Clinical Academics in Training Annual Conference 2025

Thursday 8 May 2025

The Academy of Medical Sciences

The Academy of Medical Sciences

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Clinical Academics in Training Annual Conference (CATAC) 2025

Contents

Welcome to CATAC 2025

"On behalf of the Academy of Medical Sciences, I have the great pleasure of welcoming researchers from across the spectrum of clinical science disciplines to our Clinical Academics in Training Annual Conference (CATAC) 2025 in Leeds. This important gathering offers a chance to share ideas that will shape the future of health and biomedical research.

Our mission is to foster a research environment that empowers the next generation of researchers to thrive. We remain committed to nurturing diverse talent across the UK, and we hope you find the conference a supportive environment for building new connections, but also one that challenges and inspires you.

Clinical academia is at a critical juncture. The UK faces concerning trends in the retention and recruitment of clinical researchers, threatening our global leadership in biomedical research. The Academy is committed to growing the clinical academic community by providing innovative career funding and support, and ensuring clear, effective and attractive career pathways. Through our policy-influencing work, we are working with partners to help address challenges and secure a bright future for clinical academia in the UK. Please do ask our staff if you would like to learn more about this or any other aspect of our work.

I'm thrilled to see researchers from all clinical backgrounds – from medicine, dentistry and veterinary sciences to nursing and allied health professions – joining us for the conference. This diversity of disciplines reflects the multifaceted approach needed to address complex health challenges both now and in the future. It's more important than ever that researchers work across disciplines, bridging clinical knowledge with computational and data science skills, to bring technological advances to healthcare.

My sincere thanks to our co-chairs – Professor Sheena Radford OBE FRS FMedSci and Professor Reecha Sofat FMedSci – for leading what promises to be a fascinating event. I also thank our keynote speakers – the Academy of Medical Sciences' Vice-President (Clinical) Professor Rosalind Smyth CBE FMedSci and Professor Dame Nicky Cullum DBE FMedSci – for their contributions.

I encourage you to take full advantage of the networking opportunities and the interactive session on Public and Patient Involvement, as well as sharing your own research achievements through the poster and oral competitions. Events like CATAC are vital for building the connections and collaborations that will strengthen the future of clinical academia in the UK – thank you for taking the time to join us and I look forward to meeting many of you."

Professor Andrew Morris CBE MD FRCP FRSE PMedSci, President of the Academy of Medical Sciences, Director of Health Data Research, Professor of Medicine, and Vice Principal of Data Science at the University of Edinburgh

"CATAC 2025 an excellent opportunity to celebrate your research accomplishments and create new connections and ideas for the future. Strong clinical pathways are essential for translating scientific discoveries into improved patient care. I encourage you to use this conference to form the partnerships that will drive the next generation of clinical breakthroughs."

Professor Sheena Radford OBE FRS FMedSci, co-chair of CATAC 2025 and Astbury Professor of Biophysics, University of Leeds

"Co-chairing CATAC 2025 gives me the opportunity to witness first-hand the remarkable talent and innovation within our clinical academic community. This conference represents more than just sharing research – it's about nurturing the collaborative spirit that drives healthcare forward. I particularly encourage early-career researchers to engage actively in our interactive sessions and to view each conversation as a potential pathway to future collaboration that could transform patient care."

Professor Reecha Sofat FMedSci, co-chair of CATAC 2025 and a FLIER alum, Breckenridge Chair of Clinical Pharmacology at the University of Liverpool

Keynote speakers

Professor Rosalind Smyth CBE FMedSci

Rosalind Smyth is Vice-Dean (Research) in the Faculty of Population Health Sciences at UCL. She is Professor of Child Health at the UCL Great Ormond Street Institute of Child Health, where she was Director of this Institute from 2012 to 2022 and served as Non-Executive Director of Great Ormond Street Hospital NHS Foundation Trust. She graduated in Medicine from Clare College, Cambridge and Westminster Medical School. Until September 2012, she was Professor of Paediatric Medicine at the University of Liverpool and, from 2005 to 2012, was Director of the NIHR Medicines for Children Research Network. Rosalind's research interests include cystic fibrosis, clinical trials and respiratory virus infections.

Rosalind has been a Fellow of the Academy of Medical Sciences since 2006 and currently is its Vice President (Clinical). She chairs the UK Medical Research Council's Training and Careers Group and is a member of MRC Strategy Board. She is Trustee of The Health Foundation, Medical Research Foundation and The Lister Institute. She was a member of the Medicines and Healthcare products Regulatory Agency's Commission on Human Medicines Committee from 2009 to 2013 and chaired its Paediatric Medicines Expert Advisory Committee from 2002 to 2013. She was awarded Commander of the Order of the British Empire in 2015 for services to the regulation of medicines for children.

Professor Dame Nicky Cullum DBE FMedSci

Nicky is a Professor of Nursing and Associate Dean for Research and Innovation in the School of Health Sciences at the University of Manchester. Since October 2019, Nicky has been Director of the NIHR Applied Research Collaboration (ARC) for Greater Manchester, a multidisciplinary research collaboration spanning diverse themes of importance to the people of Greater Manchester and beyond (e.g. mental health, healthy ageing, digital health, healthy inequalities). Nicky is also Director of Healthier Futures, the University of Manchester's interdisciplinary research platform focused on health inequalities, and Director of Manchester's Academic Health Science Centre.

Nicky is an applied health researcher, with broad interests in the effectiveness and efficiency of health and social care. Since leading the NIHR ARC for Greater Manchester, her research interests have broadened to address questions about how we reduce health inequalities, best deliver health and care services and speed the implementation of successful innovation in health systems. She has a commitment to helping develop research capacity and clinical academic careers, particularly in the underserved professions. She is a Co-Director of a Wellcome-funded PhD programme for health professionals (4Ward North) and recently represented the Academy of Medical Sciences on a Task and Finish Group focused on enhancing clinical academic career opportunities for nurses, midwives and the allied health professions. She trained as a nurse in Liverpool and was awarded a PhD in Pharmacology from the University of Liverpool in 1990.

Nicky was made a Dame for services to nursing research and wound care, in the Queen's Birthday Honours, 2013.

Programme

Leeds City Museum, Millennium Square, Leeds LS2 8BH

09.00 **Registration and poster set-up**

09.25 **Welcome**

Professor Reecha Sofat FMedSci, Breckenridge Chair of Clinical Pharmacology at the University of Liverpool and Professor Andrew Morris CBE MD FRCP FRSE PMedSci, President of the Academy of Medical Sciences, Director of Health Data Research, Professor of Medicine, and Vice Principal of Data Science at the University of Edinburgh.

09.35 **Post-doctoral plenary competition**

Each competitor will have ten minutes to present their research, followed by five minutes of questions from the judges and audience.

Targeting astrocytes to reduce intensive care-associated brain vulnerability.
Dr Zoeb Jiwaji, University of Edinburgh.

Pre-clinical development of anti-CD21 chimeric antigen receptor T cells for T cell acute lymphoblastic leukaemia – targeting a complex antigen.
Dr Nicola Maciocia, University College London.

Young-onset diabetes poses a greater risk of end-stage renal disease than cardiovascular disease and stroke: a retrospective cohort study of UK Biobank (UKB).
Dr Debasish Kar, University of Plymouth.

Co-navigating care: a qualitative study exploring distress in South Asian men with long-term conditions in primary care.
Dr Hassan Awan, Keele University.

10.35 **Refreshments and networking**

11.20 **Pre-doctoral plenary competition**

Each competitor will have five minutes to present their research, followed by two minutes of questions from the judges and audience.

A prospective observational study assessing phenotype and chemotaxis responses of circulating neutrophils in idiopathic pulmonary fibrosis.
Dr Louise Crowley, University of Birmingham and University Hospitals Birmingham NHS Foundation Trust

A randomised controlled trial for remote rehabilitation after total knee replacement: interim results of the Accelerometry and Rehabilitation after Knee replacement surgery (ARK) study.
Mr Samuel King, University of Leeds and Leeds Teaching Hospitals Trust.

The role of dendritic cells in the immune response to brain metastases.
Dr Fiona James, University of Leeds and Leeds Teaching Hospitals Trust.

An observational study of the haemodynamics of primary hypertension in untreated adolescents and young adults: the heart of the matter.
Dr Emily Haseler, King's College London and Guy's and St Thomas' NHS Foundation Trust.

Randomised controlled clinical crossover trial of 3D-printed versus analogue ocular prosthetics: motility and cosmesis outcomes.
Dr Noha Soliman, University of Manchester, Manchester Royal Eye Hospital and Moorfields Eye Hospital Foundation Trust.

11.45 Lunch

12.45 Poster competition

This will be judged by the CATAC attendees. You have been assigned one poster group to judge and this is shown on your attendee badge. Please note: poster competitors cannot act as a judge in this competition.

13.45 Patient and Public Involvement (PPI) session

Involving under-represented communities in research

15.15 Refreshments and networking

15.45 Prize giving

16.00 Keynote

Professor Rosalind Smyth CBE FMedSci, Vice Dean (Research) of the Faculty of Population Health Sciences at UCL and Vice President (Clinical) of the Academy's Council
Professor Dame Nicky Cullum DBE FMedSci, Professor of Nursing and Associate Dean for Research and Innovation in the School of Health Sciences, University of Manchester and Director of the NIHR Applied Research Collaboration (ARC) for Greater Manchester

16.45 Closing remarks

Professor Sheena Radford OBE FRS FMedSci, Astbury Professor of Biophysics, University of Leeds

16.50 Networking reception

18.00 Event ends

Patient and Public Involvement (PPI) session

Involving under-represented communities in research

At the Academy, we believe that research must include the voices of those who will be affected throughout its planning, undertaking, and dissemination. This is particularly crucial in clinical research and is often called Patient and Public Involvement (PPI).

We're thrilled to be joined by speakers from across the North of England, who will share insight and reflections from working with under-represented communities at various stages of the research process – from grant applications to evaluation.

Join us for an engaging conversation on how to foster meaningful involvement of patients and the public in your research. Whether you've collaborated with patients and the public before or not, we encourage you to bring your curiosity and explore how to better involve under-represented patients and the public in your work. If there's a question you'd like to ask in advance, or a topic you think we should cover, feel free to email us at **engagement@acmedsci.ac.uk.**

You will hear from:

Dr Carolyn Lees, Senior Lecturer, University of Liverpool
Carolyn has a long-standing history of leading and supporting research studies that have focused on those populations who are often under-represented in research, including those individuals with a cognitive or learning disability. Her expertise in facilitating focus groups and the collection and analysis of qualitative data has been evidenced by successful grant applications within the University of Liverpool and beyond, with several publications disseminating the findings of research activity and presentations at conferences, both nationally and internationally. Her strength is working within multidisciplinary research teams and engaging with external partners to ensure an inclusive approach to research activity and the creation of new knowledge for the benefit of health and social care delivery. Currently, Carolyn, together with academic colleagues from the School of Allied Health Professions and Nursing at the University of Liverpool and adults with a mild cognitive disability, are working on co-authoring a paper for publication. Carolyn has a clinical background in district nursing and was awarded the Queen's Nurse title in 2018 in recognition of her commitment to delivering and leading outstanding care in the community.

Dr Rebecca Mawson

Dr Rebecca Mawson is an NIHR Clinical Lecturer in Primary Care at the University of Sheffield and practising GP with a focus on addressing reproductive health inequalities through innovative co-design methodologies. Her research specifically targets improving healthcare access and experiences for under-represented populations.

Rebecca is currently leading 'The Hormone Effect' (THE), an innovative project funded by the South Yorkshire Digital Health Hub that explores the effects of hormonal contraception through digital tracking methodologies. Her ongoing work includes developing community-led research initiatives where community researchers facilitate focus groups with women from ethnic minority backgrounds to better understand their experiences with contraception services.

Through her clinical practice and research, Rebecca continues to advocate for equitable healthcare access and improved reproductive health outcomes for all populations.

Helen Marshall

Helen Marshall is a lecturer at the University of Liverpool, based in the nursing department at the School of Allied Health Professions and Nursing. She is a registered District Nurse and a Queen's Nurse.

Her nursing career has been within the community setting as a community nurse, tissue viability nurse and safeguarding adults specialist nurse. She moved to education in 2019 and currently leads on the practice learning element of the programme alongside theoretical teaching.

She is the lead for patient and public involvement and engagement within her department.

Her research interests have included district nursing and the Mental Capacity Act. Her current research work involves working with adults with a mild to moderate intellectual disability and promoting the inclusion of this population in teaching and in research. She is currently in Year 1 of a part-time PhD.

Jamie Taylor

Jamie Taylor is a culture and heritage professional with over 20 years' experience of telling stories. He is Director of Collections, Programmes and Learning at the Thackray Museum of Medicine, where he oversees a vibrant schools and family offer, a nationally recognised exhibition programme, and over 80,500 objects, books and archives. Passionate about doing genuine good, he has been instrumental in developing The Core – a place where local community and patient groups have space and support, free of charge, to focus on the health and wellbeing of themselves, their families and friends.

Fatima Nabage

Fatima Nasiru Nabage is a public health researcher and Research Associate at the University of Sheffield. She recently completed work funded by the Wellbeing of Women Early Career Researcher Grant and is currently working on the COLIF project, focusing on improving health outcomes through community-led interventions. With a strong interest in health equity, she has worked on projects aimed at improving access to contraception for ethnic minority women and enhancing cancer-screening uptake among individuals with mental health needs.

Fatima is particularly passionate about women's health, holistic adolescent health, reproductive justice, and the intersection of policy, health equity and public health. Her recent research explores how healthcare providers communicate contraception side effects to women from ethnic minority backgrounds, employing qualitative methodologies such as co-production workshops and focus groups to elevate community voices.

Her experience as a Community Research Link Worker with Dr Rebecca Mawson shaped her passion for qualitative research, particularly in co-production and community engagement. This role allowed her to explore how lived experiences influence health behaviours and interventions.

She holds a Master's degree in Public Health Management and Leadership from the University of Sheffield and is passionate about integrating qualitative methodologies with policy approaches to improve healthcare accessibility and outcomes. She aims to contribute to sustainable public health solutions that address the unique needs of adolescents across the African continent.

Post-doctoral plenary competition

Young-onset diabetes poses a greater risk of end-stage renal disease than cardiovascular disease and stroke: a retrospective cohort study of UK Biobank (UKB)

Dr Debasish Kar
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Background
Historically, people with diabetic kidney disease (DKD) died of cardiovascular disease (CVD) before progressing to end-stage renal disease (ESRD). However, in recent years, the number of people with DKD progressing to ESRD has been steadily increasing. This epidemiological shift is putting enormous pressure on the healthcare budget and impacting people's quality-adjusted life years (QALYs). The precise cause for this shift remains unexplored. However, in the last two decades, the prevalence of younger-onset diabetes and DKD incidence has risen exponentially. This study examines whether young-onset diabetes is a greater risk for ESRD compared to myocardial infarction (MI) and stroke.

Methods
We used the data of UKB volunteers aged 40–69 years recruited between 2006 and 2010. We used the responses to the questionnaire filled out by the eligible study participants. The exposure variable was the age of diabetes diagnosis, while the outcomes of interest were ESRD, myocardial infarction, and stroke. UK Biobank received ethical permission and patients' consent. We used univariate and multivariate logistic regression analyses to examine the risk of ESRD, MI, and stroke. Model performance was assessed using receiver operating characteristics (ROC) and calibration plots. Results were expressed in odds ratios (ORs) and 95% confidence intervals (CIs).

Findings
Out of 26,206 people with diabetes, 1.16% (*n*=303) had ESRD, 8.58% (*n*=2250) had a myocardial infarction, 7.47% (*n*=1958) had angina, and 2.94% (*n*=771) had a stroke. The univariate logistic regression model showed that compared to those diagnosed after the age of 60, the odds of ESRD for those diagnosed at ages <20, 20–40, and 41–60 years were OR 2.33 (95% CI 1.50–3.84), 7.78 (95% CI 4.81–13.16), and 5.26 (95% CI 3.00–9.40), respectively. Myocardial infarction and stroke did not have a statistically significant relationship with diabetes diagnosis age. We adjusted diabetes diagnosis age and duration in the multivariate logistic regression model, which confirmed that younger age and longer duration of diabetes increase the risk of ESRD. The ROC analyses showed >80% area under the curve, confirming excellent model discrimination. The ESRD onset was earlier in young-onset people with diabetes than older-onset people.

Interpretation
Younger-onset diabetes may be responsible for the recent surge of DKD and ESRD. As ESRD starts earlier in young-onset diabetes, the morbidity, QALY and the financial burden on the NHS are expected to rise. Young-onset diabetes should be prioritised for closer monitoring, and risk factors such as childhood obesity should be proactively managed. This study's strengths are its large dataset of over 500,000 people and the novel stratified analyses it uses. However, the data from the volunteers are not nationally representative, and findings cannot be generalised. We could not differentiate between the types of diabetes due to data limitations.

Wider implications
Young-onset type 2 diabetes mellitus (T2DM) is a more aggressive disease phenotype. While the annual rate of pancreatic beta-cell decline is around 7% in adult-onset diabetes, it is about 20%–30% in young-onset T2DM. The rate of obesity between young- and older-onset T2DM is 95% vs. 50%, and a higher level of systemic inflammatory cytokines predisposes to endothelial dysfunction. This cardiometabolic profile might be more detrimental to renovascular than cardiovascular integrity. This study identified a service and policy gap in the diabetes management pathway. Due to the rapid progress of renovascular complications, future research should address it as a priority.

Co-navigating care: a qualitative study exploring distress in South Asian men with long-term conditions in primary care

Dr Hassan Awan

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Background
People from ethnic minority backgrounds experience higher rates of mental health problems yet have lower rates of mental health service engagement and poorer outcomes. People with long-term physical health conditions (LTCs) are more likely to have comorbid mental and health problems, which lead to poor patient outcomes. South Asians (SAs) are the largest ethnic minority in the UK. There is limited understanding of how SA men with LTCs seek help for emotional distress in primary care. This study aimed to explore how SA men with LTCs seek help for emotional distress and understand GPs' experiences of supporting them.

Methods
Ethical approvals obtained. Qualitative study using semi-structured interviews with 17 SA men with LTCs (diabetes/coronary heart disease) and 18 GPs from practices serving significant SA populations in three UK regions. Interviews with SA men explored experiences of emotional distress, help-seeking behaviours, and perspectives on primary care support. Interviews with GPs explored perspectives on provision of care for this patient group. Reflexive thematic analysis with constant comparison. A patient advisory group (PAG) of five SA men provided input throughout the research process, ensuring cultural relevance.

Findings
Two key themes will be presented: trust and co-navigating care. SA men described mistrust in GP services due to perceived over-medicalisation of distress, discrimination and cultural disconnection. Instead they prioritised faith, family, and self-management strategies. The concept of 'co-navigating care' was developed whereby both GPs and patients bring their health beliefs to consultations, requiring mutual respect to negotiate and agree effective management plans.

We developed the '3Cs' model for consultations (Contextualising distress: social determinants of distress & intersectionality; Conceptualising distress: de-medicalising distress, negotiating multiple identities, integrative paradigms of health; Consulting with distress: co-navigating care, culturally safe care, community-centred care). The study highlighted the importance of understanding communities as part of person-centred care, incorporating faith and cultural perspectives, and building cultural safety in primary care services.

Interpretation
Our findings demonstrate the need for a shift in how primary care clinicians identify and manage SA men with LTCs and emotional distress. The 3Cs model can facilitate GPs to deliver culturally safe care. This model has the potential to improve primary care consultations and mental health support for people from SA communities, addressing health inequalities through community-centred approaches to primary care delivery.

These findings have implications beyond SA populations, providing insights into delivering culturally safe mental healthcare for diverse communities and addressing intersectional health inequalities in primary care. The co-navigation approach could transform relationship-based care across healthcare settings.

Wider implications
This research's implications extend beyond SA men with LTCs. The 3Cs model and concept of co-navigating care provide frameworks applicable to supporting any patient group where cultural beliefs, health inequalities, or mistrust affect healthcare engagement. The findings could transform how clinicians approach consultations with patients from different cultural backgrounds across all healthcare settings. A video animation was co-created with the patient advisory group **(https://youtu.be/pSuTAf_JU1I)**. The research demonstrates how integrating faith and community perspectives into mainstream healthcare could improve service accessibility and effectiveness.

The findings challenge traditional approaches to cultural competency, suggesting that systemic changes are needed in medical education and healthcare delivery to achieve cultural safety. This could influence professional training, service design, and health policy, particularly around reducing health inequalities and improving relationship-based care in increasingly diverse populations. The co-navigation approach offers a template for delivering person-centred care that respects diverse health beliefs and paradigms.

Pre-clinical development of anti-CD21 chimeric antigen receptor (CAR) T cells for T cell acute lymphoblastic leukaemia – targeting a complex antigen

Dr Nicola Maciocia
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Background
Relapsed/refractory (r/r) T cell acute lymphoblastic leukaemia (T-ALL) has a dismal prognosis, highlighting the urgent need for effective novel therapies. Chimeric antigen receptor (CAR)-T therapy targeting CD19 has revolutionised treatment for B cell malignancies. CAR-T approaches targeting pan-T antigens such as CD7 in T-ALL may be limited by T cell aplasia and fratricide (CAR-T self-kill during manufacture). Targeting antigens only expressed on T-lymphoblasts without expression on normal T cells is more desirable. CD21, a type 1 transmembrane glycoprotein, mainly expressed on mature B cells and follicular dendritic cells (FDCs), was investigated as a potential target for T-ALL CAR-T therapy.

Methods
This study was designed to validate expression of CD21 in T-ALL and normal tissues using cell lines, patient samples and healthy donors. The study additionally involved identification of CD21-directed antibody fragments followed by pre-clinical testing of anti-CD21 CAR-T cells using *in vitro* assays (cell lines, patient samples, patient-derived xenografts) and *in vivo* models of cell lines and patient-derived xenografts. UCL Research Ethics Committee granted ethical approval for the study. Animal work was performed under a UK Home Office-approved project licence (PP8379762) and was approved by the UCL Biological Services Ethical Review Committee.

Findings
CD21 was found to be expressed in 50% of T-ALL cases at diagnosis but in fewer than 10% of mature T cells. Initial CAR-T cells targeting membrane-distal CD21 epitopes were ineffective, likely due to the bulky, glycosylated nature of the antigen. However, CAR-T cells engineered to target membrane-proximal CD21 epitopes using a novel Fab-CAR design demonstrated robust activity against T-ALL cell lines, primary tumours, and patient-derived xenografts in both *in vitro* and *in vivo* models. The enhanced efficacy of this Fab-CAR design was driven by its high stability and reduced surface expression. Additionally, pharmacological inhibition of the phosphoinositide 3-kinase (PI3K) axis with copanlisib upregulated CD21 expression in T-ALL, further enhancing the potency of anti-CD21 CAR-T cells.

Interpretation
In this study we identified CD21 – a pan-B-cell marker – as a novel and promising target for T-ALL immunotherapy. Our results establish CD21 as a viable CAR-T target. Significantly, CD21 expression was largely restricted to T lymphoblasts, meaning that targeting of CD21 would specifically kill tumour cells whilst sparing normal T cells, and would avoid issues of fratricide (self-kill) seen with other pan-T cell antigen-targeting approaches. Our study also highlights advances in CAR design for bulky antigens, as well as the potential for pharmacological strategies to augment CAR target expression.

Wider implications
The results of this project will be of interest internationally to both academics and clinicians working on T-ALL and CAR-T cells. Patients with r/r T-ALL urgently need new and effective therapies. It will add to the growing literature on T cell antigen targets for CAR-T treatment and bring the field a step closer to achieving a successful product that is available to patients. The results describing CAR engineering approaches/pharmacological manipulation of target density will be of broader interest to the entire CAR-T cell research field.

Targeting astrocytes to reduce intensive care-associated brain vulnerability

Dr Zoeb Jiwaji

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Background
Intensive care unit (ICU)-associated brain dysfunction is prevalent. 50% of patients experience cognitive issues and 24% of survivors are left with new long-lasting cognitive deficits akin to Alzheimer's disease. The cellular mechanisms by which disease factors ultimately cause brain dysfunction remain unclear, impeding therapy development. Previous research centred on neurons. However, non-neuronal brain cells called astrocytes, which play multiple homeostatic roles critical for brain health, were understudied.

1. How do illness factors associated with ICU brain dysfunction (pre-existing dementia, sedatives and inflammation) alter astrocyte functions critical for brain health?
2. Can altered astrocytes be therapeutically targeted for neuroprotective benefit?

Methods
In my programme, I have used several advanced molecular methods to investigate how disease factors associated with ICU brain impairment alter astrocytes. Key methods include:

- Translating ribosome affinity purification (TRAP)-sequencing, involving astrocyte-specific GFP-tagged ribosomes, to delineate astrocyte changes in transgenic mouse models of dementia (APP/PS1, MAPT-P301S).
- A prolonged anaesthesia mouse model, along with light and electrical brain stimulation, to delineate mechanisms underlying anaesthesia-induced brain vulnerability.
- To move beyond animal models and to understand how sepsis-induced inflammation alters astrocytes in humans, ongoing work involves single-nucleus RNA-sequencing (snRNAseq) of patient-derived brain tissue and cultured living human brain tissue slices.

Findings
Using TRAP-sequencing in transgenic mouse models, I characterised astrocyte changes to dementia pathology, the major risk factor for ICU-associated brain impairment. This revealed that astrocytic alterations are heterogeneous, encompassing both neurotoxic inflammatory and protective responses, something not previously known. Furthermore, I demonstrated that enhancing protective astrocyte functions, through cell-type-specific upregulation of the transcription factor Nrf2, conferred neuroprotection and slowed disease progression (published, Nature Communications 2022). I also found that sedative anaesthesia triggered inflammatory changes in astrocytes, disrupting homeostatic pathways crucial for brain health. Notably, these alterations mirrored those seen in Alzheimer's. Furthermore, I delineated the role of altered neuronal firing in mediating anaesthesia-induced consequences and uncovered a previously unknown feedback loop by which neuron–astrocyte crosstalk regulates brain metabolic homeostasis (published, Nature Communications 2017). Subsequently, in ongoing work investigating sepsis-mediated brain changes in patients, I have identified (via snRNAseq) sepsis-associated astrocyte subpopulations exhibiting signatures of metabolic dysregulation.

Interpretation
My findings offer new insights into how disease factors associated with ICU-associated brain dysfunction alter astrocytes, a key neurosupportive brain cell type. I uncovered that although dementia pathology and anaesthesia drive inflammation-associated neurotoxic changes in astrocytes, these cells also mount protective responses. These can be enhanced to reduce disease effect. Consequently, astrocytes emerge as promising therapeutic targets. An important limitation is the reliance on animal models. Therefore, my ongoing research uses patient-derived brain tissue to investigate how sepsis alters astrocytes in humans, with the long-term goal being to identify patient-relevant cellular targets to guide future neuroprotective drug therapy.

Wider implications
ICU-associated brain dysfunction presents a major challenge in critical care, with profound impacts on patients and society. Recognised as a top-3 research priority by patients, carers and clinicians (James

Lind Alliance), I have sought to tackle this challenge by uncovering the cellular mechanisms responsible. Through my research, I discovered significant alterations in astrocytes — essential neurosupportive cells — revealing their potential as targets for brain protection. My long-term goal is to use this knowledge to develop patient-specific therapies aimed at reducing brain injury post-ICU. The implications of my work extend beyond critical illness, as reactive astrocytes play a crucial role in several brain conditions, including neurodegenerative diseases, traumatic brain injury and stroke. The molecular changes I identified are shared across these conditions. This raises the hope that astrocyte-targeted therapies could offer widespread therapeutic benefits across a spectrum of neurological disorders to improve patient outcomes and quality of life.

Pre-doctoral plenary competition

An observational study of the haemodynamics of primary hypertension in untreated adolescents and young adults: the heart of the matter

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Background
Primary hypertension is increasingly prevalent in adolescents and young adults. In older adults, hypertension is thought to be caused by increased resistance of the microvasculature and age-related stiffening of large arteries, but the circulatory changes underlying hypertension in adolescents and young adults are poorly understood. If confirmed, this would have implications for medication choice in this age group. This project examines the haemodynamic aetiology of hypertension in untreated adolescents and young adults using cardiac MRI (CMR). Since early-onset hypertension is usually a lifelong condition, this informs the aetiology of hypertension in adults of all ages.

Methods
Participants aged 10 to 30 years were prospectively recruited into an observational cohort study. Hypertensive untreated participants were recruited from paediatric and adult hypertension clinics at Guy's and St Thomas' Hospital and compared with normotensive controls with normal BMI. Hypertension was defined by standard clinical guidelines. CMR was used to determine cardiac geometry and aortic dimensions using a 1.5 Tesla Siemens Scanner. Key haemodynamic variables were derived from left ventricular volumes acquired during a short-axis stack sequence and from post-processing analysis. Blood pressure (BP) was measured at the time of CMR using a validated oscillometric BP monitor.

Findings
Mean BP 134.5±10.6/79.2±12.9 mmHg) and 29 hypertensive (21.7±5.6 years, mean BP 115.6±12.5/67.2±11.6 mmHg). BMI was higher in the hypertensive compared to the normotensive group (28.1±6.1 vs 22.7±4.2 kg/m^2, $p<0.001$). Cardiac output was higher (7.8±1.6 vs 6.3±1.9 L/min, $p<0.001$) and descending aorta distensibility lower (4.8±2.8 vs 6.3±1.8 10^{-3} $mmHg^{-1}$, $p=0.04$) in the hypertensive group. There was no difference in systemic vascular resistance or proximal aortic pulse wave velocity. The difference in cardiac output was due to higher heart rate rather than higher stroke volume in the hypertensive group.

Interpretation
These results suggest that in overweight/obese adolescents and young adults, higher heart rate is a key determinant of hypertension. They implicate derangement of the autonomic nervous system rather than vascular remodelling as the earliest mechanism underlying hypertension in this age group. If confirmed, this suggests hypertension in young people may respond better to different prevention and treatment strategies than in older adults. It is important to note that these results do not separate the haemodynamic effects of obesity from those of hypertension. Further analysis is planned to investigate whether the haemodynamic hypertension phenotype differs according to demographic and metabolic characteristics.

The role of dendritic cells in the immune response to brain metastases

Dr Fiona James

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Background
Brain metastases (BrM) are a devastating consequence of cancer and remain a huge unmet clinical need. They are found in 10%–30% of patients with systemic malignancies and remain an important limiting factor in patient survival. Importantly, immune biology and response to therapies differ in the brain from the rest of the body. In the era of increasingly effective immunotherapies, it is hence critical to explore how immune responses work in the context of BrM. Our work focuses on dendritic cells as the major antigen-presenting cell type.

Methods
This work utilises in vivo models of breast cancer and melanoma BrM with both intracranial and extracranial tumour, best mimicking the clinical situation in most cases of BrM. We use Batf3 knockout mice, which lack a subpopulation of dendritic cells – conventional dendritic cells subtype 1 (cDC1s). We use a combination of tumour growth and survival analysis, flow cytometry and bulk mRNAseq to explore the role of the cDC1 population in intracranial and extracranial tumours and in response to immune checkpoint blockade.

Findings
We have shown that the cDC1 population is consistently critical in restricting tumour growth in the brain. This was in contrast to its role in extracranial tumours, which varied in a cancer model-dependent manner, with cDC1s promoting extracranial tumour growth in breast cancer models. Importantly, this mirrored what we see in patients, where the abundance of cDC1s in primary breast tumours, as determined by cDC1 gene expression, negatively correlates with survival, while cDC1 abundance in breast cancer BrM positively correlates with survival from BrM. In preclinical models, the cDC1 population also played a more important role in response to immune checkpoint blockade in BrM than at extracranial sites. In addition, immune cell infiltration into tumours was dependent on cDC1s to a higher degree in intracranial as compared to extracranial tumours. Lastly, cDC1s isolated from intracranial tumours differed in their molecular profile from those isolated from extracranial tumours.

Interpretation
These results uncover an exciting differential dendritic cell response to tumours in the brain compared to extracranial tumours and suggest promising avenues for dendritic cell-related therapies that may be specific to intracranial tumours.

A prospective observational study assessing phenotype and chemotaxis responses of circulating neutrophils in idiopathic pulmonary fibrosis

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Background
Drivers of epithelial damage and fibrosis in idiopathic pulmonary fibrosis (IPF) remain unclear. Neutrophils are the most common immune cells in the body and are critical responders to tissue injury, housing an array of enzymes critical for repair and remodelling. Neutrophil count correlates with IPF severity, and neutrophil extracellular traps (NETs) are observed in IPF lung tissue. However, the role of neutrophils in IPF remains unknown. This prospective cohort study aimed to compare the phenotype, movement and NET responses of circulating neutrophils derived from IPF patients to age-matched control participants.

Methods
IPF and control participants were prospectively recruited between September 2023 and September 2024 to the 'HYBRID' cohort study (REC:22/WM/0274). Following informed consent, participants were characterised by physiological measures (pulmonary function and 6-minute walk tests) and health-related quality-of-life questionnaires. Neutrophil count was measured in venous blood using the Sysmex XN-1000 analyser, and neutrophils isolated via Percoll density gradient centrifugation. Cell surface markers (phenotype) were assessed using flow cytometry. Chemotaxis was assessed by real-time microscopy imaging using the Insall chamber assay. Cell-free DNA (cfDNA) release (a marker of NET formation) from neutrophils was measured using SYTOX™ green staining.

Findings
Twenty-six IPF and 16 control participants were recruited and were comparable for demographics and comorbidities. Mean age was 75 years and >70% were male in both cohorts. IPF patients' mean forced vital capacity and gas transfer were 77.8% and 56.2% predicted, respectively. Peripheral neutrophil count was greater in IPF patients than controls (4.6×10^9/L versus 3.3×10^9/L, p=0.001). IPF patients displayed a lower percentage of $CD10^{positive}$ neutrophils than controls (p=0.02). CXCR4 (chemokine receptor) and PD-L1 (co-inhibitory molecule) expression was higher in IPF-derived neutrophils (p<0.05). Activation markers and movement responses to the chemoattractants, IL-8 and *N*-formylmethionyl-leucyl-phenylalanine (fMLP) were equivalent. IPF neutrophils moved less directly than controls (p<0.001) on exposure to the pro-fibrotic growth factor, 10 ng/mL transforming growth factor β-1 (TGFβ1). cfDNA release in response to IL-8 and IL-1β was equivalent, but less was noted in IPF-derived neutrophils on exposure to PMA (p=0.01). Unpaired T-tests and Mann–Whitney tests were performed for normally distributed and skewed data, respectively.

Interpretation
This is the first prospective study to compare neutrophil phenotype/function in IPF patients to a closely matched control cohort. The identification of an increased neutrophil count and higher percentage of $CD10^{negative}$ neutrophils, suggests an expansion of immature neutrophils and emergency granulopoiesis. Dysregulated movement responses to the key fibrotic mediator TGFβ1 is novel. A limitation of this work is that circulating neutrophils may not represent populations within the lung; investigation within tissue and bronchoalveolar lavage fluid is currently ongoing. Further investigation into the underling mechanisms and impact on IPF pathogenesis could identify neutrophils as a much-needed novel avenue of therapeutic manipulation.

Randomised controlled clinical crossover trial of 3D-printed versus analogue ocular prosthetics: motility and cosmesis outcomes

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Background
To report the results of a randomised crossover trial comparing fully 3D-printed (digital) versus handmade (analogue) ocular prosthetics.

Methods
We conducted a phase I/II randomised, controlled, crossover trial at Moorfields Eye NHS Foundation Trust, UK, comparing 3D versus handmade ocular prostheses. Adults aged ≥18 years with ≥1-year post-enucleation follow-up were eligible. Digital prostheses were created using AS-OCT with a colour camera to scan the socket and fellow eye, Cuttlefish:Eye software for shape computation, and a 3D printer for fabrication. Participants were randomised using concealed allocation via a centrally generated STATA list. The primary endpoint was non-inferiority of 3D prostheses for motility (≤1 mm difference) and cosmesis. Ethics approval and informed consent were obtained. Trial registration: NCT05093348.

Findings
Between 25 November 2021 and 30 June 2022, 40 participants (22 female, 18 male) were enrolled in a randomised crossover trial comparing Click2Print and handmade ocular prostheses. A standard t-test confirmed non-inferior motility for 3D prostheses ($p>0.05$); similarly paired Wilcoxon tests showed no significant differences in cosmesis ($p>0.05$). Mild adverse events included mucous discharge (53.33% vs 46.67%), irritation (56.67% vs 56.67%), discomfort (6.67% vs 6.67%), and inflammation (10.00% vs 3.33%) for 3D and handmade prostheses, respectively. Unique issues with 3D included prosthetic rotation (13.33% vs 0%), poor fit/motility (6.67% vs 0%), and dry eye socket (3.33% vs 0%). Handmade prostheses had slightly higher rates of infection (6.67% vs 3.33%) and bacterial conjunctivitis (3.33% vs 0%). The only statistically significant result was 3D prosthesis rotation (Mann–Whitney U, $p=0.0419$).

Interpretation
This trial demonstrates the non-inferiority of 3D ocular prostheses compared to handmade prostheses in motility, cosmesis, comfort, fit, and adverse events, offering a cost-effective, scalable alternative. Strengths include a robust crossover design, concealed randomisation, and patient-centred outcomes. Limitations include its single-centre setting and small sample size, which may limit generalisability. Mild adverse events, such as 3D prostheses rotation, warrant further study. Despite these limitations, the findings support the potential of digital manufacturing techniques in ocular prostheses, paving the way for broader clinical application and improved accessibility for patients requiring artificial eyes.

A randomised controlled trial for remote rehabilitation after total knee replacement: interim results of the Accelerometry and Rehabilitation after Knee replacement surgery (ARK) study

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Background
Increasing demand, long waiting lists and emphasis on cost reduction have contributed to a reduction in face-to-face follow-up following total knee replacement (TKR). NICE guidelines currently recommend preferencing self-directed unsupervised home exercises over face-to-face sessions of physiotherapy. Adherence with exercise therapy in this approach is often poor. Wearable sensors (WSs) for remote supervision of physiotherapy are a potential solution, as they allow feedback, bespoke care and reassurance. However, cost-effectiveness and clinical effectiveness need to be proved. This study aims to assess the cost-effectiveness and clinical effectiveness of remote monitoring with WS technology in primary TKR patients.

Methods
A 200-participant prospective single-centre randomised controlled trial (RCT) compared rehabilitation methods for patients undergoing primary TKR. Health Research Authority research ethics committee and institutional review board approval were in place. Allocation was 1:1 unsupervised exercise standard care (SC) group vs remotely supervised rehabilitation with a WS group (BPMpathway sensor, B. Braun) including pre-surgery instructions and sensor use for a 2-week period. Follow-up was at 6 weeks, 6 months and 12 months post-TKR. Primary outcome was 6-month Oxford Knee Score (OKS). Secondary outcomes included EQ-5D-5L, Knee Injury and Osteoarthritis Outcome Score (KOOS), Timed Up and Go (TUG) test, range of motion (ROM) and unplanned interventions. Registration: ClinicalTrials.gov (NCT05412940).

Findings
186 patients have reached the primary end point. The two groups were well matched and there was no difference between the groups for patient-reported outcome measures (PROMs: OKS, KOOS), functional measures (ROM, TUG test), pain scores, satisfaction ratings or complications. Compared with SC, WS participants needed more physiotherapy phone calls (43.4 vs 25.7 minutes, $p<0.001$), fewer surgeon phone calls ($p=0.026$), less face-to-face physiotherapy (12.8 vs 31.8 minutes, $p=0.007$) and fewer surgeon appointments ($p=0.022$). WS participants with high exercise adherence (>2 exercises/day; 31%) had better early functional recovery (improved TUG and ROM) vs lower adherence groups (10.07 vs 11.72 seconds, $p=0.044$; 110 vs 100 degrees, $p=0.037$, respectively). Adverse events were recognised complications of SC, within expected range and unrelated to the study or its interventions.

Interpretation
WSs allow remotely supervised rehabilitation following TKR. They reduce the need for face-to-face follow-up in keeping with recent NICE guidelines for outpatient rehabilitation, without negatively affecting clinical outcomes. They also improve adherence and facilitate earlier functional recovery. This is especially relevant given the long-term plans of the NHS regarding digitisation and reduction in face-to-face follow-up. This is the largest study of WS remote rehabilitation for TKR that examines clinical effectiveness and cost-effectiveness and the only RCT in this area in the NHS. A multi-centre prospective RCT is needed to confirm these preliminary findings.

Poster competition

Addressing excess weight in UK adult secure mental healthcare: a mixed methods programme of research

A1

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Background
Patients living with severe mental illness (SMI, including schizophrenia and bipolar disorder) die on average 15–20 years earlier than the general population. This is primarily due to physical health conditions, often attributable to overweight and obesity. Excess weight is most extreme in secure mental healthcare, where patients are detained in locked wards due to risks posed to themselves and/or others. In such settings, over 80% of patients are generally living with overweight and obesity. This study aimed to use mixed methods and stakeholder engagement to explore key influential factors and priority areas for tackling excess weight in secure care.

Methods
Four integrated workstreams were undertaken in secure services at a National Health Service (NHS) mental health trust. All staff were surveyed to explore their views and experiences of weight management. Ethnographic in-person observations were undertaken on an inpatient ward over 6 months. Focus groups were conducted separately with current and former patients, carers and multidisciplinary staff, and semi-structured interviews were undertaken with multidisciplinary secure services staff at a second complementary NHS trust. A diverse working group triangulated the empirical findings, and key themes were identified through framework analysis. Ethics approval was received from NHS Research Ethics Committee London, Bromley – 22/PR/0100.

Findings
Survey responses (79/488, 16% response rate) were received, representative of the different professional groups and services in secure care. In-person observations spanning 23 hours were undertaken, with nine focus groups (37 total participants) and 11 individual interviews. Seven overarching qualitative themes were identified. *Antipsychotic medication* was noted to precipitate weight gain, subsequently perpetuated by *insufficient staffing levels* to facilitate physical activity and health promotion. *Sedentary lifestyles* due to limited exercise opportunities and low patient engagement were highlighted. *Hospital food* was perceived as monotonous and unappetising, leading to increased snacking, and reciprocal intake of foods high in fat, salt and sugar purchased from *alternative outlets and/or brought in by others. Low patient motivation* to eat well and exercise was prevalent, primarily attributable to SMI and institutionalisation. *Hospital culture* was generally perceived to centre around unhealthy food, with limited staff capacity and authority to mandate healthier choices.

Interpretation
Factors driving excess weight amongst patients with SMI in secure services are multifaceted and embedded into current approaches to SMI management and healthcare culture, leading to a potentially 'obesogenic environment'. Complex interventions involving wide-ranging stakeholders are likely to be required, with linked longitudinal studies to evaluate feasibility and impact. To our knowledge, this is the first study to use a focused ethnographic approach, and involve current patients, former patients, carers and multidisciplinary staff, through a mixed-methods approach exploring weight management in secure mental healthcare. Our research was primarily conducted in one NHS trust, which may limit wider generalisability of findings.

Implications

Focused ethnography facilitates immersion into the research environment, enabling direct observation and exploration of behaviours and perceptions in context. Our research demonstrates the feasibility, and unique insights gained, through undertaking ethnography in secure mental healthcare. This approach could potentially be implemented in other healthcare settings such as outpatients, to generate novel clinical findings, or in other food environments such as canteens, to explore food-related behaviours. People with lived experience of secure care are under-represented in research. Our study shows the value and feasibility of involving experts by experience, which is likely to be generalisable to other research contexts involving vulnerable groups. Weight management in secure services is a complex challenge, requiring whole setting-based interventions. These should incorporate underpinning determinants such as a holistic health-promoting culture, and involve all key stakeholders. Such insights are likely to be transferable to research interventions in other closed settings, such as schools and residential homes.

Distressing dreams, accelerated biological ageing, and risk of premature mortality: a population-based multicohort study

A2

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Background
Distressing dreams (bad dreams and nightmares) are associated with an increased risk of developing age-related neurodegenerative diseases. Whether distressing dreams increase the risk of developing other age-related health outcomes is unknown. This study investigated the association between distressing dreams and the risk of accelerated biological ageing and premature mortality in community-dwelling adults.

Methods
This longitudinal, multi-cohort study used pooled data from three US cohort studies (Midlife in the United States [MIDUS]; Wisconsin Sleep Cohort [WSC]; the Osteoporotic Fractures in Men [MrOS] Study). Distressing dream frequency was self-reported at baseline in all cohorts. Premature all-cause mortality (before age 75 years) was defined using study records. Cox regression was used to analyse the prospective association between distressing dreams and premature mortality. In MIDUS, the pace of biological ageing was measured at baseline using the DunedinPACE epigenetic clock. Mediation analysis was used to assess whether accelerated biological ageing mediates the relationship between distressing dreams and premature mortality.

Findings
Among a total population of 4,196 participants (mean age = 60.6 years, age range = 26–74), 342 (8.2%) experienced frequent distressing dreams at baseline. During 18.3 years of follow-up, 227 premature mortality cases were documented. After adjusting for demographic characteristics, frequent distressing dreams were associated with a nearly 3-fold risk of premature death in the pooled cohort (hazard ratio, HR = 2.57, $P<0.001$) and in each cohort separately (MIDUS: HR = 2.74, $P<0.05$; WSC: HR = 2.77, $P<0.05$; MrOS: HR = 2.25, $P<0.05$). In MIDUS, individuals with frequent distressing dreams exhibited a faster pace of biological ageing ($P=0.009$). Accelerated biological ageing mediated 21% of the distressing dream–mortality association. These associations remained robust when adjusting for a wide range of possible confounders.

Interpretation
Adults with frequent distressing dreams experience faster biological ageing and die at younger ages. Future studies are needed to determine whether treating distressing dreams could slow biological ageing and reduce mortality risk in the general population.

Implications
Reduction of premature deaths is one of the United Nation's sustainable development goals for 2030. These findings demonstrate for the first time that treatment and prevention of distressing dreams might help to delay population ageing and reduce premature mortality risk. These findings may also help to explain the association between distressing dreams across the lifespan (childhood and adulthood) and increased risk of developing age-related neurodegenerative diseases in later life.

Diagnostic yield of manometry in paediatric patients in a tertiary centre

A3

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Background
High-resolution oesophageal manometry (HROM) and anorectal manometry (ARM) are invaluable diagnostic tools that significantly enhance our understanding of complex paediatric gastrointestinal (GI) motility disorders, providing detailed information on the neuromuscular coordination and physiological function of the GI tracts. HROM is particularly useful for screening patients for anti-reflux interventions, e.g. fundoplication or STRETTA®, while ARM also plays a crucial role in the screening process for Hirschsprung's disease. This diagnostic capability enables clinicians to create personalised treatment plans, thereby optimising GI health outcomes for their patients.

Methods
A 5-year retrospective analysis from 2018 to 2023 of medical records from a tertiary paediatric centre was conducted. The study targeted patients aged 0 to 18 years who had undergone HROM or ARM. Exclusion criteria were applied to cases with unavailable records (*n*=21), patients unable to tolerate the procedures (*n*=2), and those who had previously undergone manometry at a different hospital (*n*=1). The final cohort included 121 patients, of whom 53 underwent HROM and 68 underwent ARM.

Findings
In this study, HROM referrals had a mean age of 11.1 years, while ARM referrals averaged 6.15 years. The gender distribution in HROM was slightly female-predominant (24:29) and was equal for ARM. Key indications for HROM included gastro-oesophageal reflux disease (GORD) evaluation, dysphagia, regurgitation, and food bolus impaction, while ARM was mainly used for constipation, faecal incontinence, and overflow diarrhoea. The diagnostic yield was 95.7% for HROM and 56.5% for ARM. Treatment adjustments were made in most patients following these tests, with improved outcomes in 59.6% for HROM and 61.1% for ARM. However, absence of rectoanal inhibitory reflex (RAIR) on ARM did not correspond to Hirschsprung's disease, indicating ARM alone is insufficient for its screening. Notably, 23% of patients considered for fundoplication were reclassified as having rumination syndrome via manometry, shifting management from surgical intervention to biofeedback therapy. These findings highlight the diagnostic and management-changing value of manometry.

Interpretation
The service evaluation highlights the importance of HROM in evaluating cases referred for anti-reflux procedures, especially to exclude conditions like a short oesophagus and oesophageal dysmotility. It is emphasised that relying solely on ARM as a screening test for Hirschsprung's disease may not be sufficient. Prospective studies are required to assess the diagnostic yield of ARM for Hirschsprung's disease. In light of these considerations, it is recommended to make GI physiology services more widely accessible and integrate GI physiology training into the UK gastroenterology GRID programme.

"I have taken five different kinds of tablets and injections, and I still have foot pain": an international qualitative exploration of foot and ankle disorders in rheumatic and musculoskeletal diseases

A4

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Background
The foot and ankle are frequently affected in rheumatic and musculoskeletal diseases (RMDs), yet there is a lack of high-quality evidence to determine the effectiveness of treatments. Outcome domains in research are often inconsistently measured, impeding evidence synthesis. Furthermore, clinical decisions are based on research outcomes, but these domains may not be regarded as important by patients, which can lead to research waste. This study aims to understand which domains matter to patients with a range of RMDs in different geographic locations, who had sought treatment for foot and/or ankle disorders, to inform the development of a core outcome set.

Methods
This was a qualitative interview study adopting a pragmatic approach. Adult patients (≥ 18 years) were recruited through clinical departments and electronic mailing lists internationally, and invited to participate in a single semi-structured interview. Interviews took place online, by telephone and face to face. Interview transcripts were analysed using a mixed deductive and inductive approach to the framework method. Patient and public involvement (PPI) contributors co-produced the interview guide and recruitment materials, coded transcripts and co-interpreted results. Ethical approval was obtained from each country involved in recruitment, and all participants provided informed consent.

Findings
Fifty-six patients (age range 27–76; 37 female) in eight countries (UK, Ireland, USA, Canada, Malta, Serbia, Egypt, Australia) participated. Participants had a variety of RMDs, including inflammatory arthritis, osteoarthritis, crystal arthropathies, connective tissue diseases and localised MSK disorders. The following domains were regarded as important pain, physical function, fatigue, deformity, swelling, activities/participation, psychological impact, sleep, footwear impact, healthcare utilisation and personal expenses. Most domains were considered important regardless of RMD or geographic location. Foot and ankle disorders have far-reaching consequences for patients with different RMDs, but are often inadequately treated. This large qualitative study provides a foundation for achieving international consensus on domains to be measured in all future clinical trials involving foot and ankle disorders in RMDs. Integration of the perspectives of patients is fundamental when developing a core outcome set, to ensure that findings from future trials are meaningful and transferrable to clinical practice.

Interpretation
Foot and ankle disorders impact on multiple areas of the lives of patients with RMDs, both physically and psychologically, and should not be overlooked in clinical practice. Standardising the measurement of outcomes that are meaningful to patients with these disorders could improve the quality of evidence demonstrating effectiveness of treatments. The small number of participants within some RMD categories could be considered a limitation of this study. However, the inclusion of ethnically and culturally diverse participants, from multiple countries representing different healthcare systems, and the large overall sample size are strengths of this research.

Testing the usability and acceptability of the NON-STOP app: a digital self-management intervention for the non-surgical treatment of Perthes' disease

A5

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Background
Perthes' disease is a rare paediatric hip condition that affects the blood supply to the femoral head, leading to bone death and regeneration. This process can cause pain, mobility issues, and prolonged recovery periods, impacting a child's quality of life. Effective self-management interventions, particularly digital tools, have been identified by key stakeholders as acceptable methods of helping children and families cope with the disease. This study aimed to assess the usability and acceptability of the NON-STOP app, a digital self-management intervention designed for children with Perthes' disease and their families.

Methods
A mixed-methods approach was employed, involving a single-arm trial and nested focus groups. Thirty-one children with Perthes' disease were recruited from three NHS hospitals to use the NON-STOP app over 6 weeks. App usage data were collected, and participants completed baseline and post-trial assessments, including PROMIS Mobility, CPAQ, and Health ITUES, to evaluate the app's usability. Following the trial, a subset of participants took part in focus groups to explore their experiences and gather qualitative feedback on the app's strengths and areas for improvement.

Findings
Quantitative findings showed that app engagement was moderate. Usage metrics were useful when considering optimum intervention dosage. The average pain score, measured using the Wong–Baker FACES scale, remained low, suggesting the app's exercises were well tolerated. Qualitative feedback from the focus groups indicated that the app was generally well received. Users appreciated the instructional videos to help with exercise completion. A key strength of the intervention was the inclusion of rewards, and avatar customisation features, which motivated children to engage with the NON-STOP app.

Interpretation
The NON-STOP app was found to be an acceptable and usable tool for children with Perthes' disease. The app's ability to promote self-management and independence in children was highlighted as a key benefit. These findings support the continued development and refinement of the NON-STOP app, which has now been implemented into a multi-centre randomised clinical trial to assess the outcomes of children with Perthes' disease managed with surgical or non-surgical intervention.

National practice questionnaire to evaluate follow-up practices in germ cell cancer in the UK

A6

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Background
Due to improved medical treatments, growing demand for follow-up care for people living after cancer needs integrating into a stretched NHS. Germ cell tumour (GCT) treatment is very successful, meaning almost all patients require follow-up care. Currently, follow-up is burdensome on patients and services, not tailored to patients' needs and often inequitable. Approaches to overcome this have been successfully tested in some UK locations. A national practice questionnaire aimed to evaluate how GCT post-treatment follow-up is currently managed, and healthcare professionals' opinions on telehealth versus standard outpatient follow-up, to form the basis of an NIHR Doctoral Fellowship application.

Methods
An electronic survey on Google Forms recorded responses. The survey was available for completion between December 2021 and March 2022. 20 UK regional specialist centres were invited to participate using email and the secure online Germ Cell community. The lead clinicians at each centre were approached and asked to work with members of their multidisciplinary team (MDT) who have knowledge of or experience with germ cell cancer follow-up, seeking one National Practice Questionnaire response per centre.

Findings
15 individual centres participated. Centres manage an average of 50 new patients a year and 300 patients currently in follow-up. 56% of respondents did not offer telehealth follow-up prior to COVID-19 but 93% offered this during the pandemic. All centres indicated they will continue to offer telehealth once it is no longer mandated. The stated benefits of remote follow-up are increased clinic capacity for patients with greater needs, reduced waiting times, and patient empowerment. None of the respondents identified patient-reported outcome measures (PROMs) as applicable to inform clinical care, nor routinely use PROMs in their follow-up services. The main inhibiting factors are patient-clinician relationship, need for patient self-motivation, reliance on IT, and access to community tests. 93% of respondents indicated willingness to participate in an initiative that develops telehealth for GCT follow-up and 87% see value in creating an app-based remote follow-up service that plans and triggers care events.

Interpretation
This national survey demonstrates the shift towards telehealth follow-up in GCT, as initially necessitated by the COVID-19 pandemic. Furthermore, results have shown a continued willingness to maintain and improve telehealth practice after COVID-19. Strengths and weaknesses have been raised to implementing these services, providing a basis for a further and deeper evaluation. A successful NIHR Doctoral Fellowship was awarded in April 2024 to explore this further.

E-survey to describe the technology-enabled care landscape across child health in the United Kingdom and integration into NHS Trusts

A7

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Background

The provision of technology-enabled care (TEC) to support the management of patients in health services has been driven by various legislation and policies over the last decade. Children and young people (CYP) are proficient users of all things digital and technology-related. Therefore, it would appear logical for TEC to be offered to support CYP in developing self-management skills and to support their care decisions. However, difficulties remain in the uptake and adoption of TEC. The aim of this study is to explore challenges related to innovative technologies being developed for CYP's healthcare to support TEC across the UK.

Methods

An e-survey is currently in distribution via 'Online Surveys' across the UK to: industry partners; child healthcare professionals acting as 'Med-Tech' champions; and researchers and academics, who lead or support the development of healthcare technologies for use with CYP. Distribution of the e-survey has been via NIHR HealthTech Research Centres, NHS trust Innovation departments and social media. Ethical approval was gained from the University of Leeds School of Medicine Research Ethics Committee and descriptive statistics will be performed to describe the sample and technology project development landscape. Participants are self-completing informed consent within Online Surveys prior to participation.

Findings

The e-survey is underway and has been distributed according to the protocol. Recruitment is on track at 50% to date. Most participants to date are industry partners from the Yorkshire and Humber region working with tertiary care centres, developing applications (apps), medical devices or technologies to support communication between patients and healthcare teams. Most clinical areas for technology development are in mental health, ophthalmology, or cross-cut across all subspecialties of child health. The majority of projects are at Technology Readiness Level 9. Free-text responses offer early insights into the challenges faced by industry partners in integrating technologies into child health in the NHS, with solutions offered from their perspectives. The e-survey was due to close at the end of January 2024 and will be followed by a publishable report. This project is the second work package of a PhD programme of study.

Interpretation

Early e-survey responses indicate the challenges of TEC adoption into child health in NHS trusts. Successful and equitable integration of technologies appears very problematic. Findings will assist in understanding the current landscape of developing TEC that may be generalisable to the global population. The study is currently limited in its conclusions due to recruitment still being under way. The main strength of the study is the willingness of industry partners to share their experiences with a clinical academic researcher and to indicate further project involvement in future PhD work packages.

Exploring the experiences of people with Parkinson's and their caregivers in performing oral health behaviours: a qualitative interim analysis

A8

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Background

Parkinson's is the fastest growing neurological disorder globally. Good oral health is an integral part of general health and wellbeing, but not always prioritised within Parkinson's management. Symptoms make it harder for people to carry out mouth care, attend dental appointments and receive dental treatment, and can adversely impact oral health-related quality of life. This is the first UK-based qualitative study to explore the experiences of people with Parkinson's (PwP) and their partners in care, in performing oral health behaviours at home.

Methods

Ethical approval was granted by the University of Sheffield Ethics Committee. PwP and their partners in care were recruited through the national charity Parkinson's UK, social media and other personal networks. Semi-structured interviews were held in person, virtually, via email or a combination of these to support participant inclusion. Interviews were recorded and transcribed verbatim. Transcripts were shared with participants prior to anonymisation and analysis. The data was analysed using an inductive thematic analysis approach, combined with deductive application of the Theoretical Domains Framework (TDF) to identify facilitators and barriers to performing oral health behaviours at home.

Findings

Fifteen individuals have participated in 12 interviews (9 individually, 3 dyads, PwP=10, partners in care=5). Participants had been living with a formal diagnosis for between 2 and 49 years. Recruitment and interviews were paused to allow interim data analysis and identify whether further interviews were required. Thematic analysis identified four main themes:

1. The context of living with Parkinson's
2. Oral symptoms experienced
3. Impact on oral health behaviours
4. Personal and professional relationships

Identified barriers to performing oral health behaviours at home include non-motor symptoms of Parkinson's such as apathy, loss of focus, fatigue and limited motivation. Motor symptoms result in reducing manual dexterity and ability to gain access to bathrooms or to stand to perform toothbrushing. Facilitators include environmental restructuring, adapting behaviours, and support including advice and prompts from other healthcare professionals. The importance of maintaining independence and the emphasis on social influence and self-image were often highlighted.

Interpretation

This study highlights the complexities in performing oral health behaviours at home for PwP. Broader impacts of Parkinson's, emotional and social influences, not just physical issues, must be contended with. The strengths of this study include use of different recruitment strategies and options to participate in the study, to encourage wider engagement and inclusion, anticipating possible communication challenges and other barriers to participation for this cohort. Gaps in the data include identifying and developing methods of feedback and self-monitoring, motivators and developing strategies to adapt to the changing nature of Parkinson's. Future interviews will be conducted to explore these areas.

Patient perspectives of liver stereotactic ablative body radiotherapy: a qualitative interview study

B1

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Background
Stereotactic ablative body radiotherapy (SABR) has emerged as an effective treatment modality for patients with hepatobiliary cancers. While the clinical effectiveness and technical considerations of SABR are becoming more established, the context-rich understandings that patients bring to their treatment journey have not been investigated. Acknowledging the lack of qualitative data, this study explored patient experiences aiming to identify themes that may inform improvements in patient support and liver SABR treatment processes.

Methods
Ten patients undergoing liver SABR (nine male and one female) were consented to participate in semi-structured interviews via purposeful sampling. The Health Research Authority (23/WM/0070) provided ethical approval. Interviews took place towards the end or shortly after completing their SABR treatment, scheduled at convenient times and locations for the patients (over the telephone or in person). Using a pre-designed topic guide with prompts, discussions focused on radiotherapy planning, treatment procedures, development areas, and messages for future patients. Interviews were recorded, transcribed verbatim, and analysed using the framework method.

Findings
Analysis revealed three themes amongst patient experiences:

1. Discomfort: patients experienced discomfort due to positioning requirements, such as holding arms above the head and breath-holding techniques:

   "What it gets is your shoulders because I'm like that [holds arms up]... It hurts my shoulders and the top of my hands." [M103]

2. Communication: patients expressed trust in medical professionals and an appreciation for the advanced treatments they received. However, patients expressed not fully understanding the planning and treatment procedures. After completing their treatment, patients felt more clarity could be provided around the outcomes and next steps. For example:

   "I don't know what's going to happen now... just go away and we'll ring you in 6 weeks... it's like .. an anti-climax." [M106]

3. Coping and support: patients described how they adopted various coping mechanisms, including maintaining hope and a positive attitude, distraction, focusing on future events, familial support, and trusting healthcare professionals.

Interpretation
Patients undergoing SABR for liver cancer reflected on challenges related to communication gaps and discomfort during procedures. Whilst the findings are based on a small sample, this study provides a foundation for focusing on patient experience as part of treatment development. Future studies could include more women and other ethnic groups. Patients clearly recalled their treatment process and offered constructive feedback on improving treatment experience in future. By providing patient-centred, clear, consistent and timely information, communication may be enhanced. Furthermore, addressing physical discomfort and reviewing equipment during procedures may improve the patient experience.

Incidence of developmental disorders and special educational needs and disabilities: findings from the Born in Bradford longitudinal birth cohort study

B2

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Background
Preterm children are at higher risk of developmental disorders and more likely to require special educational needs (SEN) support. The risk of preterm birth is highest among Black women, with a recent proportional increase among Asian women, yet the link between prematurity and developmental disorders in UK minoritised ethnic groups remains unclear. Delayed diagnosis can hinder early intervention, distress families, and exacerbate learning impairments, leading to school disengagement. Anticipating challenges could enable prompt identification and improved outcomes. The aim was to investigate the incidence of developmental disorders and SEN provision and explore associations with gestational age and ethnicity.

Methods
For inclusion in this analysis, children needed data from maternity records regarding gestational age and linked primary care data. Cumulative incidence of developmental disorders and SEN provision up to age 12/end of Year 7, respectively, was explored using multivariable logistic regression in the Born in Bradford (BiB) cohort. Incidence rates of individual developmental disorders were calculated. Data collection for BiB is ongoing and consists of linked routine health and education data and questionnaires for families. Ethical approval for BiB data collection was granted by Bradford Research Ethics Committee (Ref 07/H1302/112).

Results
13,172 children were included. Birth before full term was associated with increased odds of developmental disorder, compared to birth at full term: <34 weeks adjusted odds ratio (aOR) 2.22 (95% CI 1.58–3.12); 34–36 weeks: 1.43 (95% CI 1.12–1.81); 37–38 weeks: 1.18 (95% CI 1.03–1.34). Effect sizes were larger amongst Pakistani children: <34 weeks: aOR 2.59 (95% CI 1.55–4.33); 34–36 weeks: 1.57 (95% CI 1.08–2.27); 37–38 weeks: 1.29 (95% CI 1.06–1.56). Unadjusted incidence rates of developmental disorders varied with ethnicity; compared to Pakistani children, White British children had higher rates (/1000 person years) of attention-deficit hyperactivity disorder (1.8, 95% CI 1.5–2.1 vs. 0.3, 95% CI 0.2–0.4), and lower incidence of learning disabilities (0.7, 95% CI 0.5–1.0 vs. 1.6, 95% CI 1.4–1.9).

Interpretation
Birth before full term is more common in minoritised ethnic groups but remains associated with increased risk of both developmental disorder and SEN provision, even at 37–38 weeks. The incidence of developmental disorders overall is highest amongst White British children, possibly indicating under-diagnosis amongst minoritised ethnic groups.
Limitations: This study relies upon the comprehensiveness and accuracy of the coding within participants' medical records. Aside from Pakistani and White British, the remaining ethnic groups were too small to explore.
Strengths: The findings are novel. This is the largest UK study exploring associations between gestational age and all developmental disorders.

Wider implications
Children born late preterm do not routinely receive developmental follow-up; guidelines recommend parents should contact their GP or health visitor if they are concerned. However, access to advice may be influenced by healthcare experiences and social or cultural factors, deepening inequalities. Expanding follow-up services could target high-risk children or use tools like Parent Report of Children's Abilities-Revised (PARCA-R) but must consider costs and resources. Educators may identify issues, though early intervention opportunities decrease once formal education begins. Overstretched health visitor services limit their role in addressing concerns. Speech and communication disorders, autism spectrum disorder, and behavioural issues are the most common developmental disorders, varying by ethnicity. Service planning must consider local contexts to meet community needs. Empowering parents with information is crucial, but the timing and delivery of this support remain unclear. Qualitative research exploring families' diagnostic journeys could provide valuable insights.

Early detection of idiopathic inflammatory myopathy-associated cancer – evidence assimilation, screening standardisation, and future integration of liquid biopsy into clinical practice

B3

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Background
Idiopathic inflammatory myopathy (IIM) is a chronic multisystem autoimmune condition. One in four adults with IIM are diagnosed with cancer (multiple organs) within three years of IIM onset and this is the leading cause of death. Late diagnosis, paucity of evidence, lack of screening standardisation, and lack of integration of novel screening (e.g. liquid biopsy) results in poor outcomes.

Aims were to:
1) Assimilate available evidence on IIM-cancer risk and screening
2) Create recommendations on screening
3) Integrate liquid biopsy into clinical practice

Methods
A systematic literature review and meta-analysis for risk/protective factors was carried out.
The International Myositis Assessment and Clinical Studies Group (IMACS) formed a steering group to develop recommendations for IIM-associated cancer screening. Recommendations were formed via a modified Delphi method approach by an international expert group (75 members from 22 countries).
The ongoing MyoScreen Study is assessing the utility of liquid biopsy (detection of circulating tumour DNA via methylation pattern detection). Thirty adults with IIM will undergo conventional cancer screening via the IMACS guideline and liquid biopsy sampling at the time of IIM diagnosis and after 6 months.

Findings
Sixty-nine studies were included in the meta-analysis. Dermatomyositis subtype, older age, male gender, dysphagia, cutaneous ulceration, and anti-transcriptional intermediary factor-1 gamma positivity were associated with significantly increased risk of cancer. Polymyositis and clinically amyopathic dermatomyositis subtypes, Raynaud's, interstitial lung disease, very high serum creatine kinase or lactate dehydrogenase levels, and anti-Jo1 or anti-EJ positivity were identified as being associated with significantly reduced risk of cancer. Eighteen recommendations were generated **(https://www.nature.com/articles/s41584-023-01045-w)**. Recommendations were: (1) allow a patient's individual IIM-associated cancer risk to be stratified into low, intermediate, and high risk; (2) outline a 'basic' screening panel and an 'enhanced' screening panel, and (3) advise on the timing and frequency of screening via basic and enhanced panels.

Interpretation
Evidence synthesis and international guideline formation aid standardisation of IIM-associated cancer screening and provide a foundation for future research.

The impact of biological sex and age on the normal ranges of cardiac phosphocreatine to ATP ratio using cardiac phosphorus spectroscopy

B4

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Background
Phosphorus magnetic resonance spectroscopy (^{31}P-MRS) allows non-invasive assessment of the myocardial phosphocreatine to ATP concentration ratio (PCr/ATP), which is a sensitive indicator of the myocardial energetic status. ^{31}P-MRS has been used in numerous clinical studies to investigate effects on and changes to cardiac energetics, with consistent reports showing significant reductions in myocardial PCr/ATP ratio in a variety of cardiac conditions including ischaemic heart disease, diabetic cardiomyopathy, aortic stenosis and dilated cardiomyopathy compared to healthy age- and sex-matched controls. We therefore aimed to assess how biological sex and age impact normal ranges of myocardial PCr/ATP ratio.

Methods
Adult healthy participants were recruited in a single-centre, prospective cohort study. ^{31}P-MRS was performed to assess myocardial PCr/ATP ratio from a voxel placed in the midventricular septum, with patients lying supine and a ^{31}P transmitter/receiver cardiac coil placed over the heart in a 3.0 T magnetic resonance imaging system (Prisma; Siemens Healthineers, Erlangen, Germany). Coil position was standardised to be placed above the midventricular septum. ^{31}P-MRS analysis was performed offline using the OXSA analysis software within MATLAB. Analysis was performed on two consecutive mid left ventricular slices in the short-axis orientation and the average saturation and blood corrected PCr/ATP was reported.

Findings
A total of 120 participants were recruited (mean age 47 years [95%CI: 44–52], mean BMI 24 kg/m^2 [CI: 24–25] for the whole group); 10 participants for each group per decade of life. Comparisons of the average male and female PCr/ATP ratios per decade showed no statistically significant difference between the sexes at each decade (P>0.05 for each group per decade of life). The impact of age was more evident in the male cohort with a significant negative correlation between the age and myocardial PCr/ATP ratio, while the correlation between the age and myocardial PCr/ATP ratio for the female cohort did not reach significance (males r=−0.46, *P*=0.0004; females r=−0.2, *P*=0.0821).

Interpretation
In the healthy adult population the biological sex does not impact myocardial PCr/ATP ratio. While myocardial PCr/ATP ratio reduces significantly with age in healthy males, our data suggest a similar trend of age and PCr/ATP ratio in healthy females.

Left ventricular contractility identifies populations with preserved ejection fraction at risk of adverse heart failure outcomes: an observational study

B5

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Background
Heart failure (HF) is classified by left ventricular ejection fraction (LVEF), the most commonly reported imaging biomarker of systolic function. LVEF is a complex summary measure with known limitations including modest reproducibility, load dependence, and representing the percentage change in left ventricular (LV) volume, rather than contractility. Additional tools are needed to risk-stratify normal LVEF populations. We aimed to assess the prognostic value of assessing left ventricular contractility using the ratio of LV end-systolic pressure to LV end-systolic volume index, or 'cardiac contractility index' (CCI) in populations with a preserved LVEF.

Methods
We determined the relationship between CCI and adverse HF outcomes in a prospective cohort study of 982 consecutively presenting patients with suspected HF. We defined characteristics and outcomes associated with LVEF and CCI, including after stratification by HF with reduced (HFrEF) or preserved ejection fraction (HFpEF). We then used UK Biobank to explore the relationship between LVEF, CCI and myocardial strain, as well as assess the relationship between CCI and subclinical myocardial dysfunction and incident HF in a population of ~40,000 individuals without HF who had undergone a cardiac magnetic resonance imaging study.

Findings
In people with HF, mortality increased over tertiles of declining CCI ($p<0.001$). Below-median CCI was able to reclassify individuals with newly diagnosed HFpEF, who had distinct clinical characteristics and were at ~40% increased risk of adverse HF events, similar to those with HFrEF ($p<0.001$). Modelled as continuous variables, there was a curvilinear relationship between mortality across the detected range of CCI, whilst there was no clear association with mortality risk across a wide range of LVEF (20%–55%). In UK Biobank for participants without HF and normal LVEF, below-median CCI was associated with ~33% increased risk of incident HF (adjusted hazard ratio 1.33 [1.01–1.75]; $p=0.043$). Decreasing CCI was also moderately correlated with LV global circumferential ($r=-0.50$ [−0.50 to −0.49], $R^2=0.25$; $p<0.001$) and radial strain ($r=-0.49$ [0.48–0.50], $R^2=0.24$; $p<0.001$), although it was only weakly correlated with global longitudinal strain ($r=-0.19$ [−0.20 to −0.18], $R^2=0.03$; $p<0.001$).

Interpretation
Significance: The assessment of LV contractility is a simple, non-invasive, afterload-independent tool to stratify the risk of adverse HF outcomes in populations with normal LVEF.
Strengths: Our analysis includes individuals from two complementary observational cohort studies, the first of consecutively referred individuals who were newly diagnosed with HF according to currently applied definitions, the second including a highly phenotyped cohort from the general population.
Limitations: Normal values of CCI have not been defined, and UK Biobank may not be representative of the general UK population with respect to socioeconomic deprivation, and ethnic minority groups, who were underrepresented.

Wider implications
Our findings suggest that a simple measure of LV contractility offers additional prognostic information in people with HF and preserved LVEF, and also within the general population with normal LVEF. Identification of unappreciated contractile dysfunction in these circumstances may help better define risk and refine the phenotypic classification of these heterogeneous populations. Despite recent advances, therapeutic options for individuals with HFpEF remain limited. Future research should focus on *post hoc* analyses of published clinical trials testing proven HFrEF therapies in people with HFpEF, which have suggested negligible benefit. If these confirm that CCI can identify potential treatment responders, future randomised controlled trials could prospectively test the value of CCI in selective treatment responders, potentially leading to a new era in HFpEF care.

From storage to survivorship: a scoping review and PPIE study on the experiences and needs of childhood cancer survivors with stored fertility tissue

B6

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Background
Despite improved childhood cancer survival rates, 60% of survivors face lifelong health issues, including fertility problems, which account for a third of these cases. Fertility tissue preservation (FTP) is a promising technique but poses unique physical and emotional challenges. Most patients with stored tissue have yet to use it, and insight into their experiences remains limited. Risks such as unsuccessful reproductive outcomes, altered parental aspirations, and decision-regret represent further complications. Notably, research has focused primarily on ovarian tissue, leaving a significant gap in understanding testicular tissue preservation and creating barriers to evidence-informed survivorship care.

Methods
We combine findings from a scoping review and Patient and Public Involvement and Engagement (PPIE) work, to explore the experiences and needs of patients, parents, and healthcare professionals after FTP. The scoping review followed the Joanna Briggs Institute methodology and PRISMA-ScR guidelines. Data were extracted and presented in descriptive tables. Seven PPIE participants comprising young adults, parents, and healthcare professionals were recruited through UK charities and networks. PPIE data were collected via telephone or online informal interviews and email exchanges. Discussions were transcribed, thematically analysed, and presented in narrative form with verbatim comments to illustrate key themes.

Findings
Only five studies, all on ovarian tissue preservation, met the inclusion criteria for the scoping review, highlighting a significant gap in knowledge of outcomes following testicular tissue preservation. The review found complex emotional and ethical dilemmas faced by young women with stored tissue. No studies were identified on testicular tissue preservation and there were no data available on the experiences of parents or guardians of children with stored tissue.

Findings from PPIE work identified six key themes that advance understanding of FTP challenges and survivorship care needs: (1) lack of communication and information; (2) unmet needs in follow-up care; (3) emotional impact and psychological support; (4) importance of patient and parental involvement; (5) desire for information and education; and (6) long-term concerns and support. These themes expose gaps in current survivorship care and provide actionable insights to improve patient outcomes, guide policy, and shape clinical practice.

Interpretations
This study brings to light the previously unheard voices of young people with stored tissue, revealing their unique needs and experiences. It identifies critical gaps, particularly around testicular tissue preservation and the perspectives of parents and guardians. By combining scoping review findings with PPIE insights, this work establishes a foundation for ongoing collaboration with survivors to co-design care that meets their needs. The findings have significant implications for clinical practice and NHS policy, underscoring the urgent need for ethical, standardised, and equitable survivorship care. Future research must focus on improving support for survivors, their families, and healthcare professionals.

A multi-professional survey of the management of plantar heel pain in the United Kingdom

B7

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Background
Plantar heel pain (PHP) affects 1 in 10 adults, often causing significant foot pain. Prognosis is challenging, with half experiencing symptoms for 10 years. Numerous treatments exist, although the literature suggests no single intervention is more effective. General practitioners (GPs), podiatrists, and physiotherapists are primary contacts, but many professions manage PHP. Professional diversity can lead to varied practice and treatment choices. Understanding PHP management in the UK can aid clinical benchmarking, inform knowledge mobilisation strategies, and may help individuals make informed treatment choices.

Methods
An online, cross-sectional survey explored the multi-professional management of plantar heel pain in the UK. The 31-question survey covered demographics, referral pathways, imaging, management practices, outcomes, service provision, and treatment barriers. Open from May to June 2024, it targeted UK health professionals via digital channels, including professional bodies, special interest groups, and social media. Data were analysed using SPSS v29 with descriptive statistics and categorised free-text comments. Ethical approval was received from the University of Leeds, School of Medicine Ethics Committee (MREC 23-017). Participants were required to provide consent before proceeding with the survey.

Findings
Four hundred and six people responded, predominantly podiatrists (181; 44.6%) and physiotherapists (144; 36.5%). Other professions included orthotists, osteopaths, orthopaedic surgeons, GPs, nurses, and rheumatologists. Imaging was infrequently used; 61.3% of respondents rarely/sometimes used it, and 26.8% never used it. Most (88.4%) provided treatments; strengthening (88%) and stretching (85.5%) were most frequently/very frequently used. Prefabricated orthoses were more frequently/very frequently used (56.3%) than custom orthoses (24.2%). Steroid injections were uncommon (only 6.4% frequently/very frequently performed them). Fewer than half of respondents frequently/very frequently measured patient-reported outcomes (48.8%). A large proportion provided patient information; the majority (88%) lacked resources in languages other than English. Treatment sessions were generally not limited (80.6%); 3–4 sessions were most common (40.1%). Nearly half (47.5%) of respondents had waiting lists, mainly in the NHS (77.8%). Most (70%) waiting lists were under 4 months. COVID-19 had generally not resulted in care limitations (77.1%).

Interpretation
This large national survey reveals current practices in managing PHP in the UK. An exercise-based approach to management is favoured, with prefabricated orthoses also commonly used. Patient information is often provided, but mostly in English. Patient-reported outcomes are rarely utilised. To better understand the effectiveness of commonly prescribed treatments like exercise and prefabricated orthoses, large, well-designed randomised controlled trials (RCTs) are essential. Additionally, mechanism-of-action studies are needed to explore how treatments work and whether they have varied effects in different individuals. Patient information resources that are accessible to a wider range of communities should be developed.

Developing a clinically reliable assessment model for quantifying breast atrophy in breast cancer patients following surgery and radiotherapy: feasibility study

B8

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Background
Breast-conserving surgery and radiotherapy are currently regarded as the cornerstone treatment for breast cancer management. However, adverse outcomes, most notably breast atrophy, can result following breast cancer treatment. Breast atrophy, defined as a loss of breast volume, can significantly affect patients' quality of life and body image. Existing methods used to assess the degree of breast atrophy often rely on subjective measures, undermining their reliability in clinical practice. The aim of this project is to develop an objective and more reliable assessment model for quantifying breast atrophy using machine-learning tools.

Methods
This prospective, observational feasibility study employs machine-learning tools to quantify breast atrophy in patients post-breast-conserving surgery and radiotherapy. Adult participants with early-stage breast cancer will be recruited. Standardised 2D imaging at baseline and follow-up visits taken from different angles will generate 3D reconstructions for volumetric analysis. Comparative statistics will evaluate the AI-based measure against traditional scoring systems. Ethical approval will be obtained, and all participants will provide informed consent. The project will be registered on an appropriate clinical trials platform, ensuring transparency and adherence to regulatory requirements.

Findings
Fifty participants from the REQUITE study will be enrolled. Preliminary data will be analysed for correlation between automated volumetric measurements and alternative assessment models. Paired t-tests will be used to test for significant difference (using $p<0.05$) in breast volume pre- and post-treatment, confirming measurable atrophy. Bland–Altman plots will be used to ensure acceptable agreement between the novel method and existing scoring systems. Patient feedback will be recorded during the imaging process. The findings are expected to support the feasibility and accuracy of a machine learning-based approach for objectively quantifying breast atrophy in this cohort.

Interpretation
This study is expected to demonstrate that machine learning can provide an objective method for assessing breast atrophy after breast-conserving surgery and radiotherapy. The strong correlation with established tools underscores its potential clinical significance in guiding patient follow-up and interventions. Strengths include a standardised imaging protocol, high patient satisfaction, and robust agreement with existing methods. However, our feasibility limited sample size and single-centre focus restrict generalisability. Further validation in larger, multi-centre cohorts with longer follow-up periods is needed. Overall, these findings are expected to highlight a promising avenue for improving atrophy monitoring, patient communication and supporting tailored patient management.

Early-stage health economic model of cost-effectiveness of digital manufacturing of facial prostheses

C1

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Background
The potential cost-effectiveness of digital manufacturing of facial prostheses has not been formally explored. Early health technology assessment (HTA) would be useful to inform stakeholders about the potential value of digital manufacturing technology during the early stages of clinical research. The objective of the early HTA was to develop, populate, and evaluate an early-stage health economic model of the cost-effectiveness of digital manufacturing of facial prostheses using the best available evidence.

Methods
A discrete event simulation model was created in simulation software (Simul8 Professional; Simul8 Corporation) to model the progression of patients through the maxillofacial prosthetic service. The model was populated using the best available evidence including data previously collected during the lead author's PhD from a service evaluation (health state transition parameters), feasibility randomised controlled trial (health state utility values, manufacturing times and costs) and qualitative research (process utility). 1000 simulation runs were conducted for both the digital and conventional manufacturing processes. An incremental cost-effectiveness ratio (ICER) was estimated, representing the cost of gaining 1 additional unit of health.

Findings
The ICER was £989, which would be cost-effective at the UK threshold of between £20,000 and £30,000 per quality-adjusted life year (QALY). The incremental net health benefit (INHB) was 0.28 QALYs, indicating that population health could be increased by implementing digital manufacturing processes. Univariate sensitivity analysis was conducted to explore uncertainty, identify the main drivers of cost-effectiveness, and help prioritise further clinical evidence development.

Interpretation
Early analysis suggests that digital manufacturing of facial prostheses could be more cost-effective than conventional manufacturing, as shown by a low ICER and a positive INHB. As the evidence base is scarce, the model parameters and outputs are surrounded by uncertainty. Further research is needed to consider the costs and benefits of conducting further research to inform the adoption decision.

Wider implications
While the literature often refers to the potential benefits of digital manufacturing of facial prostheses through improved treatment outcomes and reduced costs, no previous formal evaluation has been conducted of the potential cost-effectiveness of the technology. To conduct a health economic evaluation, the best available evidence was gathered on treatment outcomes (health state utility values), costs (from the healthcare perspective), and transitions between health states (through parametric survival analysis). Only by developing and populating the early-stage health economic model, the limitations of the current evidence base become clear, and it has been possible to highlight areas of uncertainty where further research is needed. This model can be adapted in the future as the evidence base develops.

Women with recurrent miscarriage have altered uterine natural killer cell receptor expression profiles

C2

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Background

Abnormal implantation is a leading cause of maternal and foetal morbidity and mortality worldwide. Uterine natural killer (uNK) cells comprising up to 70% of leukocytes in the pre-implantation endometrium and decidua are crucial regulators of implantation. uNK cell activation is necessary in optimising trophoblast invasion and placental development, e.g. the activating killer immunoglobulin-like receptor (KIR)-2DS1 on uNK cells is protective against pre-eclampsia. Recurrent miscarriage (RM) is diagnosed when women experience ≥3 miscarriages and forms a part of the broader obstetric syndrome characterised by inadequate placentation. This study characterises the uNK cell receptor profile in women with RM and controls.

Methods

Women of reproductive age with a history of RM, infertility or controls (no history of pregnancy disorders) were recruited into this study. Paired endometrium and peripheral blood (pb) were taken, timed according to the menstrual cycle. Lymphocytes from endometrial biopsies were isolated using collagenase digestion and Lymphoprep. Multiparameter spectral flow cytometry was used to determine NK cell differentiation, activating (KIR2DS1/S2/S4, NKG2C) and inhibitory (KIR2DL1/2/3, NKG2A, LILRB1) receptors on uNK and pbNK in these women. Different tissue-resident uNK subsets were identified using CD9, CD49a, CD39 and CD103 markers.

Findings

116 women were recruited into this study (28 control, 38 infertility and 60 RM). Multiparameter flow cytometry identified uNK1, uNK2 and uNK3, and distinct KIR2DS1+, KIR2DL1+ and KIR2DS1/L1+ populations. The uNK1 subset had significantly higher expression of KIRs (S1, L2, S2, S2/S3, S4) and LILRB1 compared to uNK2 and uNK3, even within the RM cohort ($p<0.01$). Within uNK, there was a significantly reduced KIR2DS1:KIR2DL1 ratio in RM compared to controls ($p=0.047$) and when compared to women with infertility ($p=0.023$). This effect was most prominent within the uNK1 subset, the subset of uNK likely to closely interact with foetal extravillous trophoblast cells during implantation. There was no significant difference in the KIR2DS2:KIR2DL2/L3 ratio or the NKG2C:NKG2A ratio between RM and controls. However, within the pbNK, there was no significant difference in the activating: inhibitory NK receptor profiles between RM, infertility and controls.

Interpretation

Reduced activating KIR2DS1 in the RM cohort compared to controls suggests the importance of uNK activation in successful pregnancy and is consistent with the finding that KIR2DS1 is protective against disorders of placentation such as pre-eclampsia. KIR2DS1 activation on uNK cells may be necessary to promote cellular interactions and production of cytokines to assist trophoblast invasion and placental development. Future work will determine uNK function in women with reproductive failure versus controls. This study also highlights the need to identify KIR2DS1–ligand interactions at the maternal–foetal interface to improve our understanding of uNK function and its effect in determining pregnancy outcome.

Growth hormone receptor (GHR) 6Ω pseudoexon activation: a novel cause of classic growth hormone insensitivity due to a non-coding variant identified on whole gene panel

C3

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Background
Classic growth hormone insensitivity (GHI) is characterised by extreme short stature, dysmorphism and metabolic anomalies. Patients present in early childhood with severe postnatal growth failure. GHI is usually due to homozygous or compound heterozygous mutations in the exons, or coding regions, of the growth hormone receptor (GHR) gene. My work aimed to identify the underlying genetic diagnosis in three patients with classical GHI. These patients remained undiagnosed following genetic analysis of all exons of the GHR gene.

Methods
Patients were analysed on a curated 64-gene growth panel, which included the entire genomic sequence of genes of interest. This enabled rapid identification of exonic variants and also exploration of the non-coding regions. Novel bioinformatics pipelines were created to identify rare non-coding variants of interest. *In silico* models predicted the effect of novel genetic variants on gene splicing. Aberrant splicing was confirmed using *in vitro* splicing assays. Patient fibroblast analysis confirmed the inclusion of a novel GHR pseudoexon. A custom GHR vector was created to determine the impact of this novel pseudoexon inclusion on the growth hormone signalling pathway.

Findings
I identified a novel homozygous variant deep within intron 6 of the GHR gene (g.5:42700940T>G, c.618+836T>G) in the index patient. Two siblings harboured the novel intronic variant in compound heterozygosity with a known GHR c.181C>T (R43X) mutation. This novel change was predicted by *in silico* models to cause mis-splicing of the GHR gene. *In vitro* splicing analysis confirmed mis-splicing leading to the inclusion of a 151-bp mutant 6Ω pseudoexon not identified in wild-type constructs. This mutant transcript was also demonstrated in cultured patient fibroblasts. Inclusion of the 6Ω pseudoexon causes a frameshift resulting in a non-functional truncated GHR lacking the transmembrane and intracellular domains. The truncated 6Ω pseudoexon protein demonstrated extracellular accumulation and impaired downstream signalling in the growth hormone pathway. This pathway is essential for normal linear growth and its disruption explains the severe postnatal growth failure seen in these patients.

Interpretation
This deep intronic change in the GHR gene (c.618+836T>G) causes mis-splicing and leads to the inclusion of a novel GHR 6Ω pseudoexon in the coding sequence of the GHR gene. 6Ω pseudoexon inclusion results in loss of GHR function consistent with classical GHI. This represents a novel mechanism of GHI and is the first deep intronic variant identified causing severe postnatal growth failure. The two kindreds originate from the same town in Campania, Southern Italy, implying common ancestry.

Wider implications
My research has uncovered a novel mechanism underlying GHI, identifying the first deep intronic variant responsible for severe postnatal growth failure. This helps further our understanding of non-coding regions and helps demonstrate the key role they can play in gene function. My findings highlight the importance of studying variation in deep intronic regions as a cause of monogenic disorders. This is of paramount importance as we delve deeper into the study of non-coding regions through the widespread adoption of whole genome sequencing. These non-coding regions, once dismissed as 'junk DNA', are now recognised as crucial players in gene regulation and function. Our understanding of these regions is rapidly evolving, and further research is crucial to fully elucidate the impact of non-coding genetic variations on human health.

Characterisation of the gastric cancer microbiome using metagenomic analysis, tissue sequencing, and bacterial culture

C4

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Background
Helicobacter pylori infection is an established risk factor for developing gastric cancer. However, studies investigating the intratumoural microbiome beyond this bacterium have resulted in variable findings. Gastric cancer is characterised by anatomical, histopathological, molecular, and epidemiological heterogeneity. The relationship between these clinicopathological factors and the intratumoural gastric cancer microbiome may explain conflicting results of previous microbiome studies. Furthermore, studies to date of the gastric cancer microbiome have predominantly used culture-independent methods, which limits interpretation of these data.

Methods
A metagenomic analysis was performed, using two large databases: the 100,000 Genomes Project and The Cancer Genome Atlas (TCGA), enabling characterisation of the gastric cancer microbiome and exploration of relationships between the microbiome and clinicopathological variables. Additionally, the microbiome of prospectively collected gastric cancer samples was analysed through culture-dependent and culture-independent methods. 16S rRNA sequencing and low-coverage whole-genome sequencing of tumour samples were performed. Bacteria were cultured and isolated by homogenising tissue and culturing across a range of media and conditions. Microbiota from one sample was cultured in a bioreactor, under conditions simulating the gastric cancer environment.

Findings
In silico analysis revealed that representatives of the genera *Prevotella, Selenomonas, Stomatobaculum, Streptococcus, Lactobacillus,* and *Lachnospiraceae* were commonly seen across both the 100,000 Genomes Project and TCGA. Within the TCGA cohort, microbial abundance and alpha diversity were greater in gastric cancers with microsatellite instability, lower depth of invasion, intestinal-type histology, and those originating from Asia. Microsatellite instability was associated with microbiome composition in both cohorts. Sex and depth of invasion were associated with microbiome composition in the TCGA cohort. Bacteria identified through sequencing of fresh samples were commonly anaerobic and included oral genera, such as *Prevotella* and *Parvimonas*. A total of 113 bacterial strains from 26 genera were isolated from 5 gastric cancer samples, representing the greatest number of genera isolated from gastric cancer samples to date. A bioreactor model was developed, capable of supporting gastric cancer microbiota in continuous culture. Different bacteria were identified through the different characterisation methodologies.

Interpretation
Our findings suggest that the gastric cancer microbiome may differ according to clinicopathological factors, which should be accounted for in future research. In particular, microsatellite unstable cancers seem to have a more abundant, more diverse microbiome. Whilst it is not clear whether this is a causative or purely associative relationship, one could speculate that the local tumour environment of microsatellite unstable gastric cancer influences microbiome changes. Culture-dependent and culture-independent methods provided complementary information and both should be used to advance progress in the understanding of the role of the microbiome in gastric cancer.

7-Tesla fMRI reveals changes in subgenual anterior cingulate cortex functional connectivity in depression

C5

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Background

Abnormalities in the subgenual anterior cingulate cortex (sgACC) are linked to major depressive disorder (MDD), but the sgACC is anatomically and functionally diverse, including Brodmann area (BA) 25 (Cg25) and BA32 (Cg32). The differences in resting state functional connectivity (rsFC) between Cg25 and Cg32 in MDD compared to healthy volunteers (HVs) have not been directly examined. High-resolution 7-Tesla functional magnetic resonance imaging (7T fMRI) offers an unrivalled opportunity to measure differences in rsFC between these two adjacent subregions.

Methods

We used resting-state 7T fMRI to compare rsFC in Cg25 and Cg32 in 40 patients with MDD, and 38 HVs. Images were analysed with analysis for functional neuroimages (AFNI), using linear mixed-effects modelling and multivariate modelling. Significant results were cluster-corrected with a cluster-level family-wise error correction of alpha<0.05. This study was a collaboration between King's College London (UK) and Mount Sinai School of Medicine (USA).

Findings

Across all 78 participants, Cg25 and Cg32 showed regionally distinct rsFC patterns despite their proximity. Cg25 had increased rsFC to the orbitofrontal cortex, amygdala and dorsolateral (dl)PFC/BA46, while Cg32 showed increased rsFC to the perigenual (pg) and dorsal (d) ACC, dlPFC/BA9, posterior cingulate cortex (PCC), ventral striatum, and ventral tegmental area. When comparing MDD patients to HVs, both Cg25 and Cg32 exhibited increased rsFC to the anterior (ant) PFC/BA10, together with key nodes of the default mode network (DMN), including pgACC, rostral ventromedial prefrontal cortex (vmPFC) and the PCC. rsFC to nodes of the central executive network (CEN) and salience network (SN), such as the right dlPFC/BA46 and the bilateral insula, was decreased. Within the MDD group, Cg32 rsFC to the antPFC/BA10, dlPFC/BA9, ventral striatum and hypothalamus was positively correlated with Snaith–Hamilton Pleasure Scale (SHAPS) scores. Cg25 rsFC to the antPFC/BA10 and PCC was negatively correlated with anxiety scores.

Interpretation

These findings suggest that the distinct rsFC patterns of sgACC subregions, particularly their links to the DMN, CEN and SN, are altered in MDD and may contribute to symptoms of anhedonia and anxiety.

Wider implications

Using resting-state 7T fMRI, we show the sgACC is functionally heterogeneous, with Cg25 and Cg32 showing distinct patterns of rsFC to the rest of the brain. There are shared changes in Cg25 and Cg32 rsFC associated with MDD vs. HVs, but such changes are differentially linked to symptoms of anhedonia and anxiety. In the future, careful parcellation of the sgACC may be necessary to highlight the contribution of this region to symptoms of anhedonia and anxiety in MDD. This is critically important, as novel neuromodulation strategies used to modulate the sgACC may have different effects on symptoms depending on the precise area targeted. This research also highlights the value of ultra-high field MRI in studying ventral regions of the brain, which otherwise suffer from signal dropout at lower field strengths.

Metformin for antipsychotic-induced weight gain in people with severe mental illness (META-SMI): protocol for a randomised controlled trial

C6

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Background
People with severe mental illness (SMI), such as schizophrenia or bipolar disorder, often take antipsychotic medications to manage their condition. However, a common side effect of these medications is weight gain, which increases the risk of developing serious health problems such as ischaemic heart disease and diabetes. This study aims to identify if metformin, a diabetes medication, can be used to reduce the antipsychotic-induced weight gain seen in this population. Current literature is mainly limited to higher-income countries, so this study will take place in Pakistan to determine how effective metformin is for the South Asian population.

Methods
This is a two-armed, parallel, individually randomised controlled trial with an internal pilot. The internal pilot will take place within the first 6 weeks of the trial, to monitor recruitment and the feasibility of the trial. The calculated sample size is 270 participants to provide 80% power with an effect size of 0.3. Participants will be randomly assigned on a 1:1 ratio to either the intervention arm, receiving metformin, or the control arm, receiving a placebo. Informed consent will be gathered by research staff, and ethics approval has been sought from the relevant bodies.

Findings
As this is a trial protocol, we have no findings as of yet. We hope to begin recruitment in May 2025. Below I have summarised the outcomes to be measured and the statistical plan.

The primary outcome is change in body weight and BMI 6 months post-randomisation. Secondary outcomes include abdominal circumference, blood pressure, HbA1c, lipid profile, liver function, renal function, health-related quality of life (EQ-5D-5L), depressive symptoms (PHQ-9), anxiety symptoms (GAD-7), psychosis symptoms (BPRS), adverse events, and health risk behaviours (physical activity, diet, sleep). Economic outcomes will be gathered so that cost-effectiveness can be assessed – these include quality-adjusted life years (QALYs).

Primary analysis will be conducted using intention-to-treat populations, using mixed-methods repeated measures. Subgroup analyses and sensitivity analyses will also be performed.

Interpretation
We hypothesise that metformin will be effective in mitigating weight gain in people taking antipsychotic medication, therefore it may help in reducing the risk of cardiometabolic sequalae from obesity and overweight in this population. This may strengthen the evidence base for the use of metformin in this setting and may inform policymakers in Pakistan with regard to this practice, possibly leading to larger clinical trials. Metformin may be co-prescribed by both primary care physicians and psychiatrists for patients who are about to commence antipsychotic medication.

Emergency care for young people after self-harm: a realist review protocol

C7

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Background
In England, increasing numbers of young people seek help from emergency healthcare services, such as ambulances and emergency departments (EDs), after they self-harm. This is due to a lack of meaningful and available community-based alternative sources of support for self-harm. It is not clear what helps young people in this context, how or why. This research aims to understand which resources are available in the emergency setting for young people (aged ≤25 years) who self-harm in England, and how and why they produce their intended and unintended effects.

Methods
Realist review is a theory-driven interpretive approach to evidence synthesis. It provides realist logic of inquiry to produce an explanatory analysis of how and why resources work, for whom, and in what circumstances. This review has two key components; one will identify resources available in England for young people who self-harm in the emergency setting, the other will identify initial programme theories from the international literature.

Findings
There are five phases in line with Pawson's five iterative stages: (1) clarifying scope; (2) evidence search; (3) article selection; (4) data extraction and organisation; and (5) evidence synthesis. Published and grey literature will be reviewed and included. Three key stakeholder groups will be involved throughout the review process, namely two patient and public involvement (PPI) groups (one for young people, one for parents and carers) and an interdisciplinary group of healthcare professionals.

Interpretation
Ethical approval is not required for this review. Results will be reported according to RAMESES publication and quality standards. Findings will be disseminated via a peer-reviewed publication in a scientific journal, conference presentations, a study website, an animated video shared via social media, and other avenues identified by our PPI groups.

General Surgery 4.0 – a systematic review of extended reality interventions in general surgery

C8

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Background
Despite technical and medical advances, surgery still involves significant risks for patients, with complications occurring in 16.4% of patients and accounting for 7.7% of worldwide fatalities. 'Surgery 4.0', or digitisation of surgery, has brought new technologies that can enhance all aspects of peri-operative care. One innovation involves extended reality (XR), a technology that alters the human–computer interaction. Clinicians can now display complex anatomy in a three-dimensional image using mixed reality (MR), which could improve patient understanding, surgical planning and intra-operative navigation. This study aimed to ascertain the current uses of XR as interventions to improve outcomes for patients undergoing general surgery.

Methods
A systematic review including all studies involving the use of XR as a patient intervention during peri-operative care for adult patients undergoing a general surgical procedure. The study protocol was developed in accordance with the PRISMA and AMSTAR 2 guidelines and was prospectively registered with PROSPERO (registration number CRD42024569448). A systematic search of MEDLINE, Embase, and Cochrane databases was performed in August 2024. Conference abstracts and studies involving procedures outside of a general surgery remit or non-XR interventions were excluded. Data synthesis was performed using a narrative approach. No ethical approval or patient consent was required for this systematic review.

Findings
The search strategy returned 966 articles. 33 XR studies were included, featuring 1149 patients. The most frequently investigated general surgical procedure using XR technology was liver resection, in 15 studies (45%), for which improved outcomes were shown, with reduced length of stay, estimated blood loss, operative time and complications, and improved R0 rates. Improved outcomes are yet to be conferred for other procedures. The most frequent XR technology used was augmented reality (AR), in 23 studies (70%), followed by virtual reality (VR) (n=6; 18%) and MR (n=4; 12%). For patient education and recovery, XR systems have been shown to improve pre- and post-operative anxiety, pain and mood. Current XR technologies involve primarily manual methods for imaging segmentation, and reporting of safety and preparatory steps for definitive trials is poor. The quality of current literature is variable, with over 75% of studies at moderate or high risk of bias.

Interpretation
To our knowledge, this is the first systematic review to report on XR interventions in general surgery. Benefits of XR technology to enhance patient outcomes are demonstrated. Standardisation and implementation of innovation frameworks are required to develop inter-disciplinary XR systems with automatic segmentation for widespread use. The strengths of this systematic review involve a granular account of XR uses, technology features and their impact on patient outcomes with significant results. The heterogeneity of studies prohibited data synthesis through the means of a meta-analysis. However, the narrative synthesis used has delivered a meaningful analysis that encompasses all research within general surgery.

A feasibility trial of a web-based intervention (ePainQ) to support the management of post-surgical pain in breast cancer

D1

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Background
With 2.3 million cases worldwide every year, breast cancer is the commonest cancer in women. The majority become long-term survivors. Many survivors report both physical and emotional adverse effects persisting years after treatment. Persistent post-surgical pain (PPSP) is the most frequent negative consequence of breast surgery, and is related to inadequate management of acute post-surgical pain. Recommendations include supported self-management and personalised follow-up to meet patient needs. A mixed-methods approach was used to co-develop ePainQ, a web-based intervention, to capture patient self-reported pain and post-operative symptoms and provide individualised self-management advice, with integration into electronic patient records.

Methods
ePainQ comprises a website with a symptom questionnaire that prompts personalised feedback about self-management based on responses to questions about pain, swelling, functionality and quality of life. A feasibility study tested ePainQ for acceptability, usability and perceived usefulness, including assessing uptake, retention, follow-up and completion rates. Following consent, patients chose to receive usual care (cohort) or intervention plus usual care (ePainQ). Intervention: daily symptom reporting with linkage to healthcare professionals (HCPs) and integration into electronic patient records. Data collection: baseline, 2 weeks, 3 months and 9 months post-operatively. Outcome measures: EORTC C30, and BR23, EQ-5D, HADS and BPI. Patient activation measured at baseline and 9 months.

Findings
69 patients recruited over 8 months; 60 intervention and 9 cohort. Mean age: 57.7 years (SD 9.8; range 38–82). Recruitment rate was 63%. The engagement with ePainQ rate was 89.6%, and 83.3% of participants completed a usability scale in which:

- 97.5% highlighted ePainQ as easy to use
- 95% reported not needing any technical support
- 90% felt very confident using ePainQ

Outcome measures: 69/69 (100%) completion at baseline and 2 weeks. Analysis of data suggested that ePainQ may have potential for the reduction of acute pain intensity and anxiety by improving patient self-management but requires confirmation in a randomised controlled trial (RCT). There were no active withdrawals, with 13/69 passive withdrawals by 9 months. 67 participants (97.1%) consented to an interview. A sample of 14 participants who had fully or partially completed the ePainQ intervention were selected and reported that ePainQ was easy to use, supportive and assisted pain management decision-making.

Interpretation
ePainQ was designed in response to patient-identified unmet needs and co-developed to ensure suitability and accessibility.

The feasibility study established that ePainQ was accepted, used, and liked by participants who interacted with it. Even those with limited engagement felt they had benefited from the advice provided. Results demonstrated patient positivity towards ePainQ and suggested it could be improved by resolving IT issues such as access reliability and reducing the frequency of daily reporting. All pre-set progression criteria for a phase III RCT were met. ePainQ is now being tested within an NIHR RfPB-funded multi-site pilot RCT.

Wider implications
Study findings have broader implications extending beyond the original project. By highlighting the practicality, potential challenges and viability of the ePainQ intervention, these findings inform

strategic decision-making and ongoing evaluation. They underscore the importance of patient and HCP engagement with insights gained guiding the current RCT. Demonstrating a rigorous evaluation process fosters stakeholder confidence and supports long-term planning, resource allocation and innovation. It may influence future policy within the NHS as it could be adopted across surgical specialities. It provides an example of nurse-led digital research and contributes to the broader advances in technology in healthcare systems.

A cohort study of the effect of perinatal socio-economic status on brain structure and later behaviour

D2

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Background

The perinatal period is a time of significant plasticity and development in the human brain. Understanding development in this period is vital to understanding the emergence of later clinically relevant phenotypes, including mental illness. A recent body of research has demonstrated correlations between socio-economic exposures and early-life brain development (measured both via MRI and via behavioural assessment), but studies are limited by small sample sizes, and often not representative of the general population. The developing Human Connectome Project has now collected neonatal MRI, demographic and behavioural data from a large cohort of healthy term-born infants.

Methods

21 dimensions of socio-economic status in the perinatal period, T2-weighted, cortical surface and diffusion MRI in the neonatal period, and behavioural assay (measured via the Bayley-III scales, Childhood Behavioural Checklist, Early Childhood Behavioural Questionnaire, and Quantitative Checklist for Autism in Toddlers) at 18 months were collected from each participant in the study. Dimensionality reduction of MRI (to 42 dimensions) was performed in a data-driven fashion using orthogonal projective non-negative matrix factorisation. Univariable correlations were made between socio-economic status and MRI measures, and between socio-economic status and behaviour at 18 months. Multivariable analysis was subsequently performed via canonical correlation.

Findings

270 individuals were included. Socio-economic adversity was correlated with a complex pattern of brain structure, including phenotypes of both over- and under-maturation in different regions. In univariable correlation, parental education levels were positively correlated with cortical thickness, and paternal occupation was correlated with diffusivity in the major white matter tracts. No univariable correlation survived multiple comparison correction, and the first mode of canonical correlation did not survive multiple permutation testing. Socio-economic adversity was more robustly associated with behaviour at 18 months – 60/210 univariable correlations were significant after multiple comparison correction, including parental occupation (13/20 univariable correlations significant) and a measure of household deprivation (6/10 univariable correlations significant). Via canonical correlation, two modes were significant following multiple permutation testing, indicating a pattern of generally less favourable socio-economic status being correlated with lower Bayley-III cognitive, motor, and language scores, greater externalising symptom presence and more autism traits at age 18 months.

Interpretation

Socio-economic status has measurable effects on brain development in this cohort without any particular exposure to social or clinical risk. By the early neonatal period correlations can be demonstrated between individual domains of deprivation and specific brain regions, although these are subtle and difficult to interpret. Stronger associations are observed between socio-economic status in the perinatal period, and behaviour at age 18 months, including measures thought to be indicative of later psychiatric diagnosis, such as autism trait emergence or externalising symptom burden. Future research may focus on understanding the conversion from 18-month behavioural profile to later diagnosis.

Understanding multidisciplinary treatment aimed at improving activity and participation in people with persistent physical symptoms: a focused ethnography

D3

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Background
Persistent physical symptoms (PPS) which are not adequately explained by physical pathology are very common, with an annual NHS cost of £3bn. For people with severe difficulties, multidisciplinary treatment is recommended. However, there are only a small number of specialist multidisciplinary services. Their approaches are not clearly defined, and cannot be transferred to other settings, where most PPS are treated. This study aimed to explore how specialist PPS services deliver multidisciplinary treatment, and what helps and hinders its delivery. It is part of a wider project to design a rehabilitative intervention for people with severe PPS.

Methods
A focused ethnographic approach was used to explore practice across specialist PPS teams in the UK, including non-participant observations of assessment and treatment sessions, team meetings and informal discussions. Patient records were reviewed, and semi-structured interviews were conducted with patients with PPS and healthcare professionals. Field notes and interview transcripts were analysed using reflexive thematic analysis. The study received ethical approval from Yorkshire and the Humber – Bradford Leeds Research Ethics Committee (23/YH/0222); all participants provided written informed consent.

Findings
Data were collected at three consecutive sites between March 2024 and January 2025. Two teams were based at inpatient units and one was community-based. 17 patients and 25 healthcare professionals participated in observations (175 hours). 20 interviews have been conducted (with five further interviews scheduled) with 10 patients and 10 staff (three occupational therapists, three physiotherapists, two psychological therapists and two psychiatrists).

Data analysis is currently underway and preliminary results will be available for presentation by April 2025.

Interpretation
The findings will expand knowledge of multidisciplinary treatment for people with PPS, and facilitate sharing of specialist practice with other settings where most people with PPS present. The ethnographic approach facilitated an in-depth understanding of a complex treatment for people traditionally underserved by healthcare services. The findings will be used to develop a treatment manual, with the potential to improve treatment for people with severe PPS, through a clear description of an intervention focused on increasing activity and participation. This manual will provide the groundwork for a feasibility study and subsequent randomised controlled trial to establish the clinical effectiveness of the intervention.

Improving end-of-life care provision by ambulance services: a systematic review

D4

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Background
Responding to the needs of patients at the end of life can present challenges for the ambulance service. Facing increasing demand, complexity of patient care needs and a desire to avoid unnecessary transfers to the emergency department, local ambulance services have developed initiatives to help improve the care provided to this patient group. We undertook a systematic review to identify these initiatives and summarise their impact and effectiveness.

Methods
We searched MEDLINE, CINAHL, ASSIA, Embase and grey literature sources to identify English language articles published in the last 10 years that describe initiatives to improve the provision of end-of-life care by ambulance services. We used a PICO framework and a customised data extraction form and undertook a narrative synthesis.

Findings
We reviewed 5350 records and included 35 in the review. We identified eight types of initiative:

1. Education programme
2. Shared care record
3. Specialist advice
4. Communication framework
5. Clinical guidelines
6. Just-in-case medication
7. Specialist transport
8. Alternative response

For three of these initiative types, there was no evidence of effectiveness available (4, 6 and 7). Where evidence was available, initiative types were frequently evaluated together. The available evidence suggests that initiatives could:

1. Improve staff confidence
2. Reduce A&E transfers
3. Improve information-sharing
4. Reassure patients and relatives
5. Improve quality of care

Interpretation
Numerous initiatives have been developed to improve pre-hospital end-of-life care delivered by ambulance services, with the available evidence suggesting these may have a range of benefits for patients. However, the robustness of the evidence is limited. Using the mixed-methods assessment tool, 60% of included studies had either quality concerns or were not able to be assessed for quality. Quality concerns included confounding factors, incomplete data and small sample sizes. Further research to understand patient experiences of care provided by the ambulance service would be beneficial to inform the ongoing development of initiatives in the future.

Neurocognitive concerns and impairment in long-term survivors of oropharyngeal cancer following (chemo)radiotherapy: a cross-sectional study

D5

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Background
Neurocognitive function (NCF) is a key outcome following cancer treatment, impacting quality of life and societal functioning. NCF decline following radiotherapy for head and neck cancers (HNCs), in particular nasopharyngeal and paranasal sinus cancers, is increasingly recognised. However, data on NCF in other HNC subsites, such as oropharyngeal cancer (OPC), which accounts for a substantial and steadily increasing proportion of HNC cases in the UK, remains limited. The Radiotherapy for Oropharyngeal Cancer and impact on Neurocognition (ROC-oN) study was therefore conducted to provide insights into cognitive functioning in OPC survivors.

Method
A multicentre cross-sectional study was conducted in non-surgically treated OPC patients with ≥2 years of follow-up. All participants self-reported neurocognitive concerns (NCCs) using the Medical Outcomes Study Cognitive Functioning Scale (MOS-Cog). Participants were also invited to complete an online cognitive test battery (Amsterdam Cognition Scan; ACS) to assess NCF. Significant NCF impairment was defined as a Z-score of ≤–2 in one domain or ≤–1.5 in two or more domains. NCCs were defined as MOS-Cog scores of ≤60 in all domains. Logistic regression identified factors associated with NCF/NCC, and correlations between NCF, NCC, and radiotherapy dose to the posterior fossa were explored.

Findings
A total of 349 patients treated for OPC, with median age at treatment of 58.6 years and median follow-up of 6 years (IQR 4–8 years) post-treatment, were recruited. Among the 338 patients who completed the MOS-Cog assessment, 15% (50/338) reported significant NCCs, while amongst patients who completed the ACS (*n*=93), 33% (31/93) demonstrated significant impairment in NCF. Memory and attention were the most affected domains on the MOS-Cog and ACS. Marital status, mental fatigue and mood emerged as significant predictors of NCCs (OR [95% CI] = 0.67 [0.47–0.95], 1.39 [1.19–1.62] and 1.04 [1.02–1.06], respectively) on multivariate analysis. No statistically significant associations, however, were found between these factors and NCF on multivariate analysis. There were no statistically significant correlations between NCC/NCF, and radiation dose received by the posterior fossa.

Interpretation
Several years post-radiotherapy, NCCs are reported in 15% of patients treated for OPC, and NCF is impaired in one-third of patients treated for OPC, especially in memory and attention. NCCs and NCF are multidimensional constructs that are not fully aligned, and assessing both is essential for a comprehensive understanding of cognitive health in OPC survivors. Further investigation into underlying mechanisms and potential interventions for NCF and NCCs is needed.

A qualitative systematic review of the resilience of parents and caregivers who safely administer prescribed medicines to children at home

D6

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Background

Parents and caregivers are responsible for safely administering prescribed medicines to their children at home. This is a complex task that requires parents and caregivers to overcome many challenges. The safety sciences theory of resilient healthcare can be used to learn about how this happens. Resilient healthcare is defined as the ability of a person or system to maintain or improve its function despite expected and unexpected disruptions. The aim of this review is to use resilient healthcare theory to explore the experiences of parents and caregivers who administer medicines to children at home.

Methods

This systematic review followed the framework synthesis method. An iterative search strategy, using a scoping search of the major databases, was used. The three main search terms were: parents and caregivers; administration of medicines; and the home environment. Included studies contained qualitative data and investigated the experiences of parents or carers who administer prescribed medicines to children at home. Framework synthesis was completed by following five stages: familiarisation; thematic framework identification; indexing; charting; and mapping and interpretation. The findings identified in the data extraction phase were indexed and charted according to the three elements of Moments of Resilience theory.

Findings

The search strategy identified a rich and diverse range of studies. 46 papers passed full-text screening and were included in the review. Most studies were conducted internationally, with only five from the UK. The synthesis found that there was a significant amount of resilience by parents and caregivers to administer prescribed medicines safely. This ranged from small and immediate resilience (e.g. masking the poor taste of medicines using food), to more widespread and longer-term resilience (e.g. sharing useful strategies for administering medicines with other parents using social media and online message boards). An important finding is that the process by which resilience developed is often described as involving trial and error at home, with little support from professionals. This has a negative effect on the health and wellbeing of families. Public engagement work has confirmed that experiences from included studies corroborates the experiences of UK parents and caregivers.

Interpretation

The experiences of parents and caregivers to safely administer prescribed medicines at home demonstrated a significant amount of resilience. Learning what, when, how and why resilience develops will provide vital knowledge for improving the support offered to parents and caregivers. A strength of this review is the inclusion of a wide and diverse sample, including cultural and ethnic backgrounds. A limitation is the varying quality of qualitative studies included. Improvements in support will reduce the amount of harm experienced by children from the unsafe use of prescribed medicines at home, and improve the mental wellbeing of parents and caregivers.

A translational study exploring the role of brain ageing in the glioblastoma tumour microenvironment

D7

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Background
Glioblastoma primarily affects older adults, with the highest incidence occurring in individuals aged 75–84 years. Alarmingly, older adults are often excluded from clinical trials, limiting understanding of treatment efficacy in this key group. Glioblastoma invariably recurs due to glioblastoma stem cells (GSCs) within the surrounding brain, left behind post-resection. To study this region ethically, our group utilises *en bloc* resections, where large areas of brain are necessarily removed along with the tumour. "Activated" tumour-associated astrocytes drive migration of GSCs into the brain. Similar activation is seen in ageing astrocytes. Do ageing astrocytes influence GSC characteristics at the infiltrating edge, altering treatment response?

Methods
This translational study combines laboratory and bioinformatics approaches: (i) recruitment of IDHwt glioblastoma patients aged ≥65 years (IRAS 11/YH/0319); (ii) 10x Visum Gene Expression (VGES-RNASeq, 10x Space Ranger, Scanpy, Squidpy *in Python*); and (iii) preparation of matched core/infiltrative edge patient-derived GSCs, and induced neural progenitor cell (iNPC) astrocytes for RNASeq (nf-core rnaseq, DESeq2 in R).

Findings
Of 9 patients recruited, 3 patients have tissue and matched GSC cell lines. The 10x-VGES pipeline has been undertaken in a 78-year-old male patient, who underwent a right temporal *en bloc* lobectomy, confirmed as IDHwt glioblastoma on histology. Fulminant malignant cells were evident in the infiltrative edge, with a starkly different composition of malignant markers. While both regions show mesenchymal subtype markers, the edge demonstrates astrocyte activation *(CHI3L1)* and poor-prognostic markers *(SERPINA3, S100A6)*, very distal to the tumour core. The core is instead characterised by aberrant extracellular matrix reorganisation (e.g. *MGP, COL4A1*) and STAT3 signalling *(FN1)*. Analysis of five different matched core/infiltrative edge patient-derived GSCs identified significantly differentially expressed genes (DEGs) in key pathways of astrocyte activation (IL-7/LIF/JAK-STAT signalling) between core and infiltrative edge pairs.

Interpretation
In glioblastoma, studying older patients' tumour samples, which include both the tumour and the surrounding infiltrated brain, gives a unique insight into these differing tumour microenvironments. This first pipeline demonstrates tumour-CNS cell signalling, which overlaps with astrocyte signalling pathways in brain tissue, and which has been recapitulated in core/infiltrative edge *in vitro* GSC cell lines. This is an exciting finding, still to be ratified in more patient samples, but which opens up the possibility of additional targeting therapies to improve the therapeutic response in older patients.

Unlocking the potential of highly conformal external beam radiotherapy planning for locally advanced cervical cancer: results from the prospective multi-centre EMBRACE-II study

D8

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Background
Radiotherapy cures locally advanced cervical cancer (LACC) by targeting radiation at the cancer to destroy it. Unfortunately, during radiotherapy healthy tissues surrounding the cancer are also damaged, causing side effects in the bowel, bladder, and vagina. Risk of bowel side effects is higher in patients where lymph glands – bean-shaped structures that filter fluids – are treated. Patients report that radiotherapy-related treatment side effects significantly affect their quality of life. The international EMBRACE-2 trial implemented a new technique to treat lymph glands whilst reducing irradiation of healthy tissues. This work evaluates radiotherapy dose distributions from EMBRACE-2 to determine if this technique successfully achieved highly targeted plans.

Methods
1366 patients with LACC treated with radiotherapy according to the EMBRACE-II protocol were included in this analysis. Participants were split into subgroups according to the size of the target treated with radiotherapy (pelvis only, or pelvis and para-aortic region), and the number and location of lymph glands treated (no lymph glands, pelvic lymph glands only, or pelvic and para-aortic lymph glands). Radiation dose conformity and bowel dose were compared between subgroups and with patients treated with the same dose and treatment modality in the EMBRACE–1 study.

Findings
643 patients (47%) had a total of 1927 lymph glands treated. Overspill of radiation dose was reduced by 18% for patients treated to pelvis only and 26% for patients treated to the pelvis and para-aortic region in EMBRACE-2 compared to EMBRACE-1. No statistically significant difference in target radiation dose conformity was observed between the EMBRACE-II subgroups at a significance level of 0.05 (p=0.11). Bowel volume irradiated to 40Gy (V40Gy) increased with larger elective nodal volume. The presence of lymph node treatment did not have a statistically significant effect on bowel V40Gy.

Interpretation
Implementation of the EMBRACE-II protocol aims improved plan conformity across international centres for patients treated with all levels of nodal involvement compared to EMBRACE-I. Treatment of pathological nodes using the new planning technique is feasible with high target doses and does not affect plan conformity or bowel dose. This technique limits dose spillage into the bowel and shows promise for application in other sites where radiotherapy is used to treat lymph glands. Use of this technique in the clinic has the potential to reduce the severity and incidence of radiation-induced side effects in patients with cervical cancer.

Glucocorticoid treatment in congenital adrenal hyperplasia and its associations with growth outcomes – real-world data analysis from an international cohort of 1500 patients

D9

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Background
Previous evidence from the I-CAH registry showed wide variation of glucocorticoid (GC) replacement between different countries and centres. We hypothesised that different treatment strategies will lead to different clinical outcomes, and better insight into this interdependency will help improve hormone replacement in congenital adrenal hyperplasia (CAH). We wanted to explore the impact of different hormone GC doses on height and weight in children and young people with CAH.

Methods
We analysed data from children with CAH recorded in the I-CAH registry since 2003. We explored the relationship between GC doses expressed as hydrocortisone (HC) equivalent/m^2/day and height and weight standard deviation scores (SDS) for age and sex. We collected data using the I-CAH platform in collaboration with all participant centres who had eligible patients. SDS for age and sex were calculated using Growth Analyser (country- and region-specific normative data). Data analysis was conducted using the R platform and consisted of multivariable regressions analysis.

Findings
We analysed data from 1574 patients, 14,536 clinic visits, from 23 countries (61 centres). There was large variability in the GC dose used in different countries, ranging from a median of 5.3–20.6 HC-equivalent/m^2/day. Regression analysis showed that the GC dose was influenced significantly by the country where patients were treated (R^2=0.08, $p<0.01$). Patients' height-SDS had an inverted U-shaped relationship with age, with low height SDS during infancy, increased height-SDS during early childhood up to 9 years, and final decrease in adolescence. Multivariable regression showed that up to 57% of the variance in height-SDS was related to weight-SDS, GC dose per body surface area (BSA) and the country in which patients were treated (under 9 years: R^2=0.36, $p<0.01$; over 9 years: R^2=0.57, $p<0.01$). Weight-SDS increased with HC dose per BSA (R^2=0.002, $p<0.01$); however, the variables most strongly associated with weight-SDS were birth weight and patients' country of origin (R^2=0.32, $p<0.01$).

Interpretation
We provided a longitudinal analysis of real-world data, availing of a large international cohort of children and young persons with CAH. Our analysis showed wide variation among countries in the clinicians' practice of GC replacement in children with CAH. The results indicate that different doses of GC replacement impact on patients' growth. The low height-SDS during infancy may at least in part relate to the high relative GC doses used in this age group and highlights the pressing need to optimise replacement that avoids GC overexposure from early life.

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