

CARDIFF
UNIVERSITY

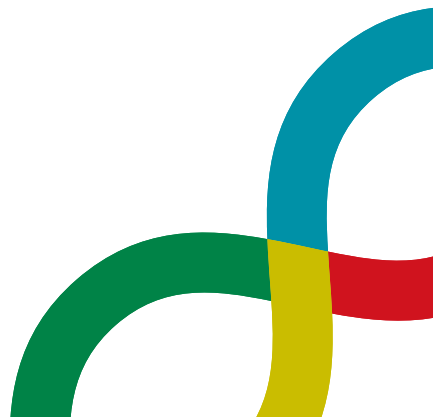
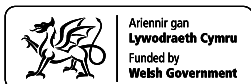
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Centre for
Trials Research

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Ymchwil Treialon

Annual Report

2021/22



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



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Glossary

CI	Chief Investigator
COPD	Chronic Obstructive Pulmonary Disease
CTR	Centre for Trials Research
CTU	Clinical trials unit
CU	Cardiff University
DCW	Domiciliary care worker
HTA	Health Technology Assessment
NIHR	National Institute for Health Research
PHR	Public Health Research
PI&E	Public Involvement and Engagement
PPI	Patient and public involvement
RCT	Randomised Controlled Trial
RDCS	Research Design and Conduct Service
UKRI	UK Research and Innovation



Executive summary

The year has seen us continue to be delivering major research into COVID-19, whilst also reinvigorating our research in other areas.

This has needed us to retain the flexibility and adaptability of previous years recognising the pressure on services and people that has been created by experiences over the pandemic. We have been reimagining how we will work for the future and establishing an approach which aims to gain the most from technology, whilst remembering how important in person connection is, for staff, students, collaborators, and everyone we work with.

A big focus this year has been our work on the PANORAMIC trial evaluating the use of novel anti-virals in the community for COVID-19. This has involved a strong partnership between three Clinical Trials Units and working closely with policy makers in both Westminster and Welsh Governments. We included over 25,000 people in a record breaking 5 months. We have also been co-producing a self-management intervention with people who are living with long COVID and are now moving forward to evaluate it. We have continued to produce results from existing COVID-19 studies,

and you can read more about the CABS and OSCAR studies in this report. Across these studies we have or will produce high quality evidence to guide policy and practice in relation to COVID-19. Many of these studies will also inform how we respond to future pandemics.

One of the challenges of the research community responding so well to the need for evidence to inform the response to COVID-19 was that other research was deprioritised. It has been wonderful this year seeing some of this important research get started again, with 28 studies having opened this year and I am delighted that we have completed recruitment on studies in acute myeloid leukaemia, neonate respiratory health and hidradenitis suppurativa to name just a few. We have also been developing our approach to making every piece of data and effort made by the people in our studies really count. There are examples of some of the secondary uses of data throughout this report, as well as some of our methodological work relating to this.





Our high-quality research is reflected by 127 peer-reviewed publications over the past year. Our programme of research has been underpinned by the inclusion of the public in the design, conduct and dissemination of research and further enabled by our Public Involvement and Engagement (PI&E) Hub. We have seen 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. Our effective resource management and success in retaining and developing our 181 skilled research and professional staff has helped us to secure £28M in funding from national and international funders (a total of 28 major awards over the current period of funding).

Thank you for taking the time to read about our work. Please do contact us if you have any thoughts, questions, or suggestions. We would like to acknowledge our funders, research partners, staff and the people who take part in our research studies without whom none of this work would be possible.

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. 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.

Key programme partners and beneficiaries

The Centre receives infrastructure funding from Health and Care Research Wales and Cancer Research UK, as well as from our host institution, Cardiff University. 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 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. 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

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). Adrian and Monica will be moving to take on new leadership challenges in summer 2022 but will remain strongly linked to the Centre.

How we work

Our researchers and professional staff work across our four divisions and within cross-cutting teams (including Statistics, Information Services, Quality Assurance & 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.

Our work plan

We place continued emphasis on the development of working practices and expert staff to ensure we meet high standards for research across our portfolio. We design new studies and win the funding to make them happen in collaboration with researchers from other organisations across Wales and beyond. All our funded studies are conducted with high quality standards that produce outputs that will make a difference to the public and we strive to develop new ways to answer important clinical questions and sustain a dynamic and professional workforce. Alongside this we support staff in the NHS and social care in Wales to develop their own research to address the important questions in the care of patients and the public. Here we showcase our work over the last year across all our divisions within the Centre for Trials Research.

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

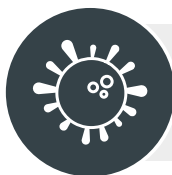


Professor Richard Adams,
Director Cancer Division



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 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: RDCS and NHS

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
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This report features examples of important areas of focus in our research. To make it easy to identify throughout the report, we include the following identifiers to highlight that activity.

	 COVID-19 Research	 Methodology
	 International Focus	 Inclusivity

Core Metrics

Reporting period: 2021/2022

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

Direct funding
awarded

£823,464



Jobs created
through direct
funding



Grants won during reporting period

Grants won	Led by group	Group collaborating
Number	13	16
Value	£6,447,972	£21,717,559
Funding to Wales	£4,544,443	£2,841,843
Funding to group	£4,239,031	£2,841,843
Additional jobs created for Wales	52.14	29.56
Additional jobs created for group	47.81	29.56



Number of publications



Number of public
engagement events



Number of public
involvement opportunities

Clinical Trials Unit metrics



29

Number of
studies awarded



15

Number of studies
led by Welsh Chief
Investigators



17,174

Total number
of participants
recruited



22.56

% participants
from Wales

WORK PACKAGE 1

Managing our work

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



The ongoing COVID-19 pandemic has brought new areas of research to the Centre using the experience and wide-ranging skills of our team.

Such trials have required the team to be fleet of foot and flexible, which they have achieved admirably under challenging working conditions. These new studies are being delivered whilst maintaining the delivery of previously and newly funded studies and we have implemented new approaches to prioritisation to ensure that we deliver.

During this year we have advertised, interviewed, employed and trained new members of staff to deliver our increasing research portfolio. Whilst most of our team work predominantly if not exclusively from home still, we are seeing an increasing number back in the office environment and have found this particularly important for new starters to help them find their feet. Notably, Carolyn Blake, our Administration and Development Officer, has led the way with her team with new starters supported by senior members of the team face to face in our offices in the Heath Park Campus.

We have also worked to diversify and integrate the skill mix more effectively with new roles such as our Data Analyst posts creating new promotional opportunities internally and linking to support our statistics team who bring a skill which has been in short supply in academic institutions across the UK. We continue to review and update our systems and approaches – this year we have installed a new data system, RedCap, alongside our other data systems and implemented it in our first study (HIDDEN 2). We are collaborating with other Clinical Trials Units to explore the best ways to utilise this software.

We have continued to optimise the efficiency and effectiveness of our core groups overseeing Risk Assessment and Quality Management with streamlined processes for low risk observational and qualitative studies and integrating data protection impact assessments to our oversight processes.

We published our response to our April 2021 stakeholder survey as a 'You Said, We Did' report in October as part of our commitment to engaging and communicating with the broader community we work with. In December 2021

we ran our “speak week” sessions giving staff the opportunity to speak freely and offer suggestions to feedback and constructively recommend changes in key areas of communication, new ways of working and our culture and values. These were well attended and utilising some of the feedback we have updated our values statements to increase the focus on sustainability and inclusivity.

We are beginning to see a return to some face-to-face learning and development opportunities but there remain several virtual events locally, nationally and internationally offering opportunities for staff development. Supporting staff to develop international links has been important and this has seen success with Dr Claire Nollett (Research Associate) awarded a travelling fellowship to Amsterdam to look at their approach to research and services to address the psychological impact of vision impairment for summer 2022 and Rebecca Milton (Research Associate) undertaking creative remote dissemination approaches for her work with Nigeria on stillbirths. Dr Charlotte Wilhelm-Benartzi (Research Fellow) has taken on a leadership role within the Centre for driving forward International Research.



Our Centre Values

Making a difference – Improving health, wellbeing and sustainability of society

Building trust and confidence – **Growing** together as partners

Aspiring and **Inspiring** – Helping everyone to be their best and to do their best

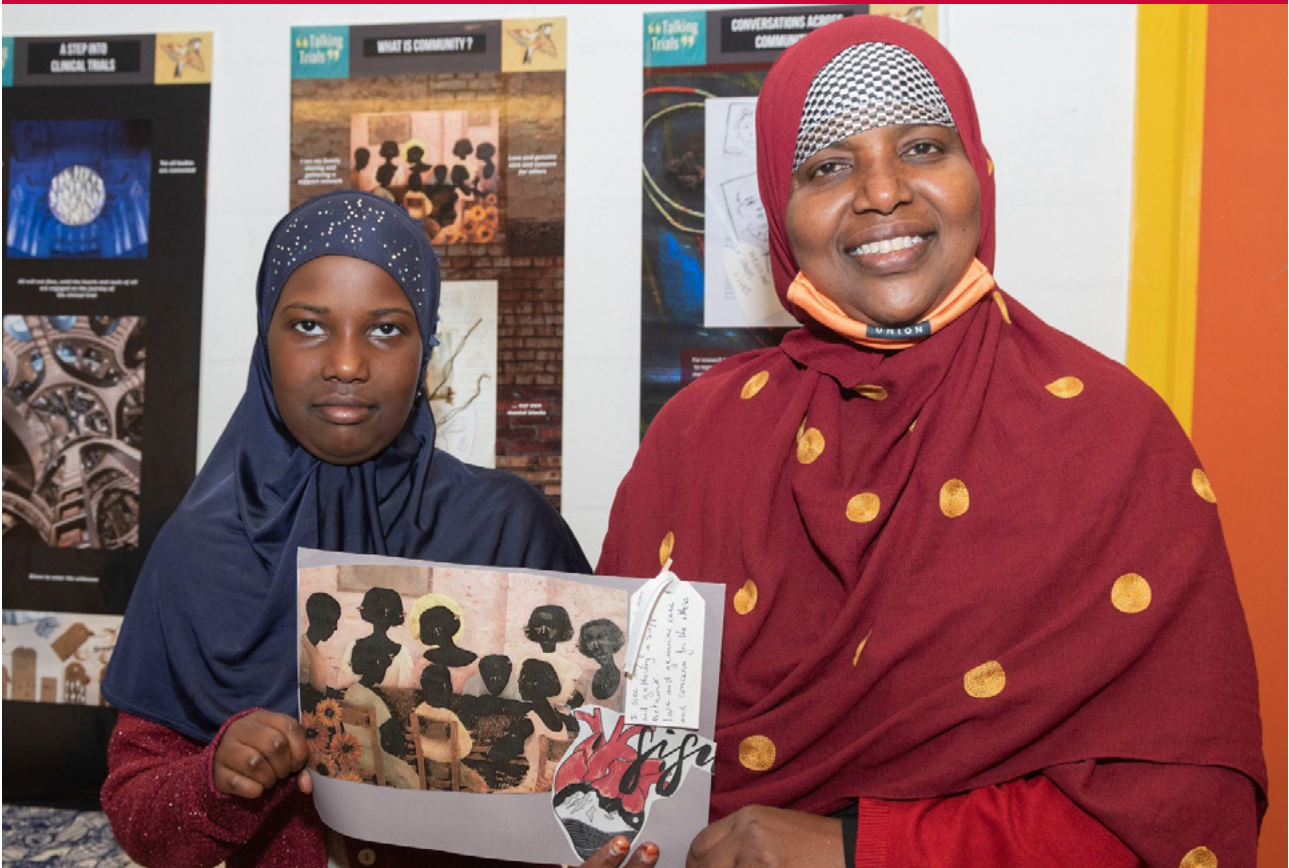
Respecting **Individuality** – Recognising different needs and aspirations of every individual in society

Innovating and Researching – Empowered to be **creative** and **questioning** in everything we do

Leading and Collaborating – Developing true **partnerships** (nobody wins unless everybody wins)

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

Recognising – **Celebrating** success, openness and transparency





WORK PACKAGE 2

Working with other groups

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



Working with groups outside of the Centre is essential to developing research that will benefit the people of Wales and the broader international community. Therefore, our second work package focuses on the connections we make with networks and organisations in bringing forward new research. In this section we use examples from each Division to show this in practice.



Cancer Division

Managing patients with cancer has been an issue over the last two years, though our trials have continued to recruit. Studies such as RAPID-PROTECTION are seeking to improve the safety of patients, preventing them developing life threatening infective complications and improving their ability to mix with loved ones. However, we have also seen a significant downturn in cancer diagnoses and subsequently later presentation of cancer.

CABS

COVID health And help seeking Behaviour Study

Chief Investigator: Professor Katherine Brain

Funder: UK Research and Innovation



The COVID health And help seeking Behaviour Study is a large-scale study to measure cancer attitudes and behaviours in adults aged 18 and older across the UK. Led by Professor Kate Brain from the Division of Population Medicine, Cardiff University, the research was funded by the Economic and Social Research Council (ESRC) as part of the UK Research and Innovation's rapid response to COVID-19.

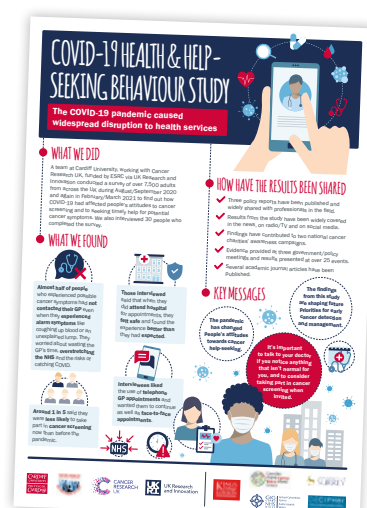
During the COVID-19 pandemic, people were less aware of the importance of seeking early medical help for signs of cancer or taking up screening, when available, to diagnose cancer sooner. People may also have been cautious about attending healthcare settings during the pandemic. Together these factors may result in more cancers being diagnosed at a later stage when treatment may be less successful.

Over 18 months the CABS study team carried out a large study to measure cancer attitudes and behaviours in adults across the UK. People were recruited from online panels including HealthWise Wales and through social media. Over 8,000 people completed the survey and 30 people were interviewed.

Study findings have been used to rapidly develop clear public health messages encouraging people to act on the early signs of cancer, take up cancer screening when it becomes available, and engage in healthy behaviours. This should help reduce the negative impact of COVID-19 on cancer

outcomes in the longer term. The study has attracted extensive media coverage with over 200 news items in national and local newspapers or news websites, and 30 pieces of coverage on local/Welsh radio. Professor Brain gave a number of media interviews including Leading Britain's Conversation radio station and ITV's Good Morning Britain.

The study was fully coordinated by the Centre for Trials Research (study lead, Dr Julia Townson, study manager, Dr Yvonne Moriarty, Division of Population Health) and is a collaboration involving researchers from Cardiff University, Cancer Research UK, King's College London, the University of Surrey and Public Health Wales.



The power of sharing data



Building on our Acute Myeloid Leukaemia (AML) trials, data has been shared internationally by

the Centre to support research to improve the lives of people with AML. These diverse projects nationally and internationally include;

- Investigating the use of a blood test biomarker called Minimal Residual Disease to validate a new endpoint in trials that can get experimental drugs to patients quicker.
- Exploring the impact of complete response to therapy versus a haematological remission in drug licensing
- Enriching international data pools holding multiple datasets for research with the HARMONY and HARMONY plus initiatives, which make data available to blood cancer research internationally
- Demonstrating the value of Patient Reported Outcome Measures. We are exploring the optimal use of Quality of Life measures prior to treatment starting in patients with Myelodysplastic Syndrome (MDS) funded by Blood Cancer UK.

We believe that by working together we can be much greater than the sum of our individual parts. In sharing anonymised data from our trials and collaborating with others we maximize the potential of each trial we undertake and optimise the contribution of every patient who has given their consent, such that their gift lives beyond the life of the trial itself.

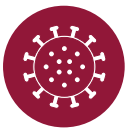






Infections, Inflammation and Immunity Division

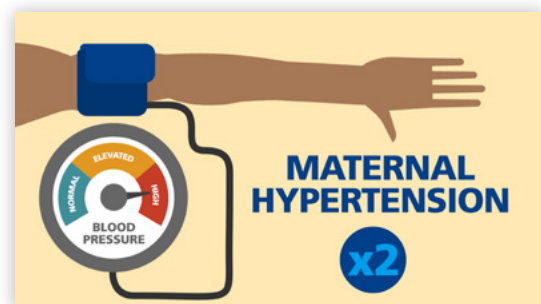
Across the Centre portfolio we have been aiming to increase our partnerships internationally and with industry. The RAPID-PROTECTION study is a collaboration with the Oxford University Hospitals NHS Foundation Trust and University of Oxford. Funded by AstraZeneca, the team led by Dr Mark Tuthill and with Centre lead, Dr Emma Thomas-Jones (Deputy Director for Infections, Inflammation and Immunity) are investigating the benefit of a long-acting antibody treatment to prevent COVID-19 infection in immunocompromised individuals.



The RAPID-PROTECTION study will recruit 350 participants with highly immunosuppressive conditions. These will include people with inflammatory disorders, solid tumours, blood cancers, kidney and liver disorders, including patients receiving transplants and dialysis. Participants will receive a long-acting antibody (AZD7442 – a combination of tixagevimab and cilgavimab) followed by an additional vaccination booster 28 days later. The immune responses from study participants will be compared to healthy controls to determine whether the combination of antibody treatment and vaccination provides protection against SARS-COV-2 infection. A successful study may help immunocompromised patients to lead less restricted lives, more akin to those not highly vulnerable to COVID-19 infection.



We have recently completed a feasibility study in partnership with the Murtala Muhammad Specialist Hospital, Kano investigating the causes of stillbirth and how this might be linked to maternal infection. This study showed that one in ten births in the hospital were stillborn and that there were a variety of potential factors associated with that. It also showed that it was possible to undertake research and collect samples at such a difficult time for the parents. The dissemination for this was intended to be face to face in Nigeria, but due to the pandemic we instead developed an animation for staff and managers at the hospital and this was shown to them in a daylong seminar on the topic with virtual attendance of the team from Cardiff, led by Rebecca Milton (Research Associate). This study will lead to a larger one on identifying causes and preventing stillbirth in Nigeria.





Mind, Brain and Neuroscience Division

Researchers from the Centre for Trials Research led by Dr Rachel McNamara, (Deputy Director for Mind, Brain and Neuroscience) are working with others from the interdisciplinary Wolfson Centre for Young People's mental Health (led from Cardiff University) on a youth depression prevention trial. Established in 2020 and funded by the Wolfson Foundation, the Wolfson Centre brings together experts in developmental and clinical psychiatry, genetics, social sciences and neuroscience.

The Wolfson Centre's work stream 3 addresses interventions in adolescents at high-familial risk and a new trial will test an enhanced psychological intervention for the prevention of youth depression. The adapted 'Coping with Stress' intervention will be tested in a trial involving 350 adolescents aged 13 to 17 years old who are at risk of depression. The study also involves optimising the treatment of parental depression prior to delivering the intervention.

The study will explore the mechanisms through which the intervention has its effect, which is delivered in groups over a nine month period. The study will assess whether a depression episode occurred during the follow-up period using a clinician rated assessment scale amongst other participant reported measures. Long-term follow up will be conducted via data linkage to routine health record data with the SAIL databank, Swansea University.

Led by Professors Frances Rice and Rudolph Uher, other members of the team include Professor Jonathan Bisson (Cardiff University), Professors Simon Murphy and Graham Moore (both from DECIPHer), Dr Rebecca Playle (Centre for Trials Research), Professors Anita Thapar and Stefan Collishaw (Wolfson Centre and Cardiff University) and Professor Ann John (Swansea University). A range of scientific collaborators from centres across the world are also involved including from the National Institute for Mental Health, US and New Zealand.





Population Health Division

Evident across our Centre portfolio are examples of our work with historically underserved populations. We embrace team-based approaches to designing trials for settings where previous attempts have been too few or viewed as too challenging. One example is that of children's social care and the Centre's partnership with CASCADE, led by Professor Donald Forester in Cardiff University. Funded by Health and Care Research Wales, CASCADE's aim is to improve the well-being, safety and rights of children and their families. The partnership brings together methodologists from our Centre with expertise in trials, routine data, and process evaluations with experts in children's social care settings. The partnership also includes researchers from Swansea University's Secure Anonymised Information Linkage Centre (SAIL) and the School of Psychology in Cardiff University.

Two current studies illustrate the role of our Centre in the CASCADE partnership. First, the social workers in schools (SWIS) study asks whether social workers linked to and based within a secondary school may enhance interagency

working, reduce risks to children and lead to better outcomes. Run with 291 schools across 21 local authorities in England, the study will compare outcomes between schools that have a social worker and those that continue as normal.

A second study is evaluating the implementation, context and effectiveness of Family Group Conferencing for children and families referred to children's social services. A Family Group Conference is a meeting where the wider family discuss children who need support and protection and decide on a plan for looking after them. The study is led by Professor Jonathan Scourfield (CASCADE) and funded by the NIHR. The study will use co-productive approaches with families to reach a consensus about the most important outcomes to measure. This will inform the design of a subsequent survey to be used across sites in Wales and England and a large-scale natural experiment in England. The study team benefits from partnership working with health economists at Oxford University (led by Professor Stavros Petrou) and a peer researcher from the London Borough of Camden (Kar-Man Au).



WORK PACKAGE 3

Developing new studies

Designing new studies and winning
the funding to make them happen



Designing new studies and winning the funding to make them happen can take time, but this last year with so many COVID-19 studies it has seemed to operate at a great pace. We have been developing new studies that are not related to COVID-19.



Cancer Division

HIDDEN 2

The HIDDEN trial aimed to investigate the prevalence of deep venous thrombosis in patients with advanced cancer.

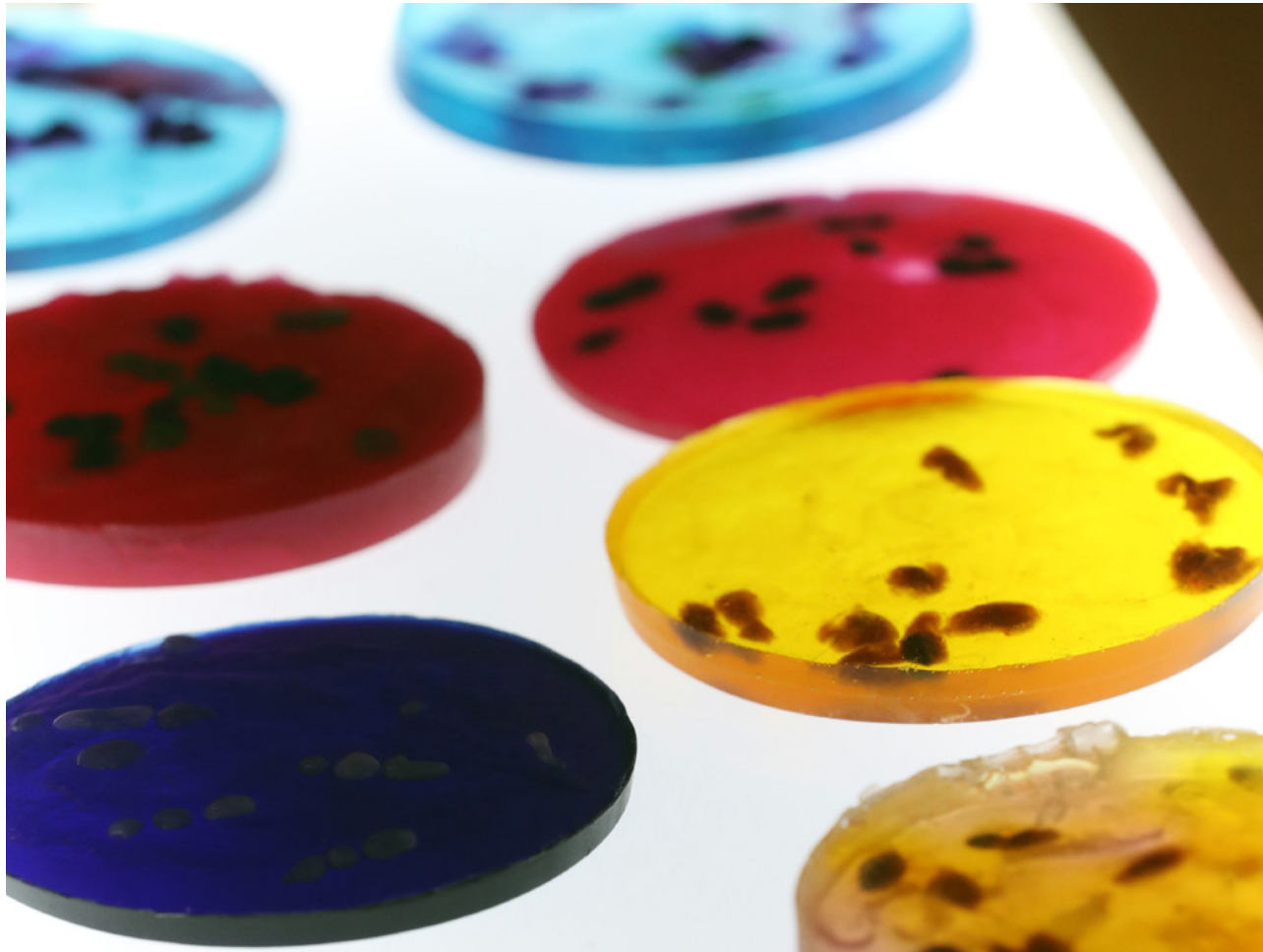
Chief Investigator: Professor Simon Noble

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

The HIDDEN 2 study (funded by Health & Care Research Wales) working in partnership with Aneurin Bevan UHB, investigates the prevalence of

deep venous thrombosis in patients with advanced cancer admitted to hospital. The original HIDDEN trial investigated this in patients admitted to specialist palliative care units (SPCUs).

The trial challenged, and changed, existing international thromboprophylaxis guidance in this population and the results were published in The Lancet. HIDDEN 2 is aiming to have a similar impact on the management of advanced cancer patients admitted to hospital.





Infections, Inflammation and Immunity Division

PLACEMENT

Perineural local anaesthetic catheter after major lower limb amputation trial.

Chief Investigators: Dave Bosanquet and Chris Twine

Funder: Health and Care Research Wales

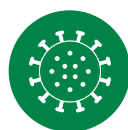
Pain after amputation is a significant problem, and comprises both acute and chronic pain, including phantom limb pain. The PLACEMENT Randomised Controlled Trial has been funded by NIHR HTA, following our successful delivery of the RfPPB funded feasibility trial. The aim of the trial is to evaluate the clinical and cost-effectiveness of the use of a perineural catheter with continuous local anaesthetic infusion, inserted at the time of lower limb amputation on postoperative outcomes, compared to standard of care. A perineural catheter, is quick and simple to insert at the time of surgery, and its placement and use for local anaesthetic infusion comes with few side effects. Opening in 2023, the trial will seek to recruit 650 adult patients undergoing lower limb amputation at recruiting centres across the UK.

PANORAMIC

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

Chief Investigator: Professor Chris Butler

Funder: National Institute for Health Research



We have continued to rapidly develop and set up studies to address COVID-19 and were key partners with the University of Oxford on PANORAMIC. This trial went from initial discussions to opening in four months and is an innovation in study delivery. Anyone can refer a potential patient; patients can self-refer; research teams can reach out to potential participants testing positive for COVID-19; registration, pre-screening and informed consent are online; anti-viral medication and study materials are delivered to participants homes; symptoms are collected and drug compliance is monitored remotely via an online patient diary and follow-up is via email and telephone. This makes the study accessible to everyone regardless of where they live.





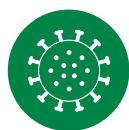
Mind, Brain and Neuroscience Division

LISTEN

Long COVID personalised self-management support co-design and evaluation.

Chief Investigators: Professor Monica Busse and Professor Fiona Jones

Funder: National Institute for Health Research



Individuals with long COVID experience a wide variety of ongoing problems such as tiredness and difficulty with everyday tasks and often struggle to return to their former lives. This is made worse by uncertainty and a lack of understanding by some healthcare professionals.

The LISTEN trial is one of among 15 projects in the UK to receive total funding of nearly £20m from the NIHR to help tackle long COVID. LISTEN is being jointly led by Professor Fiona Jones, an expert in rehabilitation research at St George's University of London and Kingston University and Professor Monica Busse at Cardiff University's Centre for Trials Research. They are working in partnership with the Bridges Self-Management social enterprise, the Wales COVID-19 Evidence Centre, PRIME Centre Wales, Health and Care Economics Cymru, Swansea University, Lincoln University, Kings Implementation Science and Diversity and Ability, a disabled-led social enterprise supporting organisations and social justice projects to create inclusive cultures. Individuals living with long COVID and a Patient and Public Involvement (PPI) panel from diverse backgrounds have shaped the LISTEN project and are involved at each stage of the study life cycle.

In the first six months of this two-year project, the trial team (led by Prof. Fiona Jones in Kingston University) have recruited people living with or recovered from long COVID, and rehabilitation practitioners to a 'LISTEN Co-design' group, helped by 'Diversity and Ability' who have expertise in reaching seldom heard populations. We used different activities such as online groups to design our intervention which includes a book, digital resources and a training package for rehabilitation practitioners to enable them to deliver the intervention.

At the same time as co-designing the intervention, Centre staff have engaged widely with potential research sites in England and Wales. We have set these up as research sites and will soon be recruiting individuals with long COVID to the entirely remote (decentralised) trial.





Population Health Division

The Population Health Division has a long history of working with socially excluded populations. We have recently had a study funded working with the charity Crisis to conduct a pilot trial of an intervention to support prison leavers at risk of homelessness.

PHaCT

Prisoners at risk of experiencing homelessness will be offered accommodation and phased support to integrate back into the community as part of a pilot study.

Chief Investigator: Dr Jim Lewsey

Funder: National Institute for Health Research



The study focuses upon prison leavers who are at risk of experiencing homelessness. Critical Time Interventions (CTIs) provide a phased level of support for people experiencing transitions and have been effectively deployed in improving the health of people leaving psychiatric inpatient care. Crisis are delivering a housing-based CTI, where settled housing is offered in combination with phased support, to prisoners at risk of homelessness.

The study's primary objective is to investigate whether it is possible to conduct a larger scale trial to evaluate the effectiveness of this housed based CTI. The Centre is coordinating this pilot study which will take place in Swansea and Liverpool. It is only the second UK based RCT working with this socially excluded population. The first, Moving On, was also led by the Centre. The study is being delivered as a collaboration between Glasgow University, Cardiff University, Herriot Watt University Glyndwr University and Crisis.



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

The FAKTION trial is a randomised controlled trial of a hormone blocking therapy fulvestrant with either a placebo or a targeted therapy Capivasertib in postmenopausal women with advanced breast cancer which has recently reported updated long-term results. This report looked at the potential survival benefits of this brand new drug as well as the molecular targets that might indicate which types of breast cancer

related to the individual patient might gain most benefit from treatment. These results were reported at the largest cancer conference in the world the American Society of Clinical Oncology (ASCO) in June of this year by Professor Robert Jones and received much media attention. Essentially, the addition of Capivasertib to standard treatment resulted in a significant survival benefit and our molecular targeted analysis indicated a group of patients who gained the most benefit overall. It is highly likely that this drug will receive a license for sale in the not too distant future, which will have been driven by the FAKTION trial and these results. The results were published in a well respected peer reviewed journal (Lancet Oncology) at the same time as the oral presentation in the United States.



AML19

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

Chief Investigators: Dr Mike Dennis and Professor Nigel H Russell

Funder: Cancer Research UK



The international phase 3 AML19 trial has been running since 2015 and is aimed at adults with acute myeloid leukaemia (AML) or high risk myelodysplastic syndrome (MDS). The trial was for younger adults mostly less than 60 years old. Patients in AML19 are allocated treatment depending on their disease features, and their response to early therapy. The trial will answer several questions: whether patients with a better prognosis should be treated with a single or a split dose of a drug called gemtuzumab ozogamicin; whether a drug called vyxeos is beneficial in patients with high risk disease; whether FLAG-Ida chemotherapy can be given in fewer treatment cycles compared to DA chemotherapy; and whether it is safe to treat patients who have a FLT3 mutation with Midostaurin plus Mylotarg. 2,150 patients have been recruited from the UK, Denmark and New Zealand including 14% black and Asian patients. In addition to the clinical outcomes including whether there is a survival benefit and whether patients can achieve complete remission, extensive quality of life data has been collected. Analysis of trial data is currently underway and we expect to publish the first outputs from the trial later this year.

PATHOS

A Phase III trial of risk-stratified, reduced intensity adjuvant treatment in patients undergoing transoral surgery for Human papillomavirus (HPV)-positive oropharyngeal cancer.

Chief Investigators: Professor Mererid Evans and Professor Terry Jones

Funder: Cancer Research UK



The phase 3 PATHOS trial will take place over 10 years and looks at whether swallowing problems and quality of life can be improved, in 1,100 patients with oropharyngeal (throat) cancer caused by Human Papillomavirus (HPV) infection. Patients are treated with surgery, which can be followed by radiotherapy or chemotherapy. The trial is assessing whether radiotherapy can be reduced in patients with a medium risk of the cancer returning and whether chemotherapy is necessary in combination with radiotherapy for patients with a higher risk of the cancer coming back. The aim is to assess whether reducing this treatment can prevent later problems with swallowing and quality of life, but without worse survival outcomes. This is an international trial recruiting from the UK, Australia, USA, France and Germany.



Infections, Inflammation and Immunity Division



We continue to collaborate across the UK to deliver COVID-19 research which is informing clinical decisions and policy. In partnership with the University of Leeds we are evaluating the way in which a biomarker (procalcitonin) has been used to guide antibiotic prescribing decisions in patients with COVID-19 in hospital (PEACH, funded by NIHR). Initial publications from the PEACH study have shown the variation in how procalcitonin (PCT) was adopted into the NHS during the first wave of COVID-19. PANORAMIC has recruited over 25,000 patients from Dec 2021-April 2022 to evaluate the benefits of Molnupirivir and is now recruiting to evaluate Paxlovid. The results of the Molnupirivir evaluation will be available in July 2022.

A few of our non-COVID-19 studies restarted and completed recruitment. The AZTEC trial of azithromycin for Chronic Lung Disease of Prematurity (funded by NIHR) is investigating if the antibiotic can improve the lung outcomes of

babies who are born at less than 30 weeks of gestational age. We have successfully reached the recruitment target of 799 premature babies and are now following them up to see the impact on their lung function. The THESEUS study (funded by NIHR) will provide vital information to answer questions that were identified as priority areas for research by patients with Hidradenitis Suppurativa and the doctors and nurses who treat them. We successfully recruited 150 patients from across England, Scotland and Wales and are currently engaging with patient groups to discuss the findings and agree on priorities for the next stage of research.

We have continued to maximise the value of completed studies and published additional papers from the PACE and PRINCESS trials. These explored in more detail the management of COPD exacerbations in primary care and the gut health of residents in care homes.





Mind, Brain and Neuroscience Division

We are preparing reports on several recently completed trials within the Mind, Brain and Neuroscience Division with the aim that once available, results will be directly relevant to patients and the public.



The SenITA trial looked at an Occupational Therapist-led play intervention for children with autism to see whether it had any impact on a range of behavioural and functional (daily living skills) outcomes. This study, run in both Wales and England, was funded by the NIHR Health Technology Assessment Programme and the project report will be available in autumn this year. We have also recently completed a trial comparing two treatments for Post-Traumatic Stress Disorder (PTSD) in partnership with the National Centre for Mental Health. One treatment is conducted face-to-face with a therapist and the other is

conducted online with some support from a therapist. We aimed to find out if both treatments are equally effective at helping people with PTSD. Results will inform the NHS about which treatments to recommend.

The PACE-HD trial, which is a study looking at physical activity and exercise outcomes in Huntington's disease, has also recently been awarded the American Physical Therapy Association Combined Sections Best Platform Presentation for "Consultative Coaching Model for Long-Term Exercise Engagement in People with Huntington's Disease".





Population Health Division

Aligned with the work of other divisions, Population Health continues its work investigating the impacts of the COVID-19 pandemic its portfolio of work on socially excluded populations. Here are two examples:

Outcomes for Social Carers: an Analysis using Routine data (OSCAR)

This study will investigate the impact of COVID-19 on the health of domiciliary care workers in Wales and develop a model for UK service planning and carer support.

Chief Investigators: Dr Rebecca Cannings-John and Professor Mike Robling

Funder: UKRI [ESRC]



Domiciliary Care Workers (DCWs) are employed in both public and private sectors to support adults at home.

The support they provide varies but often includes personal care, which demands close contact between care worker and the person being supported.

The routine health data of 15,727 care workers was analysed and 24 DCWs were interviewed to build a picture of how Wales's domiciliary care

workforce fared during last year. Interim results showed a quarter (28%) of DCWs sought medical help or received treatment related to mental ill health in the first 12 months of the pandemic in Wales from 1 March 2020. One carer said the pandemic had been the “biggest challenge” the care sector had faced. “PPE shortages, staff shortages, caring for individuals who have contracted the virus while also trying to keep yourself safe – it’s been a struggle,” Sarah Edmunds, Service Manager for Radis Community Care in Newport. Recommendations have been made on how to address the challenges faced by DCWs in a policy report. The study is led by Cardiff University, in partnership with Public Health Wales and Swansea University and supported by Social Care Wales.



WORK PACKAGE 5

Ensuring methodological and professional development

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



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

We work across five areas:

1. Outcome development and measurement

2. Trial conduct

3. Novel trial design and analysis

4. Implementation

5. Routine data

Vera-t1d

A randomised, double-blind, placebo controlled, parallel group, multi-centre trial in adult subjects with newly diagnosed type 1 diabetes mellitus investigating the effect of Verapamil SR on preservation of beta-cell function.

Chief Investigator: Prof. Thomas Pieber, MD

Funder: Diabetes Research UK



People living with type 1 diabetes (T1D) have abnormal blood sugars which is usually controlled

by a hormone called insulin. It is an auto-immune disease, which means that your body is mistaking good cells as bad cells and hence is attacking those cells involved in producing insulin. Type 1 diabetes is a relatively rare disease and treatments have the highest chance of success as soon after diagnosis as possible. In this trial such a drug, Verapamil, has shown some promising results, in a small study, with respect to handling blood sugars and maybe elongate the period where the body can still produce some insulin. The trial uses an innovative design that includes an interim analysis to allow the trial to potentially stop early for futility, or when the drug is not giving any benefit. There is a plan to randomise 120 people within the trial, but we could end the study after 50 people are randomised if the

treatment is not looking promising. This is part of the EU IMI funded INNODIA programme with the methodological innovation led by Prof Adrian Mander and Dr Charlotte Wilhelm-Benartzi.

COMORANT-UK

Consensus on methodological opportunities for routine data and trials.

Chief Investigator: Dr Fiona Lugg-Widger

Funder: Medical Research Council



The COMORANT-UK study aims to develop consensus on the key methodological opportunities for using routine data in trials. Researchers increasingly use routinely collected data to support data collection in trials. This may include information collected when providing healthcare to NHS patients, mortality data collected by the ONS, and data collected by local authorities when providing social care or educational services. The availability of routine data for research has increased and infrastructure funding has enabled much of this. However, how such data can be accessed by researchers, its adequacy for analysis, how it can be securely stored and shared in line with the requirements of regulatory bodies are amongst many suggested challenges. However, these challenges, as experienced by the wider research community, have not been systematically collected, prioritised and acted upon.

Dr Fiona Lugg-Widger (Academic Lead for Routine Data, Centre for Trials Research) is leading the COMORANT-UK study to systematically identify ongoing challenges from the perspective of key UK stakeholders. This work was funded by the MRC-NIHR Trials Methodology Research Partnership (TMRP). The study team includes colleagues at University College, London, the University of Leeds and the University of Oxford. This study is one of several in the Centre that have arisen from the partnership supported by NIHR-MRC and shows the value of this supported network which focuses on different areas of trials methods. The study also forms part of the Centre's methodological focus on using routine data in trials and observational studies. Planned work later this year aims to address highly prioritised questions to help reduce barriers to effective use of routine data in future studies.



PrinciPILs

Developing and testing participant information leaflets that inform and do not cause harm.

Chief Investigator: Dr Jeremy Howick

Funder: Medical Research Council



The way information about potential harms and benefits about trials is currently shared with patients is not standardized. Sometimes trial benefits

are not mentioned, and the focus is on potential side effects. Meanwhile, research shows that telling people about harms in the wrong way can actually cause harm. For example, some studies have shown that placebo pills (like sugar pills) can cause mild headaches if patients are told they will cause headaches. We have developed a new set of principles to use when drafting information sheets and we will test any potential clinical benefits of PrinciPILs by embedding these in five existing clinical trials via 'studies within a trial' (SWATs) and comparing them to 'standard' PILs developed by host trialists. This is funded by the MRC and led by Dr Jeremy Howick, with Martina Svobodova and Dr Nina Jacobs undertaking the implementation and evaluation.

Over the last year we have supported several students to undertake what is often their first research project, developing their interest and engagement with potentially being researchers in the future. These projects are linked to our major projects and support further exploration of datasets we hold. These students have been undertaking undergraduate and masters degrees in Population Medicine, Health Psychology and Psychiatry. This also supports our staff to develop their skills in supervision and mentoring.

CASE STUDIES

Intercalated BSc in Population Medicine

Amy Clark, supervised by Dr Rebecca Cannings-John from the Centre, undertook additional analysis of the DUTY study of acutely unwell young children (under 5) presenting to see their GP supervised by Rebecca Cannings-John. She evaluated the NICE traffic light system for GPs and showed that it did not work as intended. This was published in the British Journal of General Practice, and she gave a podcast with the editor.



Timia Raven-Gregg undertook a systematic review of the published research on trial methodology and explored the example of

ethnic minority populations' views on deferred consent, supervised by Victoria Shepherd from the Centre. She showed that research regarding attitudes toward recruitment methods like deferred consent largely fail to adequately represent ethnic minorities. Whilst deferred consent is deemed generally acceptable, analysis of patient sub-groups shows that this attitude is not universal. This was published in the journal *Trials*.

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



For the RDCS this year there has been a very gradual return to something resembling our usual pattern of work. However, with NHS and social care staff completely immersed in their people-facing practice in clinical or social care settings, research related activities have understandably been put on the back burner for most people.

Health and Care Research Wales research funding calls

In the context of the autumn of 2021 and all the service pressure on the practitioners, we were pleased to be able to support eight research groups from four different partner organisations in developing their ideas for an application to the RfPPB or the Social Care grant calls and one person in the application to the NHS research time award. These schemes are often a crucial stepping stone for practitioners into leading research projects, and so represent a really important element of RDCS work, building research capacity in Wales. We are currently working with the four teams who made it through to the second stage of the process and will hear the results in the summer.



Online Events

The team held virtual research funding application events in April and June 2021 with 52 delegates across the two workshops, including employees of our Health Board partners, Wales Ambulance, the Probation Service and Social Care Wales. We have made the most of the move online creating a virtual library of recorded presentations that people can access when they are developing their research ideas.



Chief Investigator Project

We have continued the work on the Chief Investigator project that we started last year. The aim is to develop and support people taking on the lead researcher role, known as the CI, for the first time. We have interviewed CIs at different stages of their research career to use their experiences to help us understand what they have found helpful but also to hear about any barriers that have got in their way, so we can think about how to help new CIs have a positive experience of the role.

We now have a comprehensive summary of the types of knowledge and skills that might be needed at different stages of the project lifecycle. There were clear messages about the types of support people need, which include signposting to resources, and the positive difference that mentoring by a more experienced researcher can make. We hope to use the work on the project as the foundation for building a stronger support system for people at different stages of their development as a researcher, within the RDCS and more broadly through the Centre.

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.

3

successful submissions



87

proposals



Funding

£2,001,775



14

submissions



Clients from

10

NHS organisations plus social care



Conclusion

Amidst the diverse and novel nature of studies cutting across our portfolio there are consistent threads reflecting our strategic approach. Our previously reported work on several COVID-19 related studies has continued with emergent evidence that has started to impact practice and policy (e.g. CABS, PANORAMIC, OSCAR). These have been followed by new studies that look beyond the immediate initial crisis of the pandemic to inform the care for those suffering the long-term effects of COVID-19 (e.g. LISTEN) or populations for whom the pandemic represents a particular risk (e.g. RAPID-PROTECTION). All this while staff have progressed to a hybrid model of working, sometimes meeting colleagues for the first time after joining the Centre many months ago.

Innovation in methods underpins much of our Centre work. This may be in the development of novel interventions, for example, co-productive methods used to develop a manual for patients with long COVID in LISTEN, evaluation methods such as using routine data in trials (e.g. COMORANT-UK, HARMONY) or adaptive trial design to allow earlier testing of promising new treatments for patients with Type 1 diabetes

(Vera-t1d). Designing studies that are open to all who could benefit from new treatments or forms of care has been a founding characteristic of the Centre and grows even stronger in studies across our divisions. These range from supporting patients with dementia to take part in trials of skin cancer treatments through to studies with populations defined by their disadvantage such as the PHaCT trial, whose participants are people who are homeless. Our international focus is well represented through studies such as those with the Wolfson Centre with its wide range of stakeholders and the radiotherapy trial, PATHOS with sites located across the globe.

A second underpinning core has been the development and support for research and professional services staff in our Centre and for new investigators from Wales, by whom the research of the future will be led. The latter has been the focus of our RDCS-led project and will ensure that the clinical and care needs emerging from Wales will have leaders to pick up their cause in new study ideas. The former will mean that the Centre is well prepared to partner in designing and delivering such studies.



Looking forward

Whilst it does not feel like we are really ‘post pandemic’ we are certainly moving forward into new ways of working and embedding best practice across our studies.

We are moving into our final year of our current award for infrastructure funding from both Cancer Research UK and Health and Care Research Wales and are in the process of applying for what follows. This has provided an opportunity to focus on where we want to go over the next five years and continuing to develop studies at the interface between our four divisions is a vital component, from screening, prevention, and early diagnosis of cancer (Cancer and Population Health Divisions) to sexual and reproductive health (Infection, Inflammation & Immunity and Population Health Divisions).

We will be pushing forward with engagement that opens up the ‘black box of the CTU’ as requested by our stakeholders in last year’s survey and will continue to target inclusivity and reducing burden on people who take part in studies and on services in the way we design and run our studies. Overall we aim to continue to deliver the evidence that is needed by the whole population of Wales and ensure that no one is left behind.



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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