Centre for Trials Research
Canolfan Ymchwil Treialon

Annual Report 2023/24

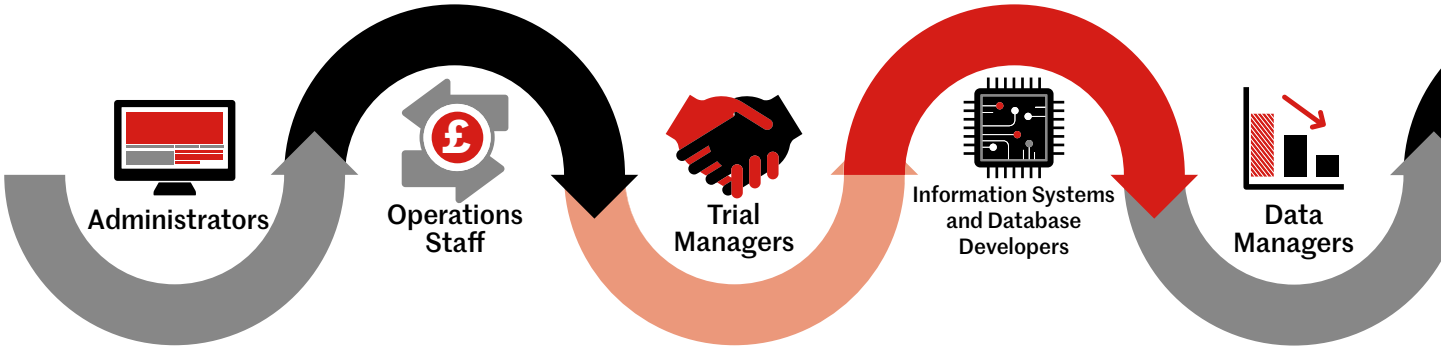
Ymchwil Iechyd a Gofal Cymru
Health and Care Research Wales

Ariennir gan Lywodraeth Cymru
Funded by Welsh Government

CANCER RESEARCH UK

www.cardiff.ac.uk/centre-for-trials-research

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

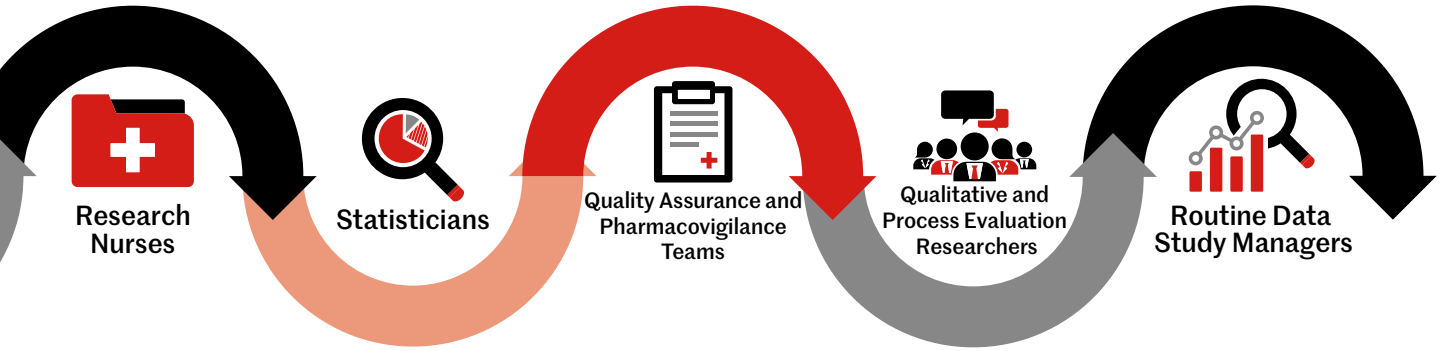


Contents

Glossary

AML	Acute Myeloid Leukaemia
CARE	The Centre for Adult Social Care Research
CI	Chief Investigator
CTR	Centre for Trials Research
CTU	Clinical trials unit
CU	Cardiff University
HTA	Health Technology Assessment
NIHR	National Institute for Health Research
PPI	Patient and public involvement
RCT	Randomised Controlled Trial
UCL	University College London
WTE	Whole Time Equivalent

This document contains hyperlinks for electronic version, and therefore not available for paper version.



Executive summary

Trials epitomise team science. We bring together the multiple stakeholders needed to provide robust answers to the questions of most importance to service users.

Yet again, this is reflected in appointments to key leadership roles within our Centre and a large number of recent promotions, awards and academic achievements. 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 existing and new partnerships with research centres across Wales and further afield, leadership in national and international methodological networks, excellent first year progress with our Treialon Cymru programme which connects Wales-based health and care practitioners with the Centre, and international connections supporting research capacity building.

The studies we feature reflect talent drawn from across Wales and beyond, as well as across all our Divisional and methodological teams.

The Centre's performance last year was remarkable and reflects huge credit to our team. We have published 129 peer-reviewed papers and the CTR team have led 48 grant submissions, and collaborated on 105 in total. Submissions led by our group have generated over £18M of funding, considerably higher than in any previous year of our current award from Health and Care Research Wales. Of this, £14M supports 163 WTE staff working in Wales - our previous highest amount was 100. With a total of over £27M grant funding awarded in the last 12 months for CTR adopted studies, we have 19 awards to Welsh chief investigators and project funded income supporting 134.51 WTE Centre staff.

This level of performance is based upon the core support of our funders, Health and Care Research Wales, Cancer Research UK and Cardiff University. More than that, it is the product of the expertise, entrepreneurship, hard work and tenacity of our teams and the fruitful partnerships that we have forged with collaborators over time and across disciplinary and organisational settings. It is even more remarkable when this has been achieved in the context of financial upheaval locally and nationally for universities and when key teams in CTR have worked under high pressure in the last twelve months. The very long list of staff successes flagged later in this report further demonstrates how the Centre's continued success is so much the result of collective excellence across every level of our organisation.

The Centre aims to drive excellence in trials and other well-designed studies, across broad research themes led by our divisions and across settings. We highlight studies that represent that diversity of methodological approach. Our report features studies in healthcare, public health, education, social care, in local, national and international settings, with populations of patients and care service users. Our studies span developmental work to explore novel interventions and novel methods, through to interventional trials or observational studies to provide convincing evidence of effectiveness. Threaded through so much of our work is our intent to address health inequality and promote meaningful inclusivity in our approach to research. Therefore, it is particularly pleasing to see the recent launch of the Centre's **inclusivity in studies web page** which brings together our expertise in this area to support better practice.

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

Dr David Gillespie
Director, Infection, Inflammation and Immunity Division

Professor Mike Robling
Director, Population Health and Social Care 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 well-being 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 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

Co-Directors are Professor Mike Robling and Professor Richard Adams. They are supported by a Divisional Directorial team including: Dr Rachel McNamara and Dr Cheney Drew (Brain Health & Mental Wellbeing Division), Angela Casbard (Cancer Division), Dr David Gillespie and Dr Emma Thomas-Jones (Infection, Inflammation & Immunity Division), Professor Jamie White (Population Health & Social Care Division). Our extended senior leadership team includes Dr Sue Channon (Treialon Cymru) and Dr Rebecca Playle (Statistics), Damian McAuliffe (Centre Management and Professional Services), Dr Lucy Brookes-Howell (Qualitative Research Group), Dr Fiona Lugg Widger (Routine Data), Dr Victoria Shepherd (Research Nurses and Inclusivity). Dr Rachel Lowe (Trial Management), Nigel Kirby (Data Management), Gareth Watson (Information Systems and Technology Solutions), Kelly Gee (Quality Assurance and Regulatory Affairs).

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

Making a difference
Improving health, wellbeing and sustainability of society

Innovating and researching
Empowered to be creative and questioning in everything we do

Building trust and confidence
Growing together as partners

Leading and collaborating
Developing true partnerships (nobody wins unless everybody wins)

Aspiring and inspiring
Helping everyone to be their best and to do their best

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

Respecting individuality
Recognising different needs and aspirations of every individual in society

Recognising
Celebrating success, openness and transparency

Centre for Trials Research Directors

Professor Mike Robling
Co-Director, Centre for Trials Research

Director, Population Health and Social Care Division

Professor Richard Adams
Co-Director, Centre for Trials Research

Director, Cancer Division

Dr Rachel McNamara
Director, Brain Health and Mental Wellbeing 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

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.

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:
Development of All Wales approach

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

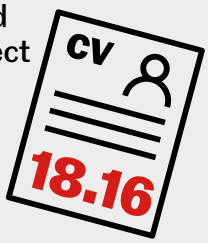
Reporting period: 2023/2024

Health and Care Research Wales Infrastructure award to the group

Direct funding awarded

£997,027

Jobs created through direct funding



Grants won during reporting period

Grants won	Led by group	Group collaborating
Number	16	18
Value	£18,121,078	£9,748,439
Funding to Wales	£14,382,439	£5,103,355
Funding to group	£12,842,319	£2,603,435
Additional jobs created for Wales	163.06	69.27
Additional jobs created for group	159.99	33.96

Number of publications

Number of public engagement events

Number of public involvement opportunities

Clinical Trials Unit metrics

34
Number of studies awarded

19
Number of studies led by Welsh Chief Investigators

3,912
Total number of participants recruited

27.89
% participants from Wales

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Work Package 1
Managing our work

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

Our successes are due to the skills of the individuals working in the CTR amplified by the team structure to which they all form a part.

Over the last year the strength of some of these individuals has been highlighted and recognised in successful appointments, promotions and awards, which include:

Academic Promotions:

- Dr Julia Townson to Principal Research Fellow
- Dr Cheney Drew to Senior Research Fellow
- Dr Fiona Lugg-Widger to Senior Research Fellow

Centre for Trials Research Appointments:

- Dr Rachel Lowe became Head of Trial Management.
- Dr Cheney Drew became Deputy Director of Brain Health and Mental Wellbeing Trials.
- Dr Fiona-Lugg Widger became Deputy Director for Data.
- Robert Trubey and Kim Munnery appointed to our two new Routine Data Study Manager posts.

Cardiff University Celebrating Excellence Awards:

- Dr Rebecca Cannings-John: runner-up, Excellence in Research
- Martina Svobodova: runner-up, Excellence in Civic Mission

School of Medicine Postgraduate Research Student Excellence Awards:

- Dr Dave Gillespie: winner, PGR Supervisor of the Year
- Dr Adam DN Williams: winner, Professor Lesley Jones PGR Excellence Award
- Dr Tim Pickles: nominee, Innovation Award

There has been significant change over the last year, including a change in Directorial leadership with Prof Kerry Hood moving to Dean of Research for a 3-year secondment and Prof Mike Robling and Prof Richard Adams moving to a Co-director model of leadership for the CTR. This has occurred during a more challenging financial time for all, requiring us to make changes and adaptations to our staffing structure as our core funding has reduced. Despite this the team have been hugely successful in both delivering their current trial/studies portfolio as well as grant writing and capture, which in line with our centre strategy will ensure our sustainability for the future.

We appointed Dr Fiona Lugg-Widger as the Centre's Deputy Director for Data. This senior role will have broad oversight for data strategy in the Centre, including for routine data. This has involved developing our new routine data study manager team – research associates and fellows with methods expertise in randomised and observational study designs using routine data. Currently we have about forty active studies in the Centre making use of routine data, including those which explore the methodologies and system required to make best and ethical use of such data in research.

Whilst delivering our work we have managed to develop new areas and expand our expertise, including: Global Health with the SunPad study in Nepal, and our "inclusivity" in trials group. We have developed the first trial in the RedCAP database for a highly regulated and complex Investigational Medicinal Product (IMP) trial "PICCOS". We have been working more closely and collaboratively across the UK but also more regionally through the GW4 initiative with universities in Bath, Bristol and Exeter.

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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 to bring forward new research. In this year's report, we focus on three projects to demonstrate locally driven innovation with national and international research and enabled by partnerships across academic, public, private and third sectors.

SunPad

SunPad is a washable menstrual pad with self-sanitising technology – a technology developed locally in Cardiff and now being trialled in rural communities in Nepal through a partnership with the Centre for Trials Research. SunPad contains a mineral based coating which when dried in the sun enables the coating to stimulate a self-sanitising effect which eliminates 99.9% bacteria. This underlying power of photocatalysis also eliminates odours and stains on the pad. SunPad is a finalist for the Royal Society of Chemistry's Emerging Technologies prize, 2024.

Globally, 500 million people who menstruate do not have access to adequate menstrual health and hygiene. This results in missed education, reduced work opportunities and increases gender disparity. SunPad was designed to create safer periods for all.

It uses sustainable and affordable components to enable local manufacture. It is a technology that is then easy to use, and does not need soap or clean water to successfully work.

The SunPad research project is funded by The Gates Foundation and is led by Dr Jennifer Edwards. The study sits across three of Cardiff University's schools: Chemistry, Medicine, and Pharmacy. The project has partner organisations in Nepal, an NGO; Global Action Nepal, an academic institution; Tribhuvan University and a local manufacturer of washable menstrual pads; Krish Proudel. The research team are fostering collaborations with a local women's co-operative group to provide additional public involvement and engagement, essential to optimising this research. In Nepal the team are conducting three streams of research including a pilot study of SunPad, focus groups with menstruators and healthcare workers and collection and analysis of used pads (non-SunPad) to inform the pilot duration.

SunPad is a fantastic example of a successful global multi-disciplinary collaboration and is rapidly attracting momentum and interest in engagement across the world. Following successful implementation and evaluation of SunPad, this has the potential to make a global impact on period poverty, reducing infection, reducing global disparity, and improving dignity and quality of life for menstruators.

QuicDNA

So much of our work is located in the NHS setting and featuring partnership working with both NHS and industry collaborators. The QuicDNA study is prime example of innovation in this collaborative space and its success was reflected at the MediWales Innovation Awards in December 2023, where the programme won the 'NHS Wales working with Industry' category.

The All-Wales Medical Genomics Service at Cardiff and Vale University Health Board and industry partner, Illumina developed a ground-breaking liquid biopsy test. The test uses circulating tumour DNA for rapid cancer genome identification. This provides the potential to bypass invasive tissue biopsies in the future. This innovation, part of the QuicDNA project, accelerates access to targeted cancer treatments, with its aim to improve patient outcomes. QuicDNA addresses the lengthy diagnostic pathway for lung cancer, aiming to deliver faster diagnostic testing in line with recommended national standards. The project has already delivered targeted treatments to lung cancer patients and will result in cost savings by reducing the need for repeat biopsies. This is particularly important for patients in Wales, where lung cancer remains the leading cause of cancer-related deaths. In Wales, patients often present late, with more advanced cancer which reduces their likelihood of one-year survival.

QuicDNA is an example of effective industry-health collaboration, aligning with the Welsh Government's vision for health and social care, and could become a standard diagnostic approach in NHS within the UK. Key industry partners include Illumina, Astra Zeneca, Amgen, Roche, with further support from the Craig Maxwell foundation, Velindre Charities and Moondance. QuicDNA was recognised for its efforts in bringing together industry partners to support the implementation and evaluation of pioneering liquid biopsy technology for lung cancer patients across Health Boards in Wales. The study is led by Dr Magda Meissner, a senior lecturer at Cardiff University and medical oncologist at Velindre Cancer Centre in Cardiff.

School-level Digital Dashboard

A research team led by Dr Jeremy Segrott from CTR has worked with the School Health Research Network (SHRN) and DECIPHer (Cardiff University, School of Social Sciences) to develop an innovative school-level digital dashboard. Their innovation has been recognised through the award of a prestigious **Wellcome Mental Health Data Prize**.

Jeremy and the team developed the digital dashboard to empower schools to use bespoke data to create environments that promote good mental and physical health. The School Level Dashboard was developed as part of a Mental Health Data Prize Project, funded by Wellcome. Every two years, SHRN conducts a national survey of student health and wellbeing in secondary schools across Wales. In 2021/22 the survey was completed by approximately 125,000 11- to 16-year-olds across 202 schools in Wales, approximately 95% of all maintained secondary schools.

The developed and now functioning dashboard enables each school to view their own data in different ways and to use it to inform how they promote healthy school environments.

This means that schools can address their own specific needs. Data are presented to schools so that individual students cannot be identified but provides summaries displayed by year group and gender.

The SHRN survey covers a range of topics. These include wellbeing and emotional health, and key factors which shape them, such as school connectedness. The survey also records physical activity, diet, school life, substance use and misuse as well as sex and relationships. The SHRN survey forms part of the international Health Behaviour in School-aged Children (HBSC) survey. Every four years, health and wellbeing surveys in 49 countries use a common set of measures to assess the health and wellbeing of young people. The School Health Research Network in Wales is one of these 49 surveys. The Dashboard therefore has strong potential to be used by other researchers across many countries. Our longstanding partnership with SHRN and DECPIHer is reflected in a number of key researcher posts that sit across both Centres, including Jeremy's.

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Work Package 3
Developing new studies

Designing new studies and winning the funding to make them happen

In this section we tell you about some of our new studies. These are drawn from across all four of our divisions and reflect some of our longest established research themes as well as newly emergent areas of focus. Featured studies reflect building programmes of research over several projects led by external local and nationally based investigators as well as those led from within the Centre by our own researchers.

Brain Health and Mental Wellbeing Division

Risk stratification for early-onset major depressive disorder

Chief Investigator:
Professor Frances Rice, Cardiff University

Funder: Wellcome Trust

Our Centre is collaborating with the Wolfson Centre for Young People's Mental Health and with colleagues across the UK, Denmark and the Unites States, on a grant awarded by the Wellcome Trust. The aim of the project is to identify children and young people whose parents have a history of mental illness and who may be at high risk of early-onset depression as a result. The project will develop a scalable risk stratification model. This can then be used to prioritise access to early intervention for those most at risk. We will test response to early-intervention in an already funded trial.
We will collaborate with lived experience experts and clinicians to ensure the risk stratification tool is acceptable and develop implementation guidance together.

Evaluating the feasibility of a samba percussion intervention for people with Parkinson's disease

Chief Investigators: Dr Cheney Drew, Dr Katy Hamana, Cardiff University

Funder: Jacques and Gloria Gossweiler Foundation

Parkinson's Disease (PD) affects areas of the brain important for regulating movement, thinking, mood, sleep and pain. Available treatments reduce some of these symptoms but are not able to stop their decline. Physical activity or repetitive beats to music (rhythmic auditory stimulation) can help PD symptoms in a clinic setting. We now want to test this in a community setting. We will perform a clinical evaluation of a community-based samba percussion activity (SParky Samba) for people with PD to see if it has potential to improve health outcomes and wellbeing. The first step will be to understand, through observations and interviews, what the key parts of SParky Samba are. Secondly, we will undertake a feasibility trial of SParky Samba in people with early to midstage PD in Wales. We will recruit 60 participants randomised to attend a SParky Samba group or a coffee morning for 12 weeks. We will measure movement, thinking and wellbeing at the beginning and end of 12 weeks. Results will inform a future larger trial.

Cancer Division

Optimise-FLT3: Optimising therapy for patients with FLT3-mutated Acute Myeloid Leukaemia

Chief Investigators: Professor Stephen Knapper (Cardiff University), Professor Richard Dillon (King's College, London)

Funder: Cancer Research UK

Acute myeloid leukaemia (AML) is an aggressive blood cancer and is the commonest form of acute leukaemia in adults. AML affects more than 3000 people per year in the UK, the majority of whom will die from the disease. Younger and fitter patients can have treatment aiming to cure the disease. The addition of various new targeted drugs for patients in specific AML sub-groups, has the potential to increase survival rates further. The OPTIMISE-FLT3 study focuses on a subgroup of patients with AML with mutations in the FLT3 gene, found in about one-third of AML patients. Clinical trials in recent years have identified several promising strategies to improve outcomes for patients with FLT3 AML including using an intensified three drug chemotherapy protocol called FLAG-Ida, adding a drug called midostaurin to inactivate FLT3, and adding a chemotherapy linked-antibody called Gemtuzumab Ozogamicin (also called GO or Mylotarg). However, these approaches have not yet been combined in a single trial.

The Optimise-FLT3 trial wants to establish the best way to treat FLT3 AML. We will compare standard treatment (called standardised intensity chemotherapy or DA) with two new combinations. Over four years, 390 newly diagnosed patients at hospitals around the UK and in partner countries will be randomly allocated to receive one of the three treatment schedules. The response of the leukaemia to treatment will be measured by standard tests of the blood and bone marrow to see whether patient outcomes are improved in terms of increased survival, reduction in rates of relapse and reduction in the need for stem cell ("Bone marrow") transplant. We will monitor for any increased side effects associated with the intensified treatment schedules. The trial is led by Professor Steve Knapper, also of Cardiff University and received funding from Cancer Research UK in 2024. The study is due to open later this year.

Infection, Inflammation and Immunity Division

VESPER: IntraVESical Preparations for Recurrent Urinary TrAct Infection Prevention

A multi- arm, multi-site open label randomised superiority trial

Chief Investigator: Professor Chris Harding (Newcastle University/Newcastle Hospitals NHS Foundation Trust)

Funder: NIHR Health Technology Assessment

For some women who suffer from recurrent uncomplicated urinary tract infections (UTI), first-line treatments for prevention do not work. The VESPER trial led by Professor Chris Harding seeks to find out how effective intravesical treatments – those that are delivered directly into the bladder (gentamicin or Glycosaminoglycan replacement compounds) - are at preventing subsequent infections when compared to standard second-line oral treatment. The study will also address whether one intravesical treatment is better than the other.

This study has been designed in response to a commissioning brief advertised by the NIHR and aims to recruit 412 participants across the UK. It is the second study the CTR have been involved with led by Professor Harding. The trial includes clinical, cost-effectiveness, and process evaluations, and incorporates a Sequential Multiple Assignment Randomised Trial (SMART) design. This means that participants who do not respond to their initial allocation can be re-randomised to another trial arm. This allows for the exploration of optimal treatment sequences which could lead to more personalised treatment plans following completion of the trial.

CLARITY: Change CLopidogrel and Aspirin after Revascularisation wIth angioplasTY for Chronic Limb Threatening Ischaemia (CLTI)

A pragmatic, adaptive multicentre open-label randomised trial

Chief Investigator: Mr Chris Twine (North Bristol NHS Trust/University of Bristol)

Host Institution: North Bristol NHS Trust

Funder: NIHR Health Technology Assessment

The CLARITY trial seeks to address the current lack of randomised controlled trial evidence for major antithrombotic regimens in UK clinical practice. The trial will examine the clinical and cost-effectiveness of three antithrombotic regimens following endovascular lower limb revascularisation for Chronic Limb Threatening Ischaemia (CLTI). This trial addresses six of the top 10 James Lind Alliance research priorities for Peripheral Arterial Disease (PAD) from the UK vascular surgery priority setting process. These include ‘What can be done to improve outcomes in CLTI?’, ‘How can we reduce progression of arterial disease?’ and ‘What is the optimal antiplatelet therapy following lower limb revascularisation?’ The CLARITY trial aims to recruit 1239 participants from about 20 sites in the UK and is the second study the CTR have been involved with led by Chris Twine. The trial includes a process evaluation, internal pilot and interim analysis using futility-stopping criteria. The adaptive design aims to improve trial efficiency by potentially dropping a less clinically effective arm early and redirecting resources to optimise patient care and recruitment.

Population Health and Social Care Division

OBS UK

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

Funder: NIHR Health Technology Assessment

The OBS UK study is jointly led by Dr Sarah Bell and Professor Peter Collins. It is funded by NIHR (£3.65M) to trial the effectiveness of a maternity quality improvement programme for reducing excess bleeding and the need for transfusion after childbirth. The study is fully coordinated by the Centre and builds on the success of the Obstetric Bleeding Strategy (OBS) Cymru programme led also by Prof Collins which launched in Wales in 2016. The treatment strategy aims to reduce excessive bleeding after childbirth and so far in Wales has seen a 29% reduction in massive postpartum haemorrhage and 160 women per year avoiding the need for a blood transfusion after birth. The programme includes a process for identifying women who are at high risk of bleeding, methods for early recognition and treatment of abnormal bleeding, and the identification of and early intervention for abnormalities in blood clotting.

The new trial aims to improve the quality of care for mothers and babies with a special focus on differences in care and outcomes for women of diverse ethnicities and backgrounds. The OBS UK study will include maternity units across Wales, Scotland, England and Northern Ireland as part of a major trial and be rolled out to 190,000 women over 30 months. Opening the study in February 2024 was a significant achievement as the stepped-wedge design required all 36 UK sites to be ready to open at the same time.

One of the aims of OBS UK is to examine excessive bleeding in relation to race, ethnicity and other elements of social diversity. Dr Julia Townson, a senior researcher in the Centre for Trials research said: *"Ensuring that the experiences of minority groups are included in this research is a major priority for the whole research team. As well as drawing on the personal experiences of individuals from minority groups, we will work with Egality Health, a community engagement agency focusing on improving inclusivity in health research."*

Spotlight on our Social Care Research

Social care research and research in social care settings has long been a feature of our work. Long-standing partnerships with Centres such as CASCADE (Children's Social Care) have been strengthened further with the first year of the new Centre for Adult Social Care Research – CARE. CARE is led from the School of Social Sciences, Cardiff University and CTR is a methodological partner, with two newly appointed research fellows in our Centre. This initiative sits alongside other capacity-building activity in some of our long-standing programmes, for example, research with populations of people with learning disabilities. Three examples illustrate recent progress:

A team led by Prof Sandy Toogood (Bangor University) and Prof Vasili Totsika (UCL) are evaluating the use of digital technology to facilitate active support for people with learning disabilities living in supported accommodation. Staff will use the trial app to provide consistent support to people with learning disabilities to enable them take part in activities of everyday life. Funded by NIHR Health Technology Assessment's research call focused on adaptation and assessment of digital technologies for social care, the study will establish the feasibility of running a larger-scale randomised controlled trial. The Centre team involved includes Dr Rachel McNamara and Dr Becky Playle.

A second example from the same NIHR funding stream is a study led by Prof Kylie Gray and Prof Richard Hastings (both University of Warwick). The study will establish the feasibility of using a randomised control trial design to evaluate an online parenting programme called Stepping Stones Triple P to support parents of children with intellectual disabilities. The study will explore the need for any additional guidance to support the online training, explore and address barriers to engaging with the online programme and establish key design features for a future trial such as how best to recruit and what outcomes should be assessed. The Centre team involved is led by Liz Randell.

A third example is a project evaluating the use of innovative assistive technology for people with dementia, led by Dr Roser Beneito-Montagut - a Reader in Cardiff University's School of Social Sciences. The project is supported by the Wales Innovation Network to develop a subsequent funding proposal to a national funder. It involves developing a network of organisations and individuals with a common interest in assistive technology in dementia care. Through workshops and other networking activities, the team are focused on how the potential benefits of novel technology can be achieved across the diverse spectrum of people who may live with dementia. As such, a key focus will be the reach of assistive technology across rural and urban environments and underrepresented people living with dementia, such as migrants, disabled, neurodivergent and LGBT+ groups. The Centre lead on the project is Dr Sofia Vougioukalou one of our new CARE research fellows

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Work Package 4
Overseeing funded studies

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

In this section we give an overview of how we oversee and deliver our funded studies to a high quality, producing outputs that will make a difference to the public.

Brain Health and Mental Wellbeing Division

STORM: Digital adaptation of the Standing up for Myself intervention in young people and adults with intellectual disabilities

Chief Investigator: Professor Katrina Scor

Funder: NIHR Public Health Research Programme

The STORM programme is a group intervention for young people and adults aged 16+ years with mild to moderate intellectual disability. Stigma contributes to the negative social conditions persons with intellectual disabilities are exposed to, and STORM is designed to help people discuss stigmatising encounters in a safe and supportive setting to increase self-efficacy in managing and resisting stigma.

The final report on the STORM programme has now been published by NIHR here.

Watch Me Play: A feasibility study of a remotely-delivered intervention to promote mental health resilience for children

Chief Investigators: Dr E Kennedy (Tavistock and Portman NHS Foundation Trust), Professor Vaso Totsika (University College London)

Funder: Foundations – What Works Centre for Children and Families

The Centre for Trials Research and the Tavistock and Portman NHS Foundation Trust are conducting a feasibility study of an intervention called Watch me Play (WMP). WMP is an early intervention programme for parents/caregivers of babies or young children and aims to protect children's mental health by enhancing child development and caregiver-child relationships. WMP involves a parent/caregiver watching their child play and talking to their child about their play for up to 20 minutes (one session). Some longer sessions are facilitated by a trained practitioner who joins the parent/caregiver in watching the child or baby either in-person or online, providing prompts to the parent/caregiver where necessary. This study aims to gain a better understanding of how parents/caregivers engage with WMP to inform a future randomised trial. We have recruited 21 parents/caregivers of children aged 0 to 8 years from early years and children's services across the UK, all of whom were offered WMP. We have now completed recruitment and analysis and submitted the final report to the funder.

Cancer Division

SCC-After: Adjuvant radiotherapy in patients with high-risk primary cutaneous Squamous Cell Carcinoma after surgery

Chief Investigator: Agata Rembielak Christie Hospital University NHS trust

Host institution: Cardiff University

Funder: NIHR Health Technology Assessment

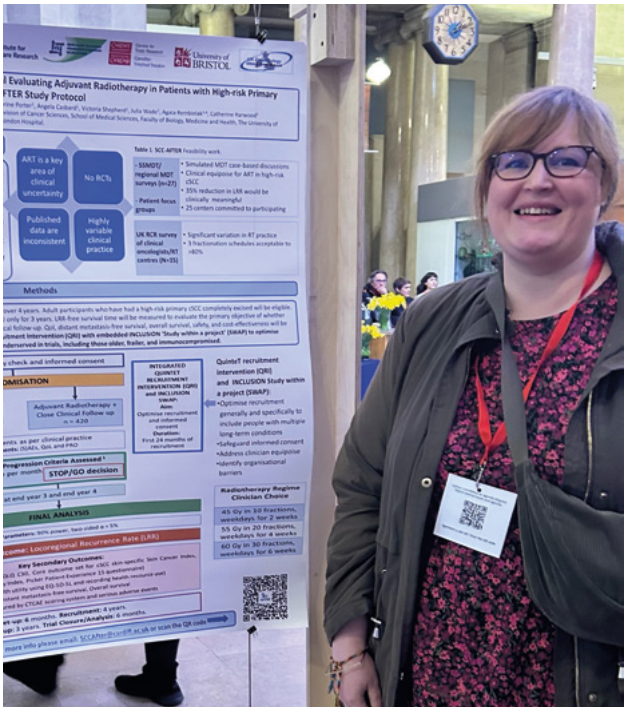
Cutaneous squamous cell carcinoma (cSCC) is a common skin cancer. In most cases it can be cured by surgery, however it can reappear in the skin where it started and/or in nearby lymph glands. This recurrence happens in about 1 in 3 people with cSCCs that are larger, have involved the nearby nerves, and/or, grown beyond the fat layer of the skin (referred to as "high-risk cSCCs"). Patients whose cSCC reappears can experience a big reduction in their quality of life.

Recurrence after surgery is often due to skin cancer cells being unknowingly left behind or cancer cells breaking away into the surrounding skin. Extra treatment such as radiotherapy to the area where the cancer was removed might destroy any remaining cancer cells, however we are not sure if this definitely helps prevent cSCC from reappearing. Despite this, some hospitals are using radiotherapy to treat high-risk cSCC after surgery.

SCC-After aims to answer the question of whether radiotherapy is helpful and better than not using radiotherapy for reducing recurrence of high-risk cSCC after surgery. Following surgery participants with a high-risk cSCC will be randomly allocated to either:

- a course of radiotherapy and close clinical follow-up;
- close clinical follow-up alone.

Both are current treatment options within the NHS for cSCC.



We will monitor all patients for cancer recurrence, treatment side effects and quality of life. If our study shows radiotherapy is effective in preventing recurrence of cSCC, we will be able to recommend its use as a routine NHS treatment.

A particular focus of this trial will be to explore the inclusion of patients with dementia who are routinely omitted from such interventional trials and may well have very different needs from those patients without dementia. By including these patients we hope that the results of this trial will be applicable to this growing group and help inform future treatment choices most effectively.

Approximately 840 patients will be recruited to the study and will be conducted across 25 UK centres.

Infection, Inflammation and Immunity Division

PEACH: Procalcitonin Evaluation of Antibiotic use in COVID-19 Hospitalised patients

Chief Investigators: Dr Jonathan Sandoe (University of Leeds), Professor Enitan Carrol (University of Liverpool)

Funder: NIHR COVID Recovery and Learning Call

The PEACH study built on the existing collaboration between the CTR and the University of Liverpool, and forged a new working relationship with the University of Leeds to deliver a mixed methods study comprising quantitative, qualitative, and health economic work packages that assessed whether the use of a Procalcitonin (PCT) test, (a blood test specific for bacterial infection), was useful in guiding antibiotic prescribing, and whether it safely reduced antibiotic use among patients who were hospitalised and suffered with COVID-19 during the first wave of the pandemic - in order to inform care during any subsequent waves of infection, and to make interim recommendations using the best available evidence.

For the main, quantitative work package, a multi-centre, retrospective, cohort study was conducted, using patient-level clinical data from patients at 11 acute hospital Trusts/Health Boards in England and Wales. Data from 5960 patients was analysed.

The summary findings of all work packages in the PEACH study can be seen here.

Baseline PCT testing was associated with a statistically significant reduction in antibiotic prescribing in hospitalised patients with COVID-19, so PCT appears to have supported antimicrobial stewardship during the first wave of the pandemic.

There was no impact on mortality or hospital/Intensive Care Unit length of stay, or resistant secondary bacterial infections. Collectively, this work highlights the need for adaptive, inclusive, wide-reaching trials of infection diagnostics to assess clinical utility before routine introduction into clinical practice.

AZTEC: The Azithromycin therapy for Chronic Lung Disease of Prematurity

Chief Investigator: Professor Sailesh Kotecha

Host institution: Cardiff University

Funder: NIHR Health Technology Assessment

The analysis of the clinical outcomes for the AZTEC study finished at the beginning of 2024, and the results have now been published in The Lancet Respiratory Medicine. AZTEC is the largest clinical trial in the world for azithromycin and chronic lung diseases in very and extremely preterm babies. The trial has provided definitive answers to whether azithromycin can decrease rates of chronic lung disease in prematurely born babies. The trial involved the recruitment of 796 babies born at less than 30 weeks' gestation from 28 neonatal intensive care units across the UK. AZTEC was a collaboration between Cardiff University's School of Medicine, the Centre for Trials Research as well as from University of Leicester, Imperial College London, University College London, University of Liverpool and Newcastle University. While the trial did not conclude that azithromycin is effective at preventing chronic lung disease in this population, follow-on work will explore its effects on longer term respiratory and neurological health.

Population Health and Social Care Division

POOL: Maternal and neonatal outcomes among spontaneous vaginal births occurring in or out of water following intrapartum water immersion

Chief Investigator: Professor Julia Sanders, School of Healthcare Sciences, Cardiff University

Funder: NIHR Health Technology Assessment

The POOL cohort study was led by Professor Julia Sanders at Cardiff University's School of Healthcare Sciences. It was funded by the NIHR HTA programme to address the question of whether for women with an uncomplicated pregnancy, having a waterbirth is as safe for them and their babies as leaving the water before birth. The POOL research team was based in the Centre and looked at the birth experiences of over 87,000 women with an uncomplicated pregnancy who used water immersion during labour for comfort and pain relief. This involved 26 NHS organisations in England and Wales. The team looked at rates of severe tears experienced by women, rates of babies needing antibiotics or help with breathing on a neonatal unit, as well as the rates of babies dying.

The main results were published in the British Journal of Obstetrics and Gynaecology and showed that rates of both maternal and infant complications were comparable for births in and out of water. The study found that around 1 in 20 first time mothers, and 1 in 100 mothers having their second, third or fourth baby, had a severe tear. Around 3 in every 100 babies needed antibiotics or help with their breathing on a neonatal unit after birth, and baby deaths were rare.

Professor Sanders commented: 'Our research was able to scientifically establish that giving birth in water was not associated with an increase in risk for mother and baby. By investigating NHS data from over 87,000 births in England and Wales, we have been able to provide information that can empower and support mothers and midwives when making decisions during labour.'

SWIS: Social workers in Schools Trial

An evaluation of school-based work

Chief Investigator: Dr David Westlake, CASCADE, Cardiff University

Funder: Department for Education through the What works centre for children's social care

The SWIS trial builds on a long-standing collaboration between the CTR and CASCADE. SWIS was one of the largest school based RCTs ever undertaken. It compared the effectiveness of having a social worker present in a school (intervention) versus usual child safeguarding services (control) in 291 secondary schools, comprising 278,858 children across 21 local authorities in England. The intervention was implemented well and acceptable to students, teachers and social workers. There was no evidence of benefit from the SWIS intervention on the primary outcome: the rate of section 47 enquiries. There was also no evidence of benefit on the secondary outcomes, nor was the intervention cost effective. The Department for Education have cited the SWIS trial in their decision not to roll out SWIS, in the UK.

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Work Package 5

Ensuring methodological and professional development

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

We have had a busy year with new appointments and several professional developments for team members; broadening and enhancing the methodological strengths, offered by the CTR.

Sadly, we have lost some members to external roles but have retained strong ongoing collaborations and affiliations. Some of our individual successes are highlighted below:

Dr Eleni Glarou achieved her PhD award

Eleni's PhD is called 'Understanding multi-party communication in therapy sessions for autistic children'. She used a qualitative method called discourse analysis to look at video recordings of actual therapy sessions collected as part of the SenITA trial. Eleni looked at how autistic children, parents and Occupational Therapists communicate with each other, how they gain rapport, etc. The PhD was funded by the School of Medicine, and Eleni was based in and supported by staff in the Centre for Trials Research.

Dr Adam Williams achieved his PhD award

Adam's PhD is titled 'Understanding the relationship between HIV pre-exposure prophylaxis, sexually transmitted infections, and antimicrobial resistance'. He used a mixed-methods design with insights from relevant literature to explore the impact of HIV pre-exposure prophylaxis provision on rates of sexually transmitted infections and antimicrobial resistance. The PhD was funded as part of the KESS 2 knowledge Economy Skills Scholarships and was supervised by CTR staff. Adam has published 3 journal articles from his PhD, received 8 awards for related artwork and presentations, including PGR Student of the Year 2023 and presented his work at national and international conferences, receiving scholarships to attend.

Trial Governance Placement scheme

CTR are embarking on a second round of the Trial Governance Placement scheme in partnership with the Health Research Board Trial Methods Research Network (HRB-TMRN). The aim of the scheme is to provide Irish researchers involved in trials in health or social care with the opportunity to learn from experts in Trial Governance across all governance committees. We have run one successful round already, with CTR trial managers and senior trial managers providing mentorship. Placements are provided with observer access to internal Trial Management Group meetings and the CTR Risk Assessment Committee as well as Independent Steering Committee and Data Monitoring meetings.

See link to website

Data management team methodological highlights

Nigel Kirby, Head of Data management led a UKCRC group which developed guidance on the use of eCRFs and forms part of the new Best Practice Guidance. Ten abstracts have been submitted to the ICTMC and/or Early Career Research network (ECR) conferences all within the area of data management methodology. These have focussed on efficiency of data management processes using case examples of trials in set-up, as well as methods employed to improve consistency, justification and the standardisation of database design. Other abstracts detail methods to enhance accessibility and working across teams not only within CTR but with the GW4 and UKCRC networks.

Qualitative Research Group (QRG) methodological highlights

Dr Lucy Brookes-Howell, Head of Qualitative Research, became Co-Lead of the Qualitative Research in Trials target group, within the MRC-NIHR Trials Methodology Research Partnership (TMRP) Trial Conduct working group. The innovative VR-Melody study, led by Dr Kim Smallman, was showcased at a CTR Celebration Event.

VR-Melody is collaborating with Rescape Innovation and explores how VR and music can be used to help reduce anxiety in adults.

Members of the QRG ran an interactive stand at the ESRC Festival of Social Science showing students from primary and secondary schools how to make sense of qualitative data and how to 'have a go' at thematic analysis.

Recent publications include a feasibility trial qualitative paper for PLACEMENT (Milosevic et al 2024) using qualitative methods to understand patients' rehabilitation experiences following major lower limb amputation. The PEACH study qualitative paper (Henley et al 2023) presents a new model to aid understanding of the complex decision-making process around antibiotic prescribing in the context of a pandemic.

Statistical team methodology highlights

Dr Philip Pallmann was invited to examine a statistics PhD in Newcastle University and also won a Reviewer Award in January.

Recent statistical methods publications:

The PERCEIVE study paper was published which evaluates and compares different prediction models. An article describing work to identify critically ill children in Malawi was published which develops and validates a new prediction model.

Routine data team methodology highlights

Our two routine data study managers started in January, which has consolidated our plan to grow this team. DELIMIT (a public engagement project) working with the public across the UK to develop recommendations on the use of synthetic data for research was funded and started 1 March 2024. A workshop has also been accepted at the international population data linkage network conference in Chicago in September on the topic of synthetic data in research.

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Work Package 6
Development of all Wales remit

In this section we describe, with examples how 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.

Treialon Cymru

We established Treialon Cymru to provide opportunities across the whole of Wales for people to engage with trials. The three components of our Treialon Cymru programme act as the mechanism to deliver the early engagement and development phases of the research development cycle.

We describe the three elements of Treialon Cymru below.

The Associate Membership Programme

This links people who work in health and social care in Wales to a trials unit via a mentoring scheme. The programme was launched this year and two cohorts of Associates are now working with their mentors. A mentoring training scheme has been rolled out to 43 people in our team, taking in a range of our staff groups. We have also initiated an ongoing programme of mentoring skills development to support this activity.

The Research Development Programme

This is designed to target emerging research areas of Welsh priority. This has been focussed on Women's Health this year. A stakeholder group has been established and the team ran a shared workshop with PRIME colleagues on Women's Health and two large-scale bids have been supported (menopause care and HPV). One early success has been the award from NIHR Health Technology Assessment for the ESTEEM study on the use of testosterone in menopause care (£2.65M, Co-Chief Investigators: Prof Mike Robling, Dr Helen Munro).

The Stakeholder Engagement Programme

This programme has been run, or co-run with local organisations, with eight webinars attended by 147 delegates and four in-person events across Wales. Webinar topics included use of adaptive trial designs, inclusivity, routine data and neurodevelopmental disorder trials.

At the end of its first year, Treialon Cymru has met or exceeded all targets for each key performance indicators. This assures delivery on our all-Wales remit for both geographical and research area coverage while providing opportunities for active participation in the Centre's activities.

Conclusion

Our annual report summarises key areas of activity and reflects achievements and progress towards our vision.

Our new studies, a snapshot of which are presented in the report, cover a broad range of work in health and social care across the life course, for example from child and adolescent mental health (SWELL) to Parkinson's (Sparky Samba). Our open studies include populations typically underserved by research, including adults with a learning disability (STORM) and children in need of support from social services (SWIS) and build on collaborations with a wide range of academic, public, industry and third sector partners. The QuicDNA study in particular received recognition for bringing together industry partners to support pioneering technology for lung cancer patients in Wales, to achieve faster diagnosis.

The report highlights our work in developing methods to improve trial design and conduct, including exploring the use and acceptability of synthetic data in research (the DELIMIT study) and a partnership with colleagues in Ireland (Health Research Board TMRN) to develop knowledge and expertise in research governance. A key success of Treialon Cymru, via the stakeholder group focussed this year on Women's Health, has been to support several large bids currently under review.

The evidence our studies produce is intended to benefit patients and the public. This informs the work we take on, how we design, fund and run our studies and how we form partnerships to put these findings into practice.

Some studies are stepping stones along this journey – feasibility studies such as Sparky Samba and STORM which will provide reassurance that the design or intervention can proceed to a larger scale evaluation. Others are definitive trials such as SWIS and in the case of that study has acted to prevent full scale roll-out of an approach that is unlikely to be beneficial. Studies such as POOL provide much needed reassurance about the safety of existing interventions – giving birth in water - that women want. Studies like QuicDNA hold the prospect of delivering quicker diagnostic results to patients who otherwise may suffer the consequences of delayed cancer treatments. Particularly exciting are exemplar initiatives such as SunPad that build international partnerships with local teams to embed and evaluate low-cost innovations that can have a major impact on the health and well-being of populations of women globally.

Our overarching approach is to work in partnership, within and across multidisciplinary teams. These collaborations are driven by Centre staff, whose expertise and skill is highlighted by the high number of promotions and awards this year, recognising excellence across career stages from students to senior researchers.

Looking forward

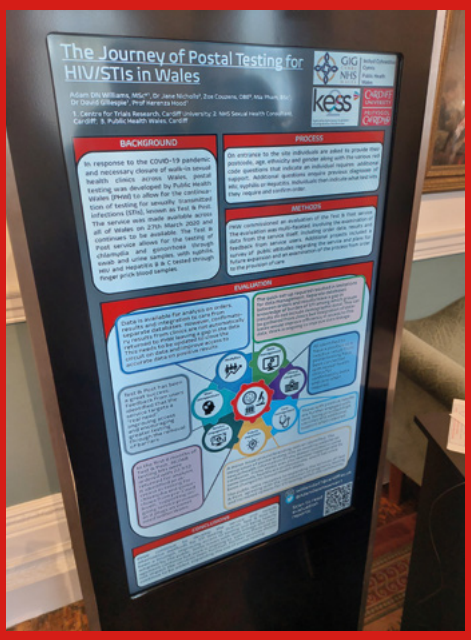
We highlight in this year's report that we have a team with great breadth and depth in research, which continues to grow in experience and expertise.

The work with a multitude of external partners and collaborators delivering a portfolio of studies and trials that will provide answers to important health and social care challenges across the UK and even across the world.

Given the financial challenges that exist, we have adapted our strategy to include a focus on sustainability. Over the next year as a component of this approach we are exploring areas where cross working both within the CTR and with our local partners will create more efficient and resilient systems whilst allowing individuals to develop specialist areas of interest and expertise. We have also developed systems to ensure that personal development and promotion have clear pathways for all concerned and hope to see this effectively implemented over the coming year.

We will continue to deliver the research we have had funded, maximizing outputs and impact from the public and patients that have taken part. We will incorporate new methods and expertise into the work we develop and deliver. We have an ongoing pipeline of applications with a steer towards larger, often longer duration, higher profile funding, building on our team strengths.

We hope to support the growth of new research themes developing within the University offering our skills and expertise to complement those of our partners.



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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