unit (ExeCTU) / University of Exeter.

International Clinical Trials Methodology Conference

Centre staff contributed to the 5th International Clinical Trials Methodology Conference (ICTMC) at Brighton.

The Centre was represented by four speakers at the ICTMC conference.

Kerry Hood and Cheney Drew presented the TRIDENT study. TRIDENT (funded by RfPPB) is particularly innovative in that it was designed to set standards for the evaluation of novel therapeutics in HD and other neurodegenerative disorders.

Vicky Shepherd presented on her work developing an intervention to support informed decision-making by family members of adults who lack capacity to consent to trials. Fiona Lugg-Widger spoke of her work which has involved developing materials to inform and engage with the public about research using routine data, which has culminated in the production of animation. Finally, Mike Robling presented on the challenges of working with healthcare data provided by NHS Digital when intending to share such data in subsequent individual participant data metanalysis or secondary analyses. In addition, several research posters were presented by Centre staff.

Our focus on methods development and sharing best practice and innovation which has then culminated in both leading presentations at the ICTMC event is directly linked to our work programme Ensuring Methodological and Professional Development.

Cardiff University Excellence in Teaching Award

The intercalated teaching course won an excellence in teaching award at Surgam 2020 which celebrate the achievements and high calibre of teaching provided by staff and NHS partners. CTR staff contribute to several research modules in this course in addition to supervising student projects and is especially valuable for early career researchers gaining teaching experience.

Cancer Research UK Annual Reception Event

Sarah Bridges attended this event to represent the CTR. The event highlighted to Senedd Cymru (Welsh Parliament) the work Cancer Research UK funds in Wales, so it was really great that the CTR was represented at the event. The Centre was mentioned by AM Janet Finch-Saunders in her speech:

“Last year we spent £4 million on research in Wales. As you can see from our exhibitors today, Cancer Research UK supports the Centre for Trials Research at Cardiff.”

United Nations Convention on the Rights of the Child

The Centre for Trials Research and DECIPHer jointly exhibited at the 30th anniversary celebration of the United Nations Convention on the Rights of the Child (UNCRC) at the Mercure Hotel, Cardiff. This event was attended by the Children's Commissioner for Wales, Sally Holland, Julie Morgan AM and the Wales First Minister, Mark Drakeford. It was also attended by a large number of both primary and secondary school children from across Wales (including a steel band from Fitzalan High School) as well as various delegates from a range of local authority, third sector and private organisations. Our stand focused on the work we undertake involving children and young people in research. CTR is a partner with DECIPHer and our researchers work with their ALPHA group (of 14-24 year olds) in developing and implementing research involving children and young people.

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



Over the year the team has received 117 requests for support and there have been 25 submissions for funding. There are four applications which have been successful this year with a total funding value of £993,780.

The Research Design and Conduct Service (RDCS) South East Wales has run their three regular events throughout 2019: 'Developing a research idea' in April, 'Building blocks of a competitive grant application' in June and the 'Grant writing' day in September. These events have attracted attendees from across nine NHS organisations in Wales and four all-Wales health and social care services – All Wales Genetic Service, Rural Health and Care Wales, Social Care Wales and Carers Trust. There has been a diverse range of specialties represented at all the open events e.g. at the grant writing day the delegates worked on nine distinct project ideas across mental health, primary care, microbiology, sexual health, epidemiology, social care and public health.

We have been involved in several targeted events: We attended the All Wales Reproductive and Childbirth Research Forum, a group led by Professor Julia Sanders in her role of Health and Care Research Wales speciality lead, to support the development of a large funding application and we have held a bespoke consultation event for midwives working in Aneurin Bevan University Health Board (UHB).

In October we provided a bespoke group consultation for Public Health Wales in connection with the NHS Research time award scheme. At the end of November, RDCS consultant Philip Pallmann presented at a collaborative research workshop entitled "Biomaterials: From Bench to Bedside" hosted by the Cardiff Institute of Tissue Engineering and Repair (CITER) and the Cardiff Materials Research Network (CMRN). The aim of this workshop was to help researchers translate their biomaterial technologies into the clinic for patient benefit, and especially to familiarise them with funding routes for clinical studies and where they can get support, including from RDCS.

The team has had exhibitor stands at a range of conferences including RCBC (Research Building Capacity Collaboration) Wales in May, Aneurin Bevan research and development (R&D) conference in June, Health and Care Research Wales Clinical Academic Forum in July, Healthcare Sciences in September, Cardiff and Vale UHB R&D conference and Health and Care Research Wales annual conference in October, Cwm Taf Morgannwg UHB R&D conference in November.

There have been two All-Wales RDCS and Welsh Health Economics Support Service (WHESS) meetings, one by audio-conference and the October meeting was held in Bangor. Alongside regular business, the focus of discussions was on the new Research for Patient and Public Benefit (RfPPB) format, recommissioning and plans for the future including streamlining meetings.

The South East Wales RDCS Steering group, with representation from organisations across health and social care, met in February to review the progress of the service over the last year and discuss the plans for the service as it moves into the new funding period.

The service supported 12 teams in their applications to the stage 1 of the RfPPB call and continues to work with the seven teams who were invited to submit a stage 2 application. These are lead from five different NHS organisations (Aneurin Bevan UHB, Cardiff and Vale UHB, Powys Teaching Health Board (THB), Velindre NHS Trust and Wales Ambulance Service NHS Trust).

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.

117

requests for RDCS consultant support



25

individuals submit research funding applications



Clients from

5

Health Boards in Wales



Successful funding applications total

£993,780



4

successful applications



Engagement



Health and Care Research Wales annual conference

RCBC Wales

Health and Care Research Wales Clinical Academic Forum

Cardiff and Vale UHB Research and Development conference

Cwm Taf Morgannwg UHB Research and Development conference

Aneurin Bevan UHB Research and Development conference

Healthcare Sciences conference



Supporting Research Capacity Building

- ✓ All Wales Reproductive and Childbirth Research Forum
- ✓ Cardiff Institute of Tissue Engineering and Repair (CITER) and the Cardiff Materials Research Network (CMRN)
- ✓ Public Health Wales bespoke event
- ✓ Bespoke event for Aneurin Bevan UHB midwives



Conclusion

The last and final year of the current Health and Care Research Wales funding period has as always been a busy and productive time for our researchers and investigators.

We have developed a range of new risk proportionate, and green initiatives to align with our goal of efficiency in research.

We have expanded our focus on public and patient involvement in research working with our newly formed Public Involvement and Engagement Hub whilst continuing with our core business of bringing together teams to win grant funding. Public involvement and engagement is now fully embedded across the Centre with public involvement fully normalised as part of our study and trial activities.

During this year we underwent the 5-year recommissioning process, alongside developing new and continued collaborations, and submitting further bids to Health and Care Research Wales.

As highlighted in this report, we have opened several major studies and a range of ongoing studies have reported results. We have continued to increase the numbers of postgraduate research students and fellows working alongside our trials and studies.

A core focus over the last year which has been very timely is that we initiated working towards becoming a greener clinical trials unit. This involved investment in remote working facilities, which have served us well as the global COVID-19 pandemic took hold in March.

Looking forward

The Centre for Trials Research has established itself at the cutting edge of complex and challenging trials, both methodologically and clinically. Its vision is to design and deliver internationally excellent, locally relevant research in health and social care, using novel and efficient methods.

The CTR was created in 2015 by the merger of three UKCRC registered CTUs with a mission to improve the health and wellbeing of society through trials and other well-designed research. The creation of the Centre has increased the critical mass of expertise in trials of medicinal products, early phase trials and novel trial designs, and both broadened and strengthened the range of skills we have to offer our partners in research. Over the next five years we will focus on ensuring our staff provide sustained benefit to the people of Wales in terms of their health and wellbeing, as well as the economy. A key part of this will be that we maximise the value of investment in research by ensuring we deliver studies as efficiently as possible, but also that our research truly changes lives by informing policy, practice and the general public.

Our strategic aim over the next five years is to be at the forefront of the changing nature of trials in health and social care, by maximising secondary use of existing data, driving efficiency in design and conduct, and even greater utilisation of novel trial designs. We will deliver this whilst continuing to grow our international reputation in the four areas of Cancer; Infections, Inflammation and Immunity; Mind, Brain and Neuroscience and Population Health. Within each of these areas we will both deliver major new studies and develop new chief investigators and methodologists, to ensure that we are providing the evidence required now by the population of Wales as well as equipping early career researchers with the skills to deliver the evidence of the future.

This aim will be achieved by maintaining and developing active and constructive partnerships within Wales with patients and the public, staff in the NHS and social care, other elements of the Health and Care Research Wales infrastructure, practitioners, policy makers in Wales and beyond, third sector and industry. We will also actively develop and engage in partnerships across the UK and internationally.

We will continue to support the development of staff in health and social care services by delivering a proactive and responsive advisory support service and contribute to the growing research culture in our partner organisations across Wales.

“Working with the Centre for Trials Research has been invaluable in securing grant funding and running a multi-centre randomised controlled trial. The Centre provides the Chief Investigator with support from day to day dealing with the funder and the recruiting sites, to regulatory approvals, finance and budgeting, sponsorship, industry liaison, and all the other bureaucracy around clinical trials.

The trial manager is the first point of contact for these issues, and deals with them on a day to day basis, thus allowing the Chief Investigator to focus on the research. Any new Chief Investigator or Principal Investigator wants to know that their research is of the highest quality, and they don't have to be bogged down with the administrative aspects of running a randomised controlled trial (RCT).

Working with the Centre gives me absolute confidence that the RCT is being conducted to the highest standards, and that the final results will be used to inform clinical practice, safe in the knowledge that current best practice in trial management has been followed throughout.”

Professor Enitan Carrol,
University of Liverpool

Chief Investigator: BATCH, PRECISE



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 “lay reps” 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.

Thank you to Seth Oliver / www.fizzievents.com / @relationalsoup for kind permission to use photos from the LEAP-MS co-production event.

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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