NIHR | Leicester Biomedical Research Centre

Part of our NIHR BRC Half Time Celebrations

# NIHR Leicester BRC and LHIIP
# PhD Scientific Symposium 2025

## Wednesday 18th June 2025

Sir Bob Burgess Building
University of Leicester
Leicester, LE2 6BF

University of Leicester
Loughborough University
wellcome
Leicester City Council
NHS University Hospitals of Leicester NHS Trust
NHS Leicester, Leicestershire and Rutland Integrated Care Board

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# EVENT AGENDA

**09:00** **Registration and Welcome Refreshments**

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|---|---|---|
| **09:30** | **Prof. Sally Singh**<br>**Dr Aarti Parmar** | **Welcome to the first BRC and LHIIP Scientific Symposium** |

## SESSION 1 - Respiratory/Environment
## Co-Chairs: Dr Linzy Houchen-Wolloff and Dr Sam Khan

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|---|---|---|
| **09:45** | **KEYNOTE SPEAKER**<br>**Dr Daniel Pan**<br>*University of Leicester* | **Rethinking infectiousness testing in respiratory virus infections – what are the implications for at risk groups?** |
| **10:15** | **PRESENTATION**<br>**Holly Drover**<br>*LHIIP \| Respiratory* | Predictors of uptake and completion of pulmonary rehabilitation in the UK |
| **10:30** | **PRESENTATION**<br>**Mathuscha Ratnasingham**<br>*BRC \| Respiratory* | The role of TRPM7 in human lung myofibroblast profibrotic function |
| **10:45** | **PRESENTATION**<br>**Robin Wroblewski**<br>*BRC \| Environment* | Development of a novel air sampler for the collection of airborne fungal spores |

**11:00** **Refreshment Break (15 mins)** *Room 0.02*

## SESSION 2 - Lifestyle/Cardiovascular/Cancer
## Co-Chairs: Prof. Thomas Yates and Dr Mark Orme

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| **11:15** | **KEYNOTE SPEAKER**<br>**Prof. Gregory Maniatopoulos**<br>*University of Leicester \| NIHR ARC EM* | **Bridging the gap between evidence and practice: Implementation research to facilitate the uptake of healthcare innovation** |
| **11:45** | **PRESENTATION**<br>**Faye Ashton**<br>*LHIIP \| Lifestyle* | The influence of acute continuous exercise and adiposity on appetite hormones and neural correlates of visual food cues (ACE CRAVE) |
| **12:00** | **PRESENTATION**<br>**Yanan Song**<br>*BRC \| Cardiovascular* | The effectiveness of different approaches to T2D remission and associated cardiovascular benefits: A systematic review and network meta-analysis |
| **12:15** | **PRESENTATION**<br>**Jean Marie Vianney Semana**<br>*BRC \| Lifestyle and Cancer* | Physical activity and fatigue in people living with and beyond cancer |

**12:30** **Lunch Break (1 hour)** *Room 0.02*

## SESSION 3 - Respiratory/Lifestyle/Cardiovascular/Data
## Co-Chairs: Dr Calvin Jephcote and Dr Nicola Paine

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| **13:30** | **KEYNOTE SPEAKER**<br>**Dr Natalie Darko**<br>*University of Leicester* | **Asking the difficult question: how do we collect data on protected characteristics?** |
| **14:00** | **PRESENTATION**<br>**Jo McAllister**<br>*LHIIP \| Respiratory* | Improving Cardiac Rehabilitation Participation Among South Asian Communities in England: An Explanatory Sequential Mixed Methods Study |
| **14:15** | **PRESENTATION**<br>**Kate Kontou**<br>*LHIIP \| Lifestyle* | Mixed methods study comprising a randomised controlled trial (RCT) with embedded qualitative component to explore the effectiveness and acceptability of face-to-face rehabilitation for patients with Long Covid who were not hospitalised with their acute infection |
| **14:30** | **PRESENTATION**<br>**Alfred Charlesworth**<br>*BRC \| Cardiovascular and Data* | Solving the antibody crisis: A novel LC-MS/MS-optimised procedure for the in-situ, label-free characterisation of antibodies |

**14:45** **Refreshment Break (15 mins)** *Room 0.02*

## SESSION 4 - Cancer
## Co-Chairs: Prof. Karen Brown and Dr Tom Wilkinson

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|---|---|---|
| **15:00** | **KEYNOTE SPEAKER**<br>**Dr Anshul Thakur**<br>*University of Oxford* | **AI in Healthcare** |
| **15:30** | **PRESENTATION**<br>**Eleanor Massey**<br>*BRC \| Cancer* | Use of Oxford Nanopore Technology liquid biopsy workflows for early cancer detection, tissue-of-origin prediction and personalising cancer treatment |
| **15:45** | **PRESENTATION**<br>**Eve Jarman**<br>*BRC \| Cancer* | Modelling Metabolic Dysregulation to Assess Colorectal Cancer Prevention Strategies |
| **16:00** | **PRESENTATION**<br>**Emmanuella Batu**<br>*BRC \| Cancer* | ctDNA meets Patient Derived Explant; Developing ctDNA predictive biomarkers for OX40 using PDE meta data |

**16:15** **Final judging (5 mins)** *Room 0.02*

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| **16:20** | **Prof. Sally Singh**<br>**Dr Aarti Parmar** | **Closing Remarks**<br>**Student Presentation and Poster Prize Winners** |

# OUR PROGRAMMES

## NIHR Leicester Biomedical Research Centre

The NIHR Leicester BRC is part of the NIHR and hosted by the University Hospitals of Leicester NHS Trust in partnership with the University of Leicester, Loughborough University and the University Hospitals of Northamptonshire NHS Group. We bring together academics and clinicians to translate scientific discoveries into potential new treatments, diagnostics and technologies.

"*We have a proud history of health research and the NIHR Leicester BRC will enable us to push the barriers of science in the quest for more answers and, ultimately, improved care for people with – or at risk of – long term conditions.*" Professor Melanie Davies, CBE, Director of NIHR Leicester BRC.

We specialise in research in six key areas:

- respiratory and infection
- lifestyle – including type 2 diabetes
- personalised cancer prevention and treatments
- environment and health
- using data to understand long term health conditions and health inequalities
- cardiovascular disease

Our plans are based on a strong foundation of discovery research and cover the understanding of the genetic causes of these diseases to investigating the benefits of lifestyle changes – especially focused on increasing different types of physical activity as both a preventative action and as a medicine for managing and minimising the disease burden.

Key to our strategy is advancing the idea of precision medicine, that is, adjusting treatments for individuals based on their personal characteristics, including their genetic make-up. This will make sure that everyone has the most effective treatment for them, while reducing the risks of side-effects.

Thanks to funding from the NIHR and our partners, we currently have 49 PhD Research Students across two cohorts. We aim to create the next generation of research leaders throughout our PhD programme.

To find out more, please visit the NIHR Leicester BRC webpage.

## Leicestershire Healthcare Inequalities Improvement Doctoral Training Programme

This prestigious PhD programme looks to address the unique health issues faced by Leicester and Leicestershire's ethnically and culturally diverse population, recently amplified by the COVID-19 pandemic.

The programme is based on challenging health inequalities in our vibrant multicultural region. It has two clear ambitions:

1. To tackle inequalities in healthcare provision;
2. To address inequalities in academic opportunities for our Health Care Professionals.

Our vision is to create a vibrant, supportive, interdisciplinary and flexible training programme to attract underrepresented healthcare professionals and to become a beacon site for nurse, midwife and allied health professional led research nationally and internationally.

Leicestershire's social and demographic features, including the highest proportion of non-white residents (55%) in the UK, provides a genuine and exciting opportunity to address major health disparities across an ethnically and culturally diverse population.

COVID-19 has shone a light on inequalities and highlighted the urgent need to strengthen action to prevent and manage ill health in ethnic minority communities. Evidence suggests that existing socio-economic inequalities, unequal access to healthcare services, lifestyle factors, and co-morbidities such as cardiovascular disease, cancer and diabetes play a key role.

Thanks to funding from the **Wellcome** we currently have 15 funded PhD Research Fellows across three cohorts and will have two more cohorts starting over the next 2 years. This provides nurses, midwives, allied health professionals and doctors the opportunity to pursue academic research.

To find out more about our programme and our current PhD Research Fellows, please visit our University of Leicester programme webpage.

# BIOGRAPHIES

## Prof. Sally Singh

Professor of Pulmonary and Cardiac Rehabilitation | *University of Leicester*
Head of Pulmonary and Cardiac Rehabilitation | *UHL NHS Trust*
Director of Training and Capacity Development | *NIHR Leicester BRC*
Programme Director | *LHIIP*

Prof. Singh's research specialisms include pulmonary and cardiac rehabilitation and digital interventions to support rehabilitation and recovery. She is leading the development and delivery of rehabilitation for patients with chronic lung disease and cardiovascular disease, including face-to-face and home-based interventions.

Prof. Singh has received research funding to understand the acceptability of manual and digital interventions for patient groups who are unable to visit medical centres for face-to-face care. Her research extends to low and middle-income countries, exploring culturally appropriate rehabilitation interventions for chronic lung disease with partners in Uganda, Malawi, India, Sri Lanka and Kyrgyzstan.

As well as being a member of the World Health Organisation's Development Group for COPD rehabilitation programme, Prof. Singh is the clinical lead for the National Asthma and COPD Audit Programme hosted by the Royal College of Physicians. She is co-lead for an NIHR Programme Grant examining the clinical and cost effectiveness of exercise-based rehabilitation in people living with multiple long-term conditions.

## Dr Aarti Parmar

NIHR Leicester BRC Manager | *UHL NHS Trust*
Honorary Fellow | *University of Leicester*

Dr Parmar earned her doctorate in Respiratory Sciences from the University of Leicester in 2013. Her research contributed to the groundbreaking identification of thymic stromal lymphopoietin (TSLP) as a key driver of asthma inflammation, evidence that supported the development of tezepelumab, a monoclonal antibody with transformative potential for patients with severe asthma.

During the COVID-19 pandemic, she managed several high-impact studies, including serving as Research Programme Manager for the NIHR/MRC-funded PHOSP-COVID study. In this role, she coordinated multidisciplinary research efforts across 26 universities and 83 NHS Trusts in the UK.

Dr Parmar brings her commitment to evidence-based medical innovation to her current role as Manager of the NIHR Leicester Biomedical Research Centre (BRC). She provides strategic leadership and oversees the delivery of cutting-edge research across six research themes and four platforms, ensuring alignment with both local and national priorities. She also leads on governance, ensuring the BRC meets its strategic goals, maintains strong partnerships, and complies with NIHR requirements. She has played a pivotal role in securing additional funding to support the BRC's research ambitions and is currently pursuing an MBA to further enhance her leadership and strategic management capabilities.

Dr Parmar plays a key role in fostering collaboration across various networks and initiatives, contributing to the Centre's broader strategic direction. She actively supports efforts to create an inclusive research environment and is involved in initiatives aimed at nurturing future talent within the research community.

## Dr Daniel Pan

NIHR Doctoral Research Fellow| *University of Leicester*
Resident Doctor in Infectious Diseases and General Internal Medicine | *UHL NHS Trust*

Dr Pan trained in Medicine at Imperial College London and completed his Academic Foundation Programme and Core Medical Training in Yorkshire and London before joining Leicester in 2019 as an NIHR Academic Clinical Fellow and Specialist Registrar.

During the COVID-19 pandemic, Dr Pan contributed to research that first identified the disproportionate impact of COVID-19 on ethnic minority groups and isolated exhaled SARS-CoV-2, directly linking it to human-to-human transmission. He has led in the design and implementation major field studies on SARS-CoV-2 transmission - including BE-DIRECT and COVMASK. COVMASK forms an essential part of his PhD, in which he has enrolled over 600 participants since 2020 and expanded to include healthcare workers and hospitalised patients with influenza, RSV, measles and mpox. Dr Pan regularly collaborates with colleagues at the Oxford Big Data Institute, Imperial College London and the Hong Kong School of Public Health.

He has led international guideline development with the World Health Organisation on the ethnic disparities in COVID-19 outcomes, with his work cited in more than 100 policy documents worldwide. His research has directly informed government policy through contributions to two national core studies on COVID-19 (themes of transmission/environment and immunity) supported by the UK Government Office for Science and has played a role in shaping debates in the UK House of Commons.

## Prof. Gregory Maniatopoulos

Director of the Centre for Healthcare Innovation, Policy and Management | *University of Leicester*
'Translating and Implementing Sustainable Service Improvement' Theme Lead | *NIHR ARC EM*

Prof. Maniatopoulos has over 15 years' experience as an applied health researcher with a track record of conducting high-quality research and teaching in healthcare innovation, implementation and change. His research explores how organisational and policy factors shape processes of appropriation of innovations in healthcare practice. He has published widely in the area of implementation, digital health, technology adoption and health systems change.

## Dr Natalie Darko

Associate Professor of Health Inequalities | *University of Leicester*
Director of Inclusion | *NIHR Leicester BRC*

Dr Darko specialises in health research and practice that addresses equality, equity, and inclusion of underrepresented and minority groups. She has extensive experience in leading and delivering research within the field of health inequalities, of which her current research projects focus on maternal health, womb cancer, social prescribing, diabetes, faith-based interventions, and dementia. She supports researchers, organisations and practitioners on how to work collaboratively with and for underserved and minority groups to inform equitable health and research practice.

## Dr Anshul Thakur

Departmental Lecturer in Clinical Machine Learning | *University of Oxford*

Dr Thakur received his PhD in 2020 from IIT Mandi, where he developed machine learning methods for audio signal analysis, including acoustic event detection and speech disorder classification. After transitioning into clinical machine learning, his work has spanned multiple aspects of healthcare AI, including the development of multimodal patient care tools, foundation models, vaccine research, federated learning, and dataset condensation. His current focus lies in building privacy-preserving, generalizable AI systems—particularly leveraging large language models (LLMs)—for clinical prediction, medical text understanding, and real-world deployment in biomedical settings.

# STUDENT PRESENTATION ABSTRACTS

## Predictors of uptake and completion of pulmonary rehabilitation in the UK

Holly Drover | LHIIP

**Background**
Pulmonary Rehabilitation (PR) is a highly evidenced intervention for individuals with chronic obstructive pulmonary disease (COPD), but uptake and completion of the programme remains a challenge. Reasons for this are complex[1], although are likely compounded by health inequalities. These are differences in health between different groups of people and the opportunities available to them for living healthy lives[2].

**Aims**
To compare the uptake and completion of PR across characteristics using a National Respiratory Audit Programme dataset from England and Wales. The uptake and completion across centre-based and home-based programmes was also explored.

**Methods**
88446 individuals with COPD attended a PR assessment between March 2019 and September 2023. Generalised linear mixed models with a logit link function were used to explore the characteristics associated with PR uptake and completion. Factors included age, gender, ethnicity, Medical Research Council (MRC) dyspnoea grade, index of multiple deprivation (IMD) quintile and programme type. Uptake was defined as attending at least one PR session in any mode of delivery. Completion was defined as attending a discharge assessment.

**Results**
72085 (82%) individuals that attended a PR assessment did uptake a PR programme and 52669 (60%) completed PR. Age<60years (OR 0.46, 95% CI 0.42-0.50, p<0.0001), female gender (OR 0.92, 95% CI 0.87-0.98, p=0.0046), MRC grade 5 (OR 0.75, 95% CI 0.67-0.85, p<0.0001) or IMD 1 quintile groups (OR 0.63, 95% CI 0.56-0.70, p<0.0001) were significantly less likely to uptake PR. Service users were 13% less likely to uptake a home-based programme of PR compared to a centre-based programme (p<0.0001), but 12% more likely to complete (p<0.0001).
Age<60 years (OR 0.51, 95% CI 0.49-0.54, p<0.0001), female gender (OR 0.92, 95% CI 0.89-0.95, p<0.0001), MRC 5 (OR 0.53, 95% CI 0.50-0.57, p<0.0001), unrecorded MRC grade (OR 0.65, 95% CI 0.60-0.71, p<0.0001), or IMD 1 quintile groups (OR 0.63, 95% CI 0.59-0.66, p<0.0001) had significantly lower odds of completing PR. Individuals that identified as Black or Asian had significantly greater odds of completing PR (Black: OR 1.48, 95% CI 1.24-1.77, p<0.0001; Asian: OR 1.20, 95% CI 1.05-1.37, p=0.0062).

**Conclusion**
Uptake and completion of PR varied across characteristics, with individuals aged <60years or with a higher MRC or a lower IMD quintile least likely to uptake or complete PR. Strategies to support individuals with characteristics less likely to uptake or complete PR would be beneficial to support health equity.

**References**
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2: Williams, E., Buck, D., Babalola, G. and Maguire, D. (2022) *What are health inequalities?*: The King's Fund. Available at: https://www.kingsfund.org.uk/publications/what-are-health-inequalities.

## The role of TRPM7 in human lung myofibroblast profibrotic function

Mathuscha Ratnasingham | BRC

**Background**

Idiopathic pulmonary fibrosis (IPF) is a progressive interstitial lung disease affecting around 5 million people globally, with a median survival of 3-4 years. Current treatments, pirfenidone and nintedanib, only slow disease progression and have significant side effects but do not stop its progression. Therefore, alternative and more effective treatments are urgently needed. IPF is characterized by excessive scarring of lung tissue, resulting from the accumulation of myofibroblasts that deposit extracellular matrix (ECM) [1]. The pathogenesis of IPF involves repeated micro injury, possibly through environmental exposure causing alveolar injury, inducing the secretion of pro-fibrotic mediators, such as TGFβ1, which trigger fibroblast-to-myofibroblast transitions and ECM deposition [2]. Recent research suggests that transient receptor potential (TRP) channels, may play a key role in regulating calcium signalling and mechanical stress, crucial in myofibroblast activation. The melastatin-type transient receptor potential 7 (TRPM7) ion channel is a bifunctional protein. It is a multimeric plasma membrane nonselective cation channel but also contains an intracellular kinase domain [3]. It is involved in $Ca^{2+}$ and $Mg^{2+}$ homeostasis, cell growth and proliferation [4]. TRPM7 promotes profibrotic activity in cardiac fibroblasts [3] Inhibition of TRPM7 has been shown to reduce wound healing in glioblastoma cell lines [5]. However, the role of TRPM7 in lung fibrosis is unclear.

**Aims / Objectives**

We aim to investigate TRPM7 expression and function in Human Lung Myofibroblasts (HLMFs) and hypothesise that targeting TRPM7 channels may hold the key to new therapeutic avenues in IPF.

**Methodology and Main Body**

HLMFs were isolated and characterised [6] from non-fibrotic (NFC) and IPF human lung tissue. TRPM7 expression (± TGFβ1) was assessed via qRT-PCR and Affymetrix Human Gene 2.1 ST genome-wide microarray in several lung cell types. TRPM7 currents were analysed using patch-clamp electrophysiology and manipulated with $Mg^{2+}$, Naltriben and TRPM7 inhibitor, Waixenicin A (500nM). TRPM7 knockdown was achieved using siRNA, and fibrotic markers (αSMA, Collagen 1, and Collagen 6) was quantified by RT-PCR. MTS assay and wound healing were utilised to assess the effects of Waixenicin A on HLMF viability, proliferation and migration.

**Results**

TRPM7 expression was examined in different lung cell types and is highly expressed in airway fibroblasts compared to other cell types cells (airway epithelial cells p=<0.0001). However, when compared to non-fibrotic controls TRPM7 is significantly downregulated in IPF HLMF (p=0.035), IPF airway fibroblasts (p=0.0004) and IPF parenchymal fibroblasts (p=0.0085). In line with this, treatment with pro-fibrotic cytokine TGFβ1 (10 ng/mL) significantly reduced TRPM7 expression in HLMFs (p=0.0319, n=11).

Patch clamp electrophysiology showed functional TRPM7 currents present in lung derived fibroblasts and these can be blocked by increasing magnesium (6 mM) (n=6 IPF and n=13 NFC) and treatment waixenicin A (500nM) (n=6 NFC). siRNA knockdown of TRPM7 inhibited TRPM7 function.

We next evaluated TRPM7s role in pro-fibrotic function using TRPM7 siRNA and TRPM7 inhibitor waixenicin A. siRNA knockdown of TRPM7 decreased expression of key fibrotic markers, α-SMA, Collagen 1 and 6 mRNA (n=8). We show that waixenicin A has no cytotoxic effects on HLMFs (n=5). TRPM7 inhibition significantly impaired HLMF wound healing (p=0.0011, n=6). In addition, changes in TRPM7 methylation were observed in airway (p=<0.019) and parenchymal (p=<0.03) fibroblasts, notably in CpGs located in regulatory regions.

**Conclusions / Implications for practice**

These findings demonstrates that HLMF express TRPM7 and possess functional channels on their membrane. Downregulation of TRPM7 is observed in IPF HLMFs, and following stimulation with TGFβ1. TRPM7 knockdown indicates a reduction in key fibrotic markers and inhibition impairs

fibroblast wound healing. There is evidence that epigenetic mechanisms may influence regulating TRPM7 in IPF. Further work is required to determine the exact role TRPM7 may play in IPF.

**References**


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## Development of a novel air sampler for the collection of airborne fungal spores

Robin Wroblewski | BRC

**Background**

Bioaerosols in the indoor environment can have a significant impact on human health due to their role in allergic, respiratory, and infectious disease (Ross *et al.* 2000; Douwes *et al.* 2003). Prolonged exposure to high concentrations of fungal spores is associated with coughing, wheezing, allergic rhinitis, fungal infection and exacerbation of chronic respiratory conditions (Schweer *et al.* 2014). The impacts of bioaerosols can be mitigated through the use of environmental sampling. As analysis of the air microbiome can enable the identification of health relevant organisms, which can be monitored to improve air quality (Martin-Sanchez *et al.* 2021).

**Aims / Objectives**

This study aimed to develop a robust and universal home sampler and sampling protocol to collect airborne fungal spores from homes for identification and analysis.

**Methodology and Main Body**

A 3D printed sampler was developed to hold a standard adhesive PCR film. A preliminary study was devised to test the sampler design. Testing was conducted in 35 participant homes under various conditions to determine the ideal sampling parameters for future use of the sampler. Participants were also issued with a questionnaire to determine the impact of daily activity and building characteristics on spore composition.

Bioaerosol concentration was then explored by excising a 1cm by 4cm section of film using sterile technique, this was loaded onto a microscope slide and stained with lactophenol cotton blue, finally fungal spore counts were recorded using a 13 vertical transverse method at 400x magnification. Additional validation of spore presence was conducted by culturing fungal colonies from the film.

**Results**

Sampling height had no significant impact on spore count (P=>0.5). Sampling time demonstrated a significant impact on spore count (P=<0.001). The room sampled demonstrated a significant impact on spore count and diversity (P=<0.01), implying that spore composition is not consistent throughout an entire property. Building time and building age were found to have no significant impact on spore quantity and minimal impact on microbiome composition (building age: P=>0.5, building type: P=>0.1). When compared to an alternative sampling method the sampler was found to collect the same spore types.

**Conclusions / Implications for practice**

This validation study has provided insight into optimal air sampling conditions using this passive sampling method. The sampler has demonstrated to be consistent in varying conditions across multiple houses although further work is ongoing to determine the consistency of the sampler at different times in the year. This sampling method has proved to be a robust, unintrusive and cost-effective method for sampling bioaerosols in homes. Future work using the sampler involves optimising a method for culturing various species of fungi from the sampler, and an ongoing pilot study analysing bioaerosol composition in the homes of COPD patients and its impact on the lung microbiome.

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## The influence of acute continuous exercise and adiposity on appetite hormones and neural correlates of visual food cues (ACE CRAVE)

Faye Ashton | LHIIP

**Background**

Appetite plays a central role in the development and progression of overweight and obesity, which remain chronic and escalating global health challenges. Regulation of appetite and energy intake is governed by an intricate network of homeostatic and hedonic mechanisms, centrally coordinated by the brain. These systems are dynamic and can be influenced by factors such as physical activity and body composition. Previous research has shown that a single bout of exercise can transiently suppress appetite, reduce levels of the orexigenic hormone acylated ghrelin, and increase concentrations of anorexigenic hormones such as peptide YY (PYY) and glucagon-like peptide-1 (GLP-1). Another gut-derived hormone, oxyntomodulin, is known to suppress appetite and enhance energy expenditure. However, the acute effects of continuous exercise on circulating oxyntomodulin concentrations in individuals with different levels of adiposity have not yet been thoroughly investigated.

**Aims / Objectives**

This study aims to determine whether acute continuous walking affects circulating oxyntomodulin levels in adults who are lean or living with overweight or obesity. In addition, the study will explore how exercise and adiposity influence other appetite-related outcomes, including hormonal responses, subjective appetite perceptions, sensory processing (taste and smell), and neural correlates assessed through functional magnetic resonance imaging (fMRI).

**Methodology and Main Body**

A total of 40 participants (20 lean and 20 with overweight/obesity) were recruited to complete two main laboratory-based trials—an exercise condition and a control (rest) condition—in a randomised crossover design stratified by weight status. Participants classified as overweight/obese had a BMI of 25–40 kg/m² and a waist circumference of ≥88 cm for women and ≥102 cm for men (with lower, ethnicity-specific cut-offs also applied), while lean participants had BMI and waist measurements below these thresholds. This study is registered at ClinicalTrials.gov (NCT06849050).

Main trial visits were spaced by at least seven days for male participants, while female participants completed their trials during the follicular phase of their menstrual cycle. The evening before each visit, participants consumed a standardised pizza meal and arrived at the lab the following morning after an overnight fast. A cannula was inserted for serial venous blood sampling every 30 minutes from 08:30 to 13:00. Subjective appetite ratings—including hunger, fullness, satisfaction, and prospective food consumption—were recorded at the same intervals. Participants also completed sensory assessments (taste and smell) at baseline, 1.5 hours, and 4 hours. The exercise intervention consisted of a 60-minute brisk treadmill walk at 60% of peak oxygen uptake; during the control trial, participants rested for the same duration. An ad libitum pasta meal was served at 2.5 hours post-baseline.

On a separate visit, participants underwent structural and functional magnetic resonance imaging (MRI) after a 10-hour fast. The fMRI session included resting state and task-based sequences, during which participants viewed images of foods varying in energy density and non-food control items.

**Results**

32 healthy adult volunteers have enrolled in the study to date. Of these, 17 participants (n = 12 females) are living with overweight/obesity (mean (SD) age 43 (±12) years, BMI 31 (±5) kg/m$^2$, waist circumference 101(±14) cm) and 15 participants (n = 10 females) are classified as lean (age 41 (±11) years, BMI 23 (±1) kg/m$^2$, waist circumference 66 (±29) cm). 25 participants have completed the two main trials, and 27 participants have undergone the MRI protocol (data to be analysed when all scans complete).

Formal statistical analysis has not been completed but preliminary observations of the data suggest that perceptions of overall appetite are suppressed during and immediately after exercise compared to control (overweight/obesity: exercise 58 (±12) mm; control 54 (±11) mm; lean: exercise 55 (±16) mm; control 55 (±16) mm).
Oxyntomodulin analysis has been completed for 10 participants (n=5 overweight/obesity; n=5 lean) which shows little difference between the two trials but a marked rise in concentrations after the *ad libitum* meal (overweight/obesity: exercise 153 (±51) pg/mL h; control 168 (±45) pg/mL h; lean: exercise 126 (±106) pg/mL h; control 107 (±73) pg/mL h). Measurements of acylated ghrelin, total GLP-1, total PYY, leptin and glucose are planned.

**Conclusions / Implications for practice**
This study will provide novel insights into the acute effects of continuous exercise on circulating oxyntomodulin concentrations and multiple appetite-related responses across individuals with different levels of adiposity. Data analysis will be completed following the conclusion of data collection in September.

## The effectiveness of different approaches to T2D remission and associated cardiovascular benefits: A systematic review and network meta-analysis

Yanan Song | BRC

**Background**

It is recognised that Type 2 diabetes (T2D) can be reversed via surgery, lifestyle and pharmacological approaches.

**Aims / Objectives**

The aim of this study was to determine the most effective approaches to achieve diabetes remission and reduce incidence of major adverse cardiovascular events (MACE).

**Methodology and Main Body**

This systematic review identified randomised control trials (RCTs) using a pre-determined search strategy applied to MEDLINE, Embase and CINAHL from database inception to January 2024. The primary outcome was diabetes remission defined as HbA1c < 6.5% following ≥3 months without any medication. Secondary outcomes were weight-loss and MACE post-intervention by remission status. The data were synthesised using network meta-analysis (NMA, MetaInsight v6.3.0).

**Results**

Twenty RCTs were identified, including 6,050 participants and median follow-up of 2 years (range: 5 months to 10 years). Different interventions and follow-up periods were categorised into a total of nine groups to permit data synthesis and produce three network analyses (NWA) by follow-up (≤1year, 1-2 years and >2years). Fourteen studies with 9 interventions and follow-up for ≤1 year were included in NWA-1, 10 studies with 8 interventions with follow-up 1-2 years were included in NWA-2 and 8 studies with 6 interventions with follow-up >2 years were included in NWA-3.
For NWA-1, Roux-en-Y gastric bypass surgery was the most effective (remission rate (RR) =64%) and demonstrated the highest weight-loss from baseline (-32kg). For NWA-2 and 3 sleeve gastrectomy was the most effective at achieving remission (RR of 69% and 43%, respectively) and demonstrating a considerable amount of weight-loss from baseline (~21kg). The least effective approaches at achieving remission and weight-loss were lifestyle plus intensive insulin therapy and incretin analogue (NWA-1: RR=21%, -5kg), lifestyle and intensive insulin therapy (NWA-2: RR=12%, -8kg), and lifestyle management (NWA-3: RR=7%, -5kg). Irrespective of intervention approach diabetes relapse increased with longer duration of follow-up.
Reporting of MACE was only included in one study for both NWA-1 and 2 and in four studies for NWA-3. However, these were not reported by remission status except in one study (comparing two lifestyle interventions) therefore data could not be pooled to form a net-work.

**Conclusions / Implications for practice**

Bariatric surgery is the most effective intervention for achieving diabetes remission which also achieves the highest weight-loss. Overtime, there is a high relapse rate, irrespective of intervention, which could be attributed to the lack of remission-maintenance support included in any of the interventions. There remains a dearth of data to the impact of diabetes remission on MACE. Future RCTs should include remission maintenance support, longer-follow-up and report MACE outcomes by remission status.

## Physical activity and fatigue in people living with and beyond cancer

Jean Marie Vianney Semana | BRC

**Background**

Cancer is an umbrella term encompassing a variety of diseases that can affect any region of the human body and can multiply and spread to other areas [1]. In 2022, around 20 million people worldwide were living with cancer, and it was one of the primary causes of global mortality, with its incidence continuing to rise [2]. People living with and beyond cancer often experience significant cancer-related fatigue (CRF), which is a distressing, continuous, and personal sense of exhaustion or weariness [3] that negatively affects their quality of life and daily functioning [4]. CRF is difficult to measure due to its subjectivity [5]. Currently, self-reported questionnaires are used for monitoring, which is not continuous and relies on the patient's memory [6]. Physical activity (PA) may be a potential intervention to alleviate CRF [7], however, the relationship between them has not been established. Although some studies have begun to explore whether accelerometers can be used to measure fatigue by monitoring PA and vital signs [8,9], existing data are still limited, with short monitoring periods. There is still a need to build a method for producing continuous accelerometer PA data collected before and during cancer therapies, and strategies for remotely monitoring fatigue. Therefore, the primary objectives of this study are 1) to describe the PA level in people living with and beyond cancer, and the relationship with fatigue using subjective and device-assessed measures, and 2) to determine the feasibility of collecting continuous accelerometer data in patients living with cancer pre- and during treatment.

**Methods**

1. **Systematic review:** Level of physical activity in people living with and beyond cancer.
2. **SELECT study:** Collecting and utili**S**ing acc**E**lerometer data from patients in ear**L**y phas**E** **C**ancer **T**rials to assess physical activity and fatigue.

**Study design:** Feasibility study.
**Population:** Patients in early-phase clinical trials, aged ≥ 18.
**Sample size:** Up to 50 patients.
**Intervention:**

- Providing an ActiGraph LEAP to wear continuously for up to 6 weeks to monitor physical behaviours and vital signs.
- Completing two types of self-reported fatigue questionnaires: a daily Numerical Rating Scale and a weekly Multidimensional Fatigue Symptom Inventory- Short Form.

**Primary outcomes:** Continuous accelerometer data collection up to 6 weeks and return of accelerometers.
**Secondary outcomes:** PA levels and patterns, and physiological parameters such as heart rate, heart variability, breathing rate, and skin temperature obtained from the accelerometer.
**Data analysis:**

- The proportion of patients recruited into the study, and who returned the devices.
- Average number of valid days, waking hours and nights.
- Description of the PA volume, intensity and patterns before and during treatment.

**Statistical plan:** Statistical summary of overall daily PA across 24 hours, and time spent in sedentary, light, moderate, and vigorous activity.

**Implications for practice**

The study will generate new data on 24-hour physical behaviours, as well as tools for continuously assessing fatigue remotely, in people living with and beyond cancer. This could provide a valuable approach for evaluating and monitoring treatment side effects, which are critical considerations in early-stage cancer trials when deciding on a treatment plan.

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## Improving Cardiac Rehabilitation Participation Among South Asian Communities in England: An Explanatory Sequential Mixed Methods Study

Jo McAllister | LHIIP

**Background**

Despite robust evidence demonstrating the effectiveness of cardiac rehabilitation (CR)[1], participation remains low[2]. Certain ethnic populations such as South Asian have a higher risk of cardiovascular disease[3], indicating an increased need for CR. There has been limited analysis of disaggregated data to understand CR engagement within individual ethnic populations. Furthermore, there is a lack of evidence-based guidance on how to tailor CR services to better meet the needs of diverse communities and enhance participation.

**Aims / Objectives**

This explanatory sequential mixed methods study aimed to evaluate CR participation among South Asian service users and to develop consensus-driven, community-informed strategies to address barriers to uptake and adherence.

**Methodology and Main Body**

In Phase I, a retrospective cohort analysis of the National Audit of Cardiac Rehabilitation database (n=421,281, between 2014-2022) compared uptake and completion rates of South Asian to White service users referred to CR, analysed using logistic regression, adjusted for age, sex, socioeconomic status and co-morbidities. Findings informed phase II, which comprised 32 qualitative semi-structured interviews (n=20 South Asian service users referred for CR and n=12 CR clinicians), and explored lived experiences, cultural and systemic barriers, and perceptions of CR services. Emerging themes guided the development of Phase III, a consensus-based nominal group technique (NGT) workshop (South Asian service users (n=20), CR clinicians (n=7), and local stakeholders (n=4)). This consensus-building approach engaged participants in co-developing and prioritising practical, culturally tailored solutions to improve CR participation, based on the 5 most prominent barriers from phase II. Findings were integrated across phases to inform tailored service recommendations and were reported following ACcurate COnsensus Reporting Document (ACCORD) guidelines.

**Results**

South Asian service users were 12% more likely to uptake CR than White Europeans (aOR 1.12, 95% CI 1.09 to 1.15), but 22% less likely to complete (aOR 0.78, 95% CI 0.75 to 0.82) suggesting factors during the exercise and education phase of CR may be contributing to disengagement. The semi-structured interviews identified prominent operational, service and patient level barriers to CR participation. Participants agreed that communication barriers, programme suitability, social and cultural influences, and psychological and emotional factors influenced both initial engagement and continued adherence with CR. The NGT workshop demonstrated participants eagerness to engage with CR and a desire for an integrated community approach to raising its profile to enhance adherence. The top ranked solutions to 5 prominent barriers included: increasing CR knowledge among other healthcare professionals; providing transport assistance; promoting CR as an essential treatment pathway; providing simple, multilingual written information highlighting CR benefits; education about medications and their interactions with exercise

**Conclusions / Implications for practice**

Persistent inequalities hinder South Asian service users from CR participation. Findings from all phases were integrated to develop evidence-based, community-endorsed recommendations aimed at informing service delivery and policy. This study provides a model for culturally responsive intervention development and contributes to the broader goal of reducing health inequalities in cardiovascular care.

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# Mixed methods study comprising a randomised controlled trial (RCT) with embedded qualitative component to explore the effectiveness and acceptability of face-to-face rehabilitation for patients with Long Covid who were not hospitalised with their acute infection

Kate Kontou | LHIIP

**Background**

Long Covid is a term used to describe a multi-system condition that presents with a myriad of physical and psychological symptoms that continue or develop after acute COVID-19 infection(1). Long Covid is a significant public health problem because of the nature of the illness, it's negative impact on everyday functioning and work, and the healthcare inequalities evident in access and experience, notably in terms of ethnicity and socioeconomic status (2, 3).

There is equipoise about the benefits and harms of exercise-based rehabilitation in this community. Evidence in patients hospitalised with their acute infection suggests exercise-based rehabilitation can improve exercise tolerance, respiratory symptoms, fatigue, and cognition (4). However, research is needed to determine whether exercise-based rehabilitation is effective and acceptable for patients with Long Covid who were not hospitalised.

**Aims / Objectives**

he primary objective of this study is to determine whether face-to-face rehabilitation increases exercise tolerance compared to usual care alone in non-hospitalised patients with Long Covid. Secondary objectives include:

- Determining the acceptability of the intervention through seeking to understand patients' perceptions of the barriers and facilitators
- Exploring the effectiveness on other symptoms commonly associated with Long Covid to include fatigue, breathlessness, reduced physical activity, health related quality of life (HRQoL), anxiety, depression and pain.
- Using a healthcare inequalities lens to explore which demographic groups may be under-represented within Long Covid rehabilitation, with the qualitative work expanding on why this may be the case.

**Methods**

A mixed methods enquiry has been employed to ensure there is an equal focus on outcomes and experiences.

For the RCT, patients will be randomised to either the intervention or control group (1:1) via a computerised randomisation system.

Individuals in the intervention group will complete an individualised symptom-titrated programme of exercise and self-management education twice/week for 6 weeks. The supervised exercise component comprises of aerobic (walking and cycling) and resistance training (upper and lower limbs). Exercise intensity and duration will be tailored to the individual's current abilities, and symptoms monitored to guide progression. In addition, patients will be asked to perform home-based exercise to include: daily walking, three aerobic exercise sessions and one resistance exercise session each week. Each rehabilitation session includes an educational discussion (approx. 30–60 min) delivered by a member of the multidisciplinary team.

Participants in the control arm will receive usual care for 6 weeks. Routine clinical care will continue such as medical follow-up, mental health service provision and other specialist services.

An Acceptability Framework (5) has been used to inform the topic guides for both qualitative components. Interviews will be conducted with those who decline or drop-out to explore the barriers to attendance. Completers in the intervention group will be invited to take part in a focus group to explore the facilitators to attendance. The data gathered from qualitative components will be used to explore any healthcare inequalities that may be evident.

**Implications**

This study will provide guidance for services delivering Long Covid Rehabilitation. The findings may also be transferrable to help inform the development of effective rehabilitation programmes in other long-term health conditions.

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## Solving the antibody crisis: A novel LC-MS/MS-optimised procedure for the in-situ, label-free characterisation of antibodies

Alfred Charlesworth | BRC

**Background**

The current antibody market includes over six million available antibodies for uses in quantification, detection, enrichment and/or perturbation of a target protein. Despite this, it is estimated that *approx.* 50% of commercial antibodies do not meet basic standards for characterisation, with many of these defective antibodies being found in published studies. Binding characterisation of antibodies is typically done using labelling techniques (e.g.,ELISA) that signal substrate binding, or in vitro with optical sensors (e.g., SPR) that study binding in environments outside of those to be used. Immunoprecipitation and capture-based workflows are becoming increasingly common in clinical mass spectrometry (e.g., SISCAPA). We therefore developed a simple, depletion-based LC-MS/MS workflow that monitored the loss of SARS-CoV-2 nucleocapsid (NCAP) peptides in the addition of SISCAPA antibodies. Calculating the bound proportion, we successfully determined antibody saturation, rate kinetics, and selectivity between polyclonal and monoclonal antibodies in a method that can be easily used to discern in situ binding characteristics. Quantifying binding characteristics also allows for optimisation of workflows and limits the quantities of costly antibodies needed.

**Aims / Objectives**

We sought to develop a new method by which binding kinetics between antibodies and COVID peptides could be measured, with the intention of carrying this method over to validate antibody binding specificity for laboratory and commercial use. This method should be repeatable and applicable to any laboratory with a LC-MS/MS.

**Methodology and Main Body**

Monoclonal (MAb) and a polyclonal (PAb) SISCAPA antibodies for SARS-CoV-2 NCAP peptides (AYN, DGI, and ADE) were tested in a series of depletion experiments to characterise binding. Saturation was investigated by incubating 5 µL of either peptide at a variable concentration (0.05 to 2500 fmol/µL) with 5 µL of respective SISCAPA MAb or PAb (0.05 – 0.25 µg/µL) and 15 µL ammonium acetate (pH 8.5) for 30 minutes at room temperature. SISCAPA Abs were removed using a magnetic array, before the unbound fraction was analysed on a Waters Xevo TQ-XS. Triplicate, Ab-free controls were analysed in parallel to allow for calculation of total bound peptide. Empirical adsorption isotherms describe the binding relationship as discrete (homogenous surface/finite sites) or continuous (heterogenous, infinite sites). Utilising Langmuir (discrete) and Freundlich (continuous) models to account for heterogeneity and number of binding sites. Scatchard plots based on bi-Langmuir are often utilised first to visualise the heterogeneity present in the binding process.

Adsorption was investigated similarly, but by maintaining a constant amount of peptide and antibody during incubation, while incubating at various time intervals (0-30 mins). First-order and second order kinetic models were used to describe the rate of binding. Selectivity was investigated by incubating each Ab with non-target viral peptides (*e.g.,* AYN-MAb with ADE).

**Results**

Results indicate that the Langmuir model provides a better fit for AYN and DGI monoclonal antibodies (MAbs), whereas the Freundlich model is more suitable for polyclonal antibodies (PAbs). The saturation capacity (BMax) was variable across the antibodies, MAb- AYN 26997 fmol/µg, MAb DGI 18080 fmol/µg, and MAb ADE 10034 fmol/µg. There was also variability between PAbs Bmax, PAb DGI 3115 fmol/ µg and PAb ADE 7361 fmol/ µg, indicating lower specific binding compared to MAbs. First-order kinetics were observed for AYN and ADE MAbs. Association rate constant (K) for MAb AYN was 13.03, whereas it was much lower for ADE (3.63) and DGI (5.25), dissociation constant (tau) for MAb AYN was lower (0.07) compared to ADE (0.27) and DGI (0.19). Second-order kinetics

are favoured by AYN and DGI PAbs, affinty was higher for AYN PAb (4.63) compared to ADE (2.77) and DGI (1.26) As expected, PAb- AYN dissociation was lower (0.21) compared to ADE (0.36) and DGI (0.79).Selectivity experiments showed high specificity of DGI and ADE peptides for their corresponding MABs, while AYN exhibits selectivity for both AYN and DGI antibodies. However, overall PAb selectivity is lower, with only the DGI peptide showing selectivity for its respective antibody. Quantifying binding characteristics allows for optimisation of workflows and limits the quantities of costly antibodies needed.

**Conclusions / Implications for practice**

Using mass spectrometry, we developed a novel, label free method by which the binding characteristics of Ab could be elucidated using LC-MS/MS, this method is repeatable and could be applied to other antibodies including those used for immunoprecipitation assays for mass spectrometry. This method provides an *in-situ* view of binding, without having to rely on other detection systems such as ELISA or SPR.

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## Use of Oxford Nanopore Technology liquid biopsy workflows for early cancer detection, tissue-of-origin prediction and personalising cancer treatment

Eleanor Massey | BRC

**Background**

Liquid biopsy workflows utilising circulating free DNA (cfDNA) have the potential to enable minimally invasive detection of early-stage cancer. Oxford Nanopore technology could assist in this detection by enabling comprehensive profiling of aberrant DNA methylation detected in a single sequence run enabling the identification of novel biomarkers. However, the identification of robust epigenetic biomarkers from high dimensional and complex data is considered the major challenge.

**Aims / Objectives**

The aims of this project are to develop machine learning workflows that can aid in the accurate detection and classification of cancer samples and healthy samples through epigenetic profiles in liquid biopsy samples; to ensure biological relevance of the identified biomarkers from these workflows and to assess the overall applicability and generalisability of these models in additional tasks such as tissue of origin prediction.

**Methodology and Main Body**

To achieve the aims a variety of ML-based methodologies were trained and evaluated for the classification of cancer and normal samples based on primary tissue and cfDNA methylation profiles. In addition, feature selection techniques using publicly available data (TCGA-BRCA) were utilised to determine the best combination of processes that will achieve the optimal performance metrics and biologically relevant selections. All potentially successful models and biomarkers were validated across different datasets to ensure generalisability. Successful models will be evaluated to determine if biomarkers can be applied in differing tasks such as tissue of origin prediction as well as tumour detection.

**Results**

Initial ML-modelling utilised the TCGA-BRCA dataset and feature selection techniques were compared to determine the best model. This was achieved through the application of a variety of supervised learning methods to determine the effects on performance metrics when classifying 726 tumour stage and subtype against 94 normal samples. Results indicated the best performing model was the combinatory power of Elastic Net feature selection, correlation analysis to identify wider selection of features, and Support Vector Machine for classification. This achieved an accuracy between 86-95% for binary classification tasks of normal samples and differing stages of breast cancer, whilst also maintaining high recall sensitivity scores (86-93%). These results are currently in the process of validation to determine the generalisability and robustness of the 18 chosen biomarkers out of 354,667 probes within the larger METABRIC breast cancer dataset.

Beyond binary classifications, the potential influence of immune infiltration on the predictive power of ML models was investigated by comparing differing deconvolution techniques and cell-specific reference methylation profiles to determine whether noise from different cell-types would have a significant effect on a model's ability to categorise samples as tumour or normal. This was achieved through categorising samples as pure/impure based on thresholding CD4 and CD8 infiltration and comparing the performance metrics of an optimised SVM model. Overall, no significant changes were observed, suggesting cell specific noise would not significantly affect the predictive power.

Going forward, complex modelling using Convolution Neural Network may potentially have a high capability of handling complex and highly dimensional data in comparison to SVMs when analysing Oxford Nanopore methylation data. However, the same process of investigation as initial modelling is being adhered to.

**Results**

Initial ML-modelling utilised the TCGA-BRCA dataset and feature selection techniques were compared to determine the best model. This was achieved through the application of a variety of supervised learning methods to determine the effects on performance metrics when classifying 726 tumour stage and subtype against 94 normal samples. Results indicated the best performing model was the combinatory power of Elastic Net feature selection, correlation analysis to identify wider selection of features, and Support Vector Machine for classification. This achieved an accuracy between 86-95% for binary classification tasks of normal samples and differing stages of breast cancer, whilst also maintaining high recall sensitivity scores (86-93%). These results are currently in the process of validation to determine the generalisability and robustness of the 18 chosen biomarkers out of 354,667 probes within the larger METABRIC breast cancer dataset.

Beyond binary classifications, the potential influence of immune infiltration on the predictive power of ML models was investigated by comparing differing deconvolution techniques and cell-specific reference methylation profiles to determine whether noise from different cell-types would have a significant effect on a model's ability to categorise samples as tumour or normal. This was achieved through categorising samples as pure/impure based on thresholding CD4 and CD8 infiltration and comparing the performance metrics of an optimised SVM model. Overall, no significant changes were observed, suggesting cell specific noise would not significantly affect the predictive power.

Going forward, complex modelling using Convolution Neural Network may potentially have a high capability of handling complex and highly dimensional data in comparison to SVMs when analysing Oxford Nanopore methylation data. However, the same process of investigation as initial modelling is being adhered to.

**Conclusions / Implications for practice**

The current results demonstrate the potential for utilising ML workflows alongside liquid biopsy and ONT sequencing for the detection of robust biomarkers. By optimising and refining these workflows they could be utilised in early cancer detection in a less-invasive manner to improve the high false positive/negative rate of mammograms as well as potentially improving cancer classifications and tumour of origin predictions using comprehensive profiles with powerful ML workflows.

## Modelling Metabolic Dysregulation to Assess Colorectal Cancer Prevention Strategies

Eve Jarman | BRC

**Background**

Colorectal cancer remains a significant global health challenge and is the second leading cause of cancer death (1). The COLO-PREVENT trial platform investigates preventive interventions in high-risk individuals identified through bowel cancer screening, focusing on aspirin, metformin, and resveratrol. Given the high prevalence of overweight and obesity in similar screening populations, metabolic dysregulation may influence the efficacy of these interventions (2). This study aims to investigate the impact of dietary patterns and metabolic status on the growth of pre-malignant colorectal cells and their interaction with COLO-PREVENT therapies.

**Aim**

To investigate the impact of metabolic dysregulation, specifically alterations in lipid metabolism, on the efficacy of preventive therapies for colorectal adenocarcinoma.

**Objectives**

To determine the effects of preventive therapies; Resveratrol, Metformin, and Aspirin on an immortalised colonic tubular adenoma cell line.
To create a model of metabolic dysregulation using palmitic acid and oleic acid, and determine physiologically relevant concentrations.

**Methodology and Main Body**

An *in-vitro* model was developed using the AA/C1/SB10C cell line, a non-tumorigenic immortalised cell line derived from a colonic tubular adenoma, to assess the effects of preventive therapies and lipids on cell viability. Cell viability was assessed using MTT assays following exposure to aspirin, metformin, and resveratrol, both individually and in combination to evaluate the impact and combination therapies at varying concentrations. An *in-vitro* model of metabolic dysregulation was created using palmitic acid (PA) and oleic acid (OA) to mimic the lipid imbalances observed in obesity and related metabolic disorders. Cytotoxicity, free fatty acid levels, reactive oxygen species (ROS) production, and morphological changes were measured. Furthermore, the effect of the drugs on cell viability was tested, and IC50s of PA and OA were calculated based on logarithmic dose-response curves.

**Results**

Initial results indicated that clinically achievable concentrations of COLO-PREVENT therapies increased cytotoxicity under normal culture conditions. After 72 hours, single agents, particularly 1 µM aspirin, significantly reduced cell viability ($p \leq 0.05$). Low-dose combinations further enhanced cytotoxicity, with 0.5 µM aspirin and 0.005 µM resveratrol increasing cytotoxicity to 37%, while 0.625 µM metformin and 0.0005 µM resveratrol increased cytotoxicity to 65% compared to the control.
Exposure to PA and OA, mimicking high fat intake, revealed enhanced cytotoxicity with PA, while OA had a weak proliferative effect. High concentrations of PA (1mM), quickly and significantly reduced cell viability, with an IC50 of 935.5 µM and an IC30 of 870.75 µM. OA exhibited weak proliferative activity across most tested concentrations.

**Conclusions / Implications for practice**

Metabolic dysregulation appears to influence the growth of colorectal adenomas and modulate the efficacy of preventive therapies. The tested drugs had greater activity when combined than alone. Low concentrations of aspirin and resveratrol increased cytotoxicity by 37%, while metformin and resveratrol achieved 65% cytotoxicity. Further studies are warranted to investigate mechanisms underlying potential interactions and how this might influence precision prevention within the COLO-PREVENT framework. Future work will extend these drug studies with the model of metabolic

dysregulation and then into primary organoid cultures of human colorectal polyps and patient-derived explants to provide a more complete microenvironment alongside the model.

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## ctDNA meets Patient Derived Explant; Developing ctDNA predictive biomarkers for OX40 using PDE meta data

Emmanuella Batu | BRC

**Background**

Breast cancer (BCa) is a heterogenous disease and many patients still lack effective treatment options (1), highlighting need for novel therapeutic approaches. The αOX40 agonist is a novel anti-cancer agent that enhances T cell proliferation, survival and cytokine production, boosting the immune system to attack tumours (2).

Accurate prediction of immunotherapy responses requires preclinical models with intact immune microenvironments, but most existing models fails to recapitulate this, leading an incomplete assessment of drug efficacy (3).

Breast Cancer Patient-Derived Explants (BC-PDEs) represents a physiologically relevant ex-vivo model that maintain the tumour-stromal and immune landscape. PDEs have been shown to be predictive of patient outcomes to standard of care therapeutics, giving confidence they can be used to assess novel anti-cancer agents.

**Aims**

To generate phenotype-genotype correlations between αOX40- treated BC-PDEs, Whole Exome Sequencing (WES), and multiplex immunofluorescence parameters, to create a novel predictive circulating tumour DNA (ctDNA) panel to guide rationale design of a stratified clinical trial.

**Methodology**

BC-PDEs were derived from 49 patients, treated with α-OX40 at 3 concentrations (1ug/ml, 10ug/ml, and 100ug/ml) for 24 hours, formalin fixed and FFPE sections stained with markers for proliferation (Ki67), apoptosis (CPARP), tumour cells (cytokeratinAE1/AE3). Slides were digitised using an Akoya Biosciences PhenoImagerHT, and analysed using digital pathology solutions to generate drug performance data. Drug performance data was correlated with matched WES data to identify novel predictive markers of drug efficacy.

**Results**

α-OX40 (1ug/ml and 100ug/ml) significantly induced apoptosis with a range of responses, although no dose-response was observed across three viability parameters: apoptosis, necrosis and proliferation. Unsupervised hierarchical clustering was used to classify patient samples as α-OX40 sensitive (14) or resistant (35), which demonstrate 29% of breast cancers were susceptible to α-OX40-induced tumour cell killing. An unbiased Fisher's Exact Test across the whole exome, identified 223 genes with significant copy number variations (CNV) genes associated with treatment response. Pathway enrichment analysis identified key genes in defensins-related pathways, implicated in modulating immune response.

**Conclusions**

BC- PDEs are a robust patient-relevant preclinical model that can be used to evaluate immunotherapy responses ex-vivo, due to maintenance of the immune microenvironment. Notably, pharmacologically-relevant α-OX40 concentrations (1ug/ml and 100ug/ml) induced marked tumour cell death in 29% of patient samples. Furthermore, integration of genomic profiling identified novel breast cancer CNVs involved in modulating the tumour microenvironment, conferring resistance/sensitivity to α-OX40 insult. These findings support the use of PDEs in translational research to inform personalised immunotherapy strategies and improve rationale design of stratified clinical trials.

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# STUDENT POSTER ABSTRACTS

## Ethnic differences in healthcare utilisation and diagnosis after first presentation with breathlessness: an epidemiological study using UK primary care records

Harini Willis | LHIIP

**Background**

Previous studies have shown that people of non-white ethnicity are more likely to report experiencing breathlessness. However, the influence of ethnicity on the healthcare pathway after presentation with breathlessness is unknown.

**Aims / Objectives**

To investigate the influence of ethnicity on the healthcare pathway after a coded first presentation with breathlessness in primary care records, including incidence rates of primary care consultations, outpatient referrals into secondary care, hospital admissions, and receipt of coded explanatory diagnosis.

**Methodology and Main Body**

Clinical Practice Research Datalink (CPRD) GOLD data linked to hospital episode statistics (HES) and death registries were used to identify adults with a first-recorded code for breathlessness (index date) presenting between 2007 and 2017. Rates of primary care consultations, secondary care referrals and hospital admissions within six and 24 months after index date were examined using negative binomial regression. Logistic regression was used to estimate odds of receiving an explanatory recorded diagnosis for breathlessness during these timeframes. Models were adjusted for age, sex, socioeconomic status and presence of ≥2 long-term conditions.

**Results**

Amongst 88,857 patients identified, 3,336 (3.8%) were of South Asian and 1,506 (2.7%) of Black ethnicities. Patients of South Asian and Black ethnicities were significantly younger compared to patients of White ethnicity (median age 47, 48 and 61 years respectively). Patients of South Asian ethnicity had significantly higher incidence rate ratios (IRR) of primary care consultations in all models (24-month IRR 1.13 95% CI 1.10 - 1.16) and non-urgent referrals into secondary care within 24 months from index date (IRR 1.10 95% CI 1.05 - 1.14), compared to White ethnicity. Conversely, patients of Black ethnicity had significantly lower IRR of primary care consultations within 24 months from index date (IRR 0.95 95% CI 0.92 - 0.99), compared to patients of White ethnicity. However, in all models both groups had significantly higher IRR of all-cause unplanned hospital admissions (South Asian 24-month IRR 1.34 95% CI 1.25 - 1.45; Black 24-month IRR 1.33 95% CI 1.19 - 1.49) and significantly lower odds of receiving an explanatory diagnosis for breathlessness (South Asian 24-month OR 0.82 95% CI 0.77 - 0.89); Black 24-month OR 0.78 95% CI 0.70 - 0.87), compared to patients of White ethnicity.

**Conclusions / Implications for practice**

We observed significant ethnicity-based differences in healthcare utilisation and receipt of an explanatory diagnosis following presentation with breathlessness. Further qualitative work is planned to explore the underlying factors contributing to these differences, including in symptom perception, relevant health behaviours, healthcare professionals' perspectives, and experiences of healthcare received after presentation with breathlessness.

## Characterizing potential exposure triggers in people of South Asian ethnicity diagnosed with Hypersensitivity Pneumonitis (HP)

Gunjan Rajes Jaiaprasat| BRC

**Background**

Hypersensitivity Pneumonitis (HP) is a type of Interstitial Lung Disease (ILD) characterised by a disproportionate inflammatory response of the lung parenchyma due to inhaled environmental antigens (Hamblin, Prosch and Vašáková, 2022). Where there is persistent antigen exposure, this inflammation can lead to irreversible lung fibrosis (De García Alba *et al.,* 2015). ~50% of HP cases are cryptogenic, i.e. the specific trigger is unknown (Walters *et al.,* 2019). This study explores potential HP triggers within the South Asian community in Leicester, where there is high prevalence of chronic cryptogenic HP, disproportionately affecting women.

**Aims / Objectives**

To identify and evaluate potential HP triggers in the inhalational environments of individuals of South Asian ethnicity with chronic HP, with a focus on those likely to be increased in this demographic due to specific cultural practices.

**Methodology and Main Body**

I have used initial community engagement (Patient and Public Involvement and Engagement, PPIE) strategies with focus group discussions involving community members. These have identified potential triggers for which the South Asian population would tend to have enhanced inhalational exposure, e.g. burning incense sticks, specific cooking practices involving the use of ghee (clarified butter), textile work. Survey findings defined commonly used brands and fragrances of incense sticks and candles, as well as types of ghee and traditional oil lamps (diyas). We are now assessing these products for particulate matter (PM) and volatile organic compound (VOC) emissions using a controlled chamber. Real-time PM emissions will be analysed using an Optical Density Sizer (OPS) and the VOCs will be collected on sorbent tubes for analysis. Further environmental sampling of PM and VOCs is planned for the homes of South Asian individuals in Leicester to assess real-world exposure levels and correlate with the emissions profiles identified in the laboratory.

**Conclusions / Implications for practice**

This community-informed research will enhance our understanding of the specific environmental triggers of HP within South Asian populations in Leicester. This study aims to contribute to culturally informed identification and prevention strategies of the triggers by linking prevalent product use with their emission characteristics and real-world exposure levels. Future steps include correlating environmental finding with clinical data and exploring patient perspectives for better respiratory health outcomes.

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# The effect of lifestyle activity and pulmonary rehabilitation on chronic systemic inflammation in individuals with Chronic Obstructive Pulmonary disease (COPD) of different ethnicities: A Study Proposal

Hannah Polak | LHIIP

**Background**

Chronic obstructive pulmonary disease (COPD) is an inflammatory airway disease characterised by persistent symptoms and largely irreversible airflow limitation. In addition to localised airway inflammation, COPD is associated with chronic systemic inflammation with adverse consequences for the cardiovascular, metabolic, and neuromuscular systems.

Elevated levels of systemic inflammation markers are associated with increased risk of comorbidities and mortality in COPD (1). Therefore, interventions that reduce systemic inflammation in individuals with COPD may have the potential to delay disease progression, reduce the risk of comorbidity onset or development, and provide mortality protection.

In healthy individuals, physical activity and exercise are known to reduce markers of chronic systemic inflammation and inflammatory responses by provoking the release of pro-and anti-inflammatory cytokines (2, 3).

There is limited data on the effect of a single bout of exercise/exercise training on inflammatory markers in individuals with COPD, who typically display sedentary behaviour.

There is no data to determine if ethnicity impacts upon acute or chronic exercise responses. The South Asian (SA) ethnicity is associated with higher markers of chronic inflammation, independent of other inflammatory risk factors (4, 5) as well as increased risk of comorbidities.

**Aims / Objectives**

1. Determine the effect of an acute bout of exercise on circulating markers of chronic systemic inflammation in individuals with COPD of SA and White European (WE) ethnicities.
2. Determine the effect of participation in a pulmonary rehabilitation (PR) programme (i.e. exercise training) on circulating markers of chronic systemic inflammation in individuals with COPD of SA and WE ethnicities.

**Methodology and Main Body**

Forty-four individuals with a diagnosis of COPD who are eligible for PR will be recruited and divided into two groups based on ethnicity: WE and SA. Participants will attend three study visits before and after a 6-week PR programme. Baseline questionnaires and physiological measurements will be completed during the first visit. A ramp-incremental exercise test will be conducted at visit two to assess peak oxygen uptake, enabling prescription of a heavy-intensity exercise bout. This bout, completed on the third visit, will be ergometer-based. Blood samples will be drawn at rest, immediately after, and 45- and 90-minutes post-exercise to assess inflammatory biomarker levels. Samples will be analysed using Enzyme-Linked Immunosorbent Assay (ELISA) to determine biomarker concentrations. The primary outcome is the change in IL-6 concentration after an acute bout of heavy-intensity exercise following PR. Secondary outcomes include changes in CRP, white cell count (including eosinophils), fibrinogen, IL-5, IL-8, IL-10, IL-33, and TNFα.

A repeated measures ANOVA will assess within-subject changes over time and between-group differences.

**Discussion / Potential implications for practice**

The future of COPD treatment lies in a more targeted approach, informed by biological insights alongside phenotypic and endotypic characteristics (6). It is hoped that the results of this study will contribute to a deeper understanding of the heterogeneous inflammatory pathways involved in COPD, as well as the potential anti-inflammatory effects of lifestyle activity and pulmonary rehabilitation. Importantly, the proposed study design may also provide evidence supporting the effectiveness of pulmonary rehabilitation specifically within the SA COPD population, addressing a gap in current research.

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## Evaluating the Cardiovascular Effects of Multiple Environmental Exposures

Kritika Anand | BRC

**Background**

Urban environmental exposures - temperature, noise, air pollution, and green space (TANG), have been known to affect development and exacerbation of non-communicable diseases. However, their interactions are complex and inconsistently assessed impacting comparability across epidemiological studies. Most existing research focuses on individual exposures, with limited consideration of their joint effects, especially in settings with varying socio-economic and environmental conditions. There is a paucity of studies in the United Kingdom (UK) and lower middle-income countries such as India, examining the health effects of simultaneous exposure to urban environmental stressors. Rising pollen counts linked to climate change and urban landscaping have led to increased symptom severity and hospitalisations, especially among patients with asthma or chronic respiratory conditions. Furthermore, these exposures are often spatially correlated and disproportionately burden disadvantaged communities.

By conducting a comparative analysis between Delhi, India, and Leicester, UK, this project will contribute to methodological advancements in co-exposure research and provide insights on health impacts of urban environmental exposures in different socio-economic and geographical settings. This project aims to address these gaps by leveraging high-resolution exposure datasets, population-based cohorts, and appropriate statistical techniques for analysing the effects of TANG.

**Methodology and Main Body**

The study will be based on two large population-based cohorts – the Centre for Cardiometabolic Risk Reduction in South Asia (CARRS) cohort in India and Extended Cohort for e-health, Environment and DNA (EXCEED) cohort in Leicester, comprising of approximately 10,000 participants. Environmental exposures will be estimated at residential addresses of the participants using from high resolution spatiotemporal models for air pollutants ($PM_{2.5}$, $NO_2$, $O_3$), noise (UK only) and temperature. In Delhi, land use regression model will be developed to estimate noise exposure. Greenspace exposure will be measured using normalized difference vegetation index (NDVI) within 500m buffer around the residences. Socio-economic status (SES) will be assessed at both individual (income, education) and neighbourhood levels (deprivation index). Health outcomes include the incidence of cardiometabolic diseases (hypertension, diabetes or hypercholesteremia).

**Analysis**

We will first review the literature to examine methodological approaches to co-exposures analysis in environmental health research, focusing on interactions, theoretical and mechanistic underpinnings, statistical considerations, and implications for interpreting health associations. The statistical methods will be guided by a literature review focusing on models that can handle repeated measures, multiple correlated exposures and non-linear interactions. A longitudinal analysis will be conducted to explore how SES modifies the cumulative effect of urban environmental exposures on risk of developing cardiometabolic diseases. Additionally, a times series analysis will be performed to assess the interaction between pollen, air pollution and temperature on the risk of hospital admissions among individuals with respiratory illnesses.

**Conclusions / Implications for practice**

Our study improves understanding of environmental determinants for improving patient care, recovery, and clinical outcomes. While most studies conducted in the past have isolated these exposure effects, our approach offers realistic insights into their contributions on health in varied geographical contexts and exposure profiles. We will also highlight how upstream determinants of population health such as environmental exposures intersect with social inequalities.

## The impact of cooking-related household air pollution on the risk of lung cancer in non-smoking women of different ethnicities

Bría McAllister | LHIIP

**Background**

Lung cancer is increasingly being diagnosed in the non-smoking population, with mounting evidence that women of Asian ethnicity are at greater risk. Exposure to cooking fumes has been identified as a driving factor, however the majority of studies have been carried out in low- and middle-income countries, with little exploration of the topic in high-income countries.
This project aims to actively explore how cooking practices affect air quality in household environments, with a focus on ethnicity and cultural practices.

**Aims / Objectives**

The aim of this project is to determine whether South Asian households are exposed to higher levels of cooking-related HAP compared to households of White British ethnicity, leaving them at a greater risk of non-smoking lung cancer.
Objectives:

- To characterise the indoor environment of participants' homes
- To evaluate the impact of ethnicity and cooking practices on household air pollution.

**Methodology and Main Body**

A systematic review of available literature was performed to explore the risks of lung cancer posed by HAP for never-smokers in high-income countries. The review returned only three papers, all exploring Chinese cooking practices in Taiwan and Hong Kong, and highlighted a lack of research in high-income economies in Europe, America and Australasia.
Twenty households have been recruited to the study within the Leicestershire area, with WB, and SA families equally represented among participants.
Kitchen air quality is monitored for pollutants including particulate matter (PM), VOCs and fungal spores using a combination of active and passive methods. Air sampling is conducted over a week, once in winter and once in summer to account for seasonal variation.
Participants complete a daily diary noting activities related to cooking, cleaning and ventilation. A home survey is completed noting structural features e.g., age and style of house, layout of living spaces, floor coverings and renovation work.
This study is ongoing, with the first round of data collection completed in January 2025, and the second round scheduled to begin in May '25. This data includes accurate, real time air quality measurements allowing for direct comparison with the daily activity diaries to assess the impact of cooking on kitchen air quality, as well as analysis of the impact of ethnicity and cultural practices on the quality of household air in non-smoking households.

**Results**

Initial findings have shown that while average 24hour exposure levels in kitchens are within WHO recommended exposure levels, all households regularly breach the WHO recommended exposure levels for $PM_{2.5}$ and $NO_2$ during cooking events, with SA households having higher overall exposures. Households of WB heritage are exposed to higher levels of Benzene, Toluene and Xylenes (BTX) than households of SA heritage. BTX are a group of VOCs strongly linked to respiratory disorders and cancers.

**Conclusions / Implications for practice**

To the best of our knowledge, this is the first UK study to explore how cooking practices affect the presence and concentrations of PM, VOCs and mould in kitchen environments, with a focus on ethnicity and cultural practices. It will provide valuable data on how cooking-related air pollution affects the risks of non-smoking lung cancer in a high-income country.

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## The impact of particulate pollutants on host-pathogen-commensal interaction

Angelica Aleksandar | BRC

**Background**

Air pollution is one of the world's most significant environmental and health issues, affecting nearly the entire human population. Outdoor air pollution comprises several components, one of the most well-researched and harmful being aerosolised liquid and solid particles known as particulate matter (PM). Exposure to PM and its inhalation cause damage to the respiratory tract and lungs through decreased ciliary beating, increased mucous production, increased disruption to the lung epithelial barrier, and increased cellular inflammation, among other immune responses. Damage caused comes with an increased risk of infection and possible subsequent exacerbations of respiratory diseases such as chronic obstructive pulmonary disease (COPD). However, not only does PM negatively impact the physical epithelial barrier, but it has also been shown to have a direct impact on the balance in abundance and diversity of naturally occurring 'good' (commensal) and 'bad' (pathogenic) bacteria in the respiratory tract. In some cases, this imbalance, or dysbiosis, can cause the lung state to shift from healthy to diseased. In a diseased lung state, there is a higher microbial density and lower microbial diversity, characterised by a disproportionate abundance of opportunistic pathogens, such as *Haemophilus influenzae* or , compared to commensals, including those of the *Streptococcus spp.*

**Aims & objectives**

Aim:

Investigate how pm could affect the balance of commensals and pathogens and how it impacts the host

Objectives:

- Establish how PM affects commensal behaviour
- Determine how PM affects bacteria-bacteria interaction
- Establish how PM affects commensal-host interaction using 2D and 3D models of colonisation

**Methodology and Main Body**

The work undertaken in my project utilised black carbon (BC) as a model of PM to study its effect on the growth and colonisation ability of various commensals and pathogens often found in the respiratory tract. Commensals studied were *Streptococcus mitis* and *Rothia mucilaginosa,* as well as the pathogen *Haemophilus influenzae.* The ability of colonisation was studied through adhesion with human epithelial cells and biofilm assays in BC. As well as this, previous work on NTHI375, a strain of non-typable *Haemophilus influenzae,* has shown an unexpected iron-starvation response to BC exposure. Therefore, several clinical isolates of NTHI were looked at for the differential gene expression of genes hitA, a periplasmic iron-binding protein; TonB, involved in the transport of heme into the cell; and ftnA, involved in iron storage**.**

**Results**

Growth of neither commensals nor any NTHI isolates was impacted by BC. However, s. Mitis showed a biofilm dose response when grown with BC, whereby less biofilm was formed at higher concentrations of BC. The same was seen with some NTHI isolates, but interestingly, not all isolates showed a dose response like NTHI375 did. In terms of epithelial adhesion, the adhesion of *S. mitis* was significantly increased when co-exposed to BC during the adhesion assay, whereas two different isolates of NTHI showed no significant increase in adhesion, unlike NTHI375, where the condition in which the bacteria had been pre-grown in BC had increased adhesion. Finally, differential gene expression of the previously mentioned genes when exposed to BC varied greatly between NTHI isolates, though the general pattern of upregulation in HitA and downregulation with TonB and FtnA was seen as with NTHI375.

**Conclusions / Implications for practice**

Although the negative impacts of PM have been studied and identified to impact the microbiome at almost any site in the body, the impact of PM on these commensals and pathogens in the microbiome is significantly understudied; therefore, my project aims to study this with a particular focus on how bacterial colonisation and virulence are altered.

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## Analysing properties of Patient Reported Outcomes Measures (PROMs) that measures breathlessness within respiratory diseases: A Systematic Review

Iridu Basnayake | BRC

**Background**

People with Respiratory diseases experience a variety of symptoms, with breathlessness being most commonly reported. Breathlessness is a debilitating multifactorial symptom that is complex in nature, making it difficult to assess, understand and treat. As an attempt to understand breathlessness, measurement and quantification tools have been developed. Among those tools, Patient Reported Outcome Measures (PROMs) have been found particularly useful. PROMs are tools or questionnaires that provides answers about a patient's health, quality of life, symptoms or functional abilities subjectively. These PROMs are used to assess patient reported breathlessness with variation to validity, reliability and sensitivity. Although, there is lack of agreement about which measurements are appropriate and widely accepted. Hence, it can be said that there is a requirement for a systematic review that will provide a detailed summary of the available PROMS on their validity, reliability and sensitivity.

**Aims / Objectives**

The aim of the study is to provide a detailed summary of breathlessness measurement tools validity, reliability and sensitivity. By providing this outline, the study will also help to identify the most appropriate and widely accepted PROMs that would encourage and promote standardised measurement practices when it comes to assessing breathlessness in research and healthcare settings.

**Methodology and Main Body**

Searches were conducted using medline, cochrane, embase and cinahl databases. The searches were conducted to identify studies that assessed the development or evaluation of measurement properties of tools that measured breathlessness in a variety of different diseases such as Chronic Obstructive Pulmonary Disease (COPD), asthma, Interstitial Lung Disease (ILD), bronchiectasis and Breathing Pattern Disorder (BPD). The eligibility criteria is as follows,

Inclusion criteria

1. Adults over the age of 18 years
2. Published literature that are full text
3. Assesses a prom designed to assess breathlessness
4. Assesses validity, reliability or sensitivity

Exclusion criteria

1. Non-respiratory conditions
2. Studies that do not include a PROM that measures breathlessness
3. Randomised Controlled Trials
4. Books chapters, conference abstracts and poster sessions

Once full text screening is completed, the data extraction will be performed using an excel form that was created adopting the JBI data extraction tool. Upon completing the data extraction, the COSMIN risk of bias tool will be used to assess for the quality of the data.

**Results**

In total there were n=2912 records initially identified from the 4 databases. n=1960 were identified after removing duplicates. Title and abstract screening were conducted where n=360 were included and n=1600 were excluded. Currently the systematic review is at the full text screening stage.

**Conclusions / Implications for practice**

The findings of this review will support clinicians in selecting the most appropriate tool that will help improve clinical decision making and patient care. It will also support researchers in selecting high quality tools that will enhance the credibility of the study findings.

## PRC2-DNMT1 as a synthetic lethal target in BAP1 inactivated mesotheliom.

Yue Lin | BRC

**Background**

Mesothelioma is a rare, lethal cancer originating from the lining of lungs, abdomen, or heart, which is mainly caused by asbestos. A lack of reliable predictive markers makes treatment stratification challenging, limiting therapeutic options and reducing patient survival. BRCA1-associated protein 1 (BAP1) has been revealed as the most commonly mutated tumour suppressor gene in mesothelioma. Investigating the downstream effects of BAP1 mutations might help identify therapeutic vulnerabilities in this aggressive disease.

Enhancer of Zeste homologue 2 (EZH2), which is the component of Polycomb Repressive Complex 2 (PRC2) and the methyltransferase of H3K27, may be synthetic lethal in BAP1 mesotheliomas [1,2,3], however inter-patient heterogeneity has been observed [2]. Additionally, EZH2 inactivation was observed synthetic lethal with DNMT1 inactivation, highlighting a vulnerability through DNMT1 [4]. Preliminary evidence suggests that DNMT1 inhibition indeed has a lethal genetic interaction with BAP1, but this has not been explored in mesothelioma, and the mechanisms likely to confer an exceptional response or resistance are unknown.

**Aims / Objectives**

This project aims to determine novel therapeutic targets in BAP1-inactivated mesothelioma.

**Methodology and Main Body**

To explore the in vivo transcriptomic modulation associated with BAP1 inactivation as a basis for novel drug target identification, Gene Set Enrichment Analysis (GSEA) was conducted in a large Leicester Mesothelioma cohort of surgically resected pleural mesotheliomas (MEDUSA), the tumour genome atlas and cell lines. In parallel, in vitro studies were performed by silencing BAP1 using siRNAs in patient-derived primary cell lines to investigate gene–gene interactions at the protein level.

To explore the inter-patient correlation of BAP1 and EZH2, patient derived mesothelioma explants (from our MEDUSA cohort) were treated with EZH2 inhibitor Tazemetostat. Genomic, transcriptomic and immune correlates of response are being explored to further refine biomarkers of sensitivity as a basis to optimising precision therapy.

**Results**

Results revealed that BAP1 inactivation enhanced polycomb repressor complex 2 (PRC2) mediated histone marks (H3K27me3) evidenced by its upregulated transcriptional signature, which is mediated by EZH2. Furthermore, BAP1 loss correlates with the downregulation of DNA methyltransferase I (DNMT1), suggesting a potential combinatorial vulnerability to DNMT1 inhibitors.

**Conclusions / Implications for practice**

PRC2-DNMT1 axis could present a synthetic lethal vulnerability to BAP1 inactivated mesothelioma, and further investigations are underway to confirm its therapeutic potential to confirm a robust actionable interaction. The outcomes of the project are expected to catalyse an industrial collaboration to underpin the execution of a phase II trial, and contribute to the development of personalised treatment for mesothelioma patients.

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## Development of an *in vitro* culture system to study the lung microcosm in airway diseases

Miles Oke | BRC

**Background**

The project and associated work detailed in this abstract is funded by the Leicester National Institute of Health and Care Research (NIHR) Biomedical Research Centre (BRC).

Chronic respiratory diseases (CRDs) are the third leading cause of death globally, responsible for approximately 4 million deaths in 2019 (GBD 2019 Chronic Respiratory Diseases Collaborators, 2019). Across England one in five people are affected by CRDs, with lung cancer, pneumonia, and chronic obstructive pulmonary disease (COPD) being the biggest causes of death (NHS England, 2025). The combined annual economic burden of asthma and COPD on the NHS is estimated at almost £5 billion. The lung microbiome is home to a diverse ecosystem of microbes and their communities, constantly alternating between states of low microbial presence and resilient microbial colonization, representing a unique, dynamic system (Natalini, et. al., 2022). Lung ecology has been linked with CRDs and the wide range of pathophysiological mechanisms they encompass, highlighting the importance of microbial ecology in disease development. Though tremendous advances have been made in discovering differentially abundant species in disease, there remains a vague understanding of the link between microbial ecology, microbiome assembly, and disease pathophysiology. Currently, there is a lack of model systems that allow testing of microbial ecology and the extent to which they contribute to disease. This gap in insight represents a major barrier in being able to translate discoveries to applicable microbiome-based interventions for improved health outcomes. By developing a model system to study the lung microcosm in airway diseases, we hope to address this gap to identify disease-specific niches and characterise microbial interactions to understand the roles they play in CRDs and develop potential microbiome-based interventions such as bacteriophage therapy.

**Aims / Objectives**

1. Characterise complex interactions of microbes and viruses within the lung microcosm.
2. Gain mechanistic insight about the role of the lung microbiome as a driver of chronic airway diseases and their exacerbations.
3. Identify microbiome-based interventions to improve health outcomes.

**Methodology and Main Body**

To study the lung ecology, we have chosen bacterial species relevant in CRDs with a focus on COPD. We aim to understand the growth kinetics of these species in general growth medium and artificial sputum medium (ASM). The monoculture data will inform our ability to co-culture species, increasing the number of different species together, to examine interspecies dynamics and understand how these interactions shape wider microbial communities. Data will also be used in mathematical modelling to describe these interactions to a further extent in whole artificial microbial communities. We also plan to study the effect of bacteriophages on microbial communities, introducing phage specific to the community and observing downstream effects on the community. In developing the model system, we will adapt the methodology originally published by Robert Quinn, et. al., in 2014 using Winogradsky columns (Quinn, et. al., 2014). The columns are scaled down to 1 mm diameter glass capillary tubes, mimicking the diameter of the bronchiole, and would be inoculated with monocultures and co-cultures in ASM. The resulting system (termed WinSCosms) would be useful in studying the spatial effect on growth dynamics of species and communities in an environment analogous to the lung microcosm.

**Results**

**Growth kinetics of species**

Bacterial species relevant in COPD were chosen to be used, namely a laboratory strain of *Klebsiella pneumonia (K. pneumoniae)* - ATCC 13883, a strain of *Staphylococcus aureus* (*S. aureus)* isolated from blood – LEI0011 – and an environmental strain of *Pseudomonas aeruginosa* (*P. aeruginosa)* -

UCL1. To determine the growth kinetics of these species, they were grown in brain heart infusion (BHI) broth as a general growth medium suitable for all three species. Optical density (OD) at 600 nm was measured over 72 hours using a spectrophotometer, with measurements taken every hour for the first eight hours and at 12, 24, 36, 48 and 72 hours.

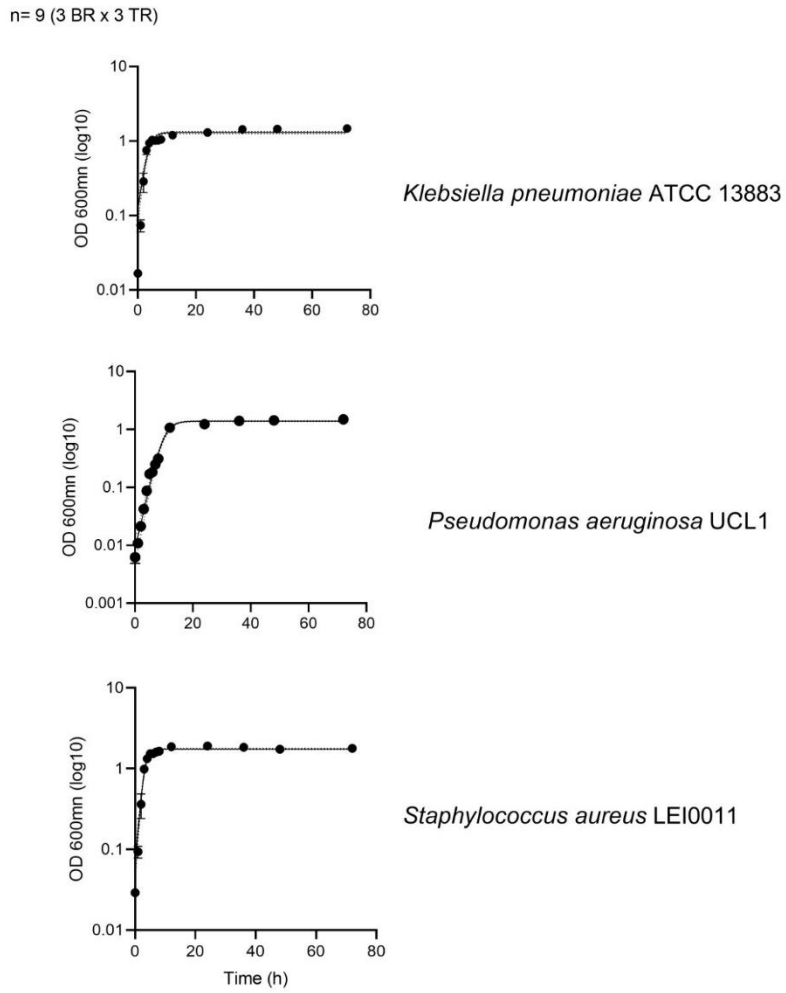


**Figure 1 –** Growth curves of *Klebsiella pneumoniae* strain ATCC 13883, *Pseudomonas aeruginosa* strain UCL1, and *Staphylococcus aureus* strain LEI0011 in BHI broth over 72 hours. Non-linear regression of mean OD at 600nm of nine replicates (three biological replicates with three technical replicates each) is plotted, with 95% confidence interval bands around the curve and error bars plotted. OD is plotted on a log base 10 scale.

To determine the growth parameters of these species, the OD data was inputted into 'Dashing Growth Curves', an online open-source web application for the analysis of microbial growth curves (Reiter and Vorholt, 2024). From OD, several growth parameters were calculated: maximum growth rate, lag time, doubling time, doublings (the number of doublings from lowest to highest measured population size), yield (maximum OD), and doublings in log-phase. A two-way ANOVA analysis was carried out followed by Tukey's multiple comparison in GraphPad Prism to determine if there was a significant difference across growth parameters between any two of the species at a time (GraphPad, 2025).

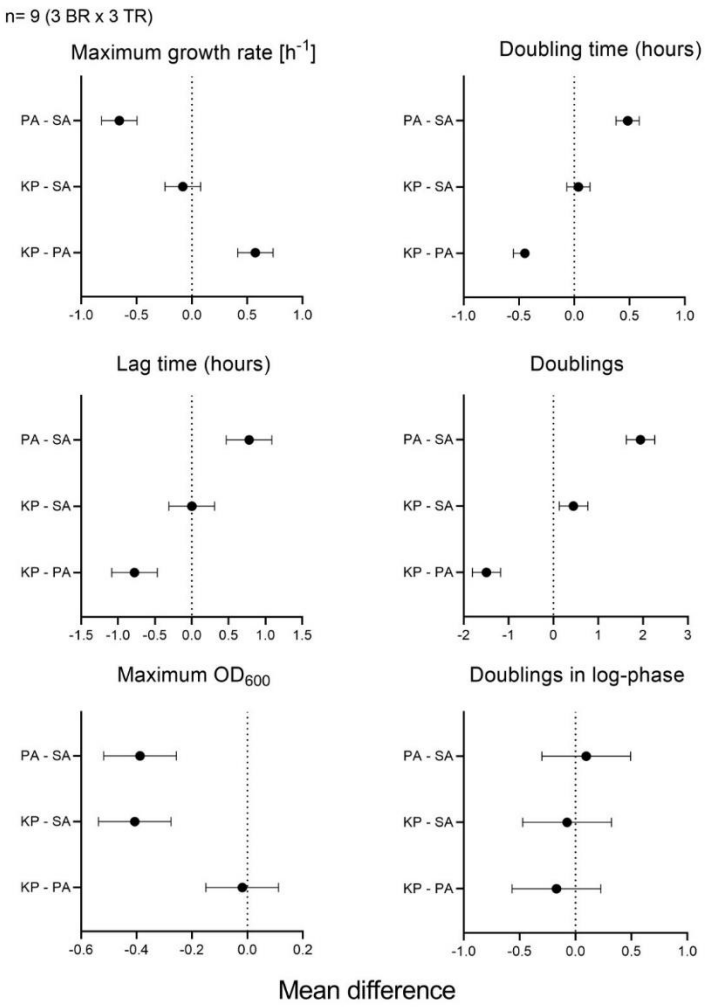


**Figure 2 –** Mean difference of growth parameters between *K. pneumoniae* ATCC 13883 (KP), *S. aureus* LEI0011 (SA), and *P. aeruginosa* UCL1 (PA), calculated using Tukey's multiple comparison test. Error bars indicate standard deviation.

By understanding the growth kinetics of the species in BHI broth, this information will be used to inform the design of co-culture experiments and wider community experiments as well data for mathematical modelling of these.

**Conclusions / Implications for practice**

Data produced from this project will be valuable in describing ecology of relevant species in CRDs and interspecies interactions, in pairs and beyond, to understand how they underpin whole microbial communities. The WinSCosm model will be valuable in describing complex microbial dynamics and interactions in airway diseases and the response to bacteriophage therapy as a potential microbiome-based intervention

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## The role of myokines in airway smooth muscle relevant to its dysfunction in obstructive lung diseases

Yasmin Farrant | BRC

**Background**

Obstructive lung diseases, such as COPD and asthma, share features including reduced airflow, airway inflammation and remodelling, and airway smooth muscle (ASM) dysfunction, which is a key player in both diseases[1-2].

Approximately 10% of asthma patients respond sub-optimally to standard treatments[3]. Despite novel biologics being developed, most target eosinophilic asthma – however 30-50% of asthmatics are non-eosinophilic and 10-25% of recipients are non-responders[4-5]. No drugs are specifically licensed to reduce ASM mass, and ASM-reducing bronchial thermoplasty is being discontinued due to low uptake[6-7]. In COPD, airway obstruction is typically steroid-resistant and treatments remain palliative, highlighting the need for therapies directly targeting ASM[8].

Circulating myokines are dysregulated in sarcopenia[9-10], which is common in COPD and emerging in asthma[11]. Systemic effects of myokines are emerging; including regulation of inflammation, metabolism, and tissue repair[12-13]. IGF-1 and irisin are two such myokines[14]. Irisin appears protective in lung function[15], whereas IGF-1's role is more contradictory[16-17]. This project explores the role of myokines on ASM function, potentially offering new therapeutic strategies for obstructive lung diseases.

**Aims / Objectives**

To investigate the role of myokines, including IGF-1 and Irisin, in ASM pathophysiology relevant to asthma and COPD, including effects on ASM mass, contractility, inflammatory mediator release and ROS production, with clinical relevance assessed through serum measurements across healthy, asthmatic and COPD donors.

**Methodology and Main Body**

MTS assays were performed to assess myokine cytotoxicity. Cells were seeded at 7,500/well in fibronectin-coated 96-well plates, cultured in DMEM + 10% FBS for 24h, serum-starved in DMEM + 0.2% BSA for 24h, then treated with IGF-1/Irisin (1-0.0003 µg/mL) for 24h. MTS reagent was added for 2h before measuring absorbance at 490 nm.

DCFDA-labelled cells were treated under the same conditions to assess ROS generation in response to IGF-1/irisin, with fluorescence measured at 523nm at 0, 1, and 24h post-treatment.

For flow cytometry, ASM cells were seeded in 12-well plates at 5000/well in 10% FBS media for 24h, serum-starved for 24h, then treated with IGF-1 (0.01-0.3µg/ml) in DMEM with 2.5% FBS or CS-FBS for 5 days. Cells were harvested, stained with Sytox Orange and run on the Attune NxT. Supernatants were saved for future analysis.

**Results**

The MTS assay measures cell metabolic activity and was used to assess the cytotoxicity of the IGF-1 and Irisin treatments. The data represents the mean with SEM from 11 donors (healthy (n=5) and asthmatic (n=6)). Normality was assessed using Shapiro-Wilk test. Staurosporine, used as a positive control for cell death, resulted in a significant difference ($p<0.0001$) compared to media control when assessed using a paired t test (IGF-1/Irisin raw data, mean ± SEM: 0.07 ± 0.03, staurosporine versus 0.73 ± 0.06, media control). Significant differences in the irisin dataset were assessed using the non-parametric Kruskal-Wallis test (overall $p<0.0001$) followed by Dunn's multiple comparisons. Irisin induced a statistically significant increase in the MTS absorbance compared to VC at 0.3 and 1µg/mL (percentage change vs media, mean ± SEM: 0.59 ± 2.25, VC versus 11.35 ± 3.45, 0.3µg/mL irisin, 13.89 ± 4.04, 1µg/mL irisin). For IGF-1, significant differences compared to VC were tested using the one-way ANOVA test (overall $p<0.0001$) followed by Dunnett's multiple comparisons test. The three highest concentrations of IGF-1 showed a significant increase in absorbance relative to the VC (percentage change vs media, mean ± SEM: 1.68 ± 3.00, VC versus 19.91 ± 4.33, 0.1 µg/mL IGF1,

21.60 ± 4.13, 0.3 µg/mL IGF1, 20.10 ± 4.40, 1µg/mL IGF1). This increase in metabolic activity could suggest that irisin and IGF-1 increase cell viability, cell size or cell number.

The DCFDA assays across 11 donors (asthmatic and healthy) showed no significant difference in ROS production between the VC and the treated ASM cells, even when the measured values were normalised to the media controls. Ordinary one-way ANOVA with multiple comparisons was used to assess whether there were significant differences between the VC and Irisin/IGF-1 treated populations. No significance was found between the groups ($p > 0.05$). The lack of significant difference implies that irisin and IGF-1 did not alter the ROS production acutely in ASM under these experimental conditions. $H_20_2$ significantly increased ROS versus media alone, demonstrating that the ASM cells were capable of producing ROS and proving the DCFDA loading procedure to be successful (DCF fluorescence (523 wavelength), mean ± SEM: 33850 ± 4904, $H_20_2$ versus 5170 ± 630.8 media control). A Wilcoxon test showed significant difference ($p < 0.05$).

Flow cytometry was used to further explore the effect of IGF-1 on cell viability, cell number, cell size (FSC) and internal complexity (SSC) across 7 donors (3 healthy, 4 asthmatic). A paired t test showed a significant increase ($p<0.05$) in cell number between the 0h baseline and 10% FBS positive control at 120h (mean ± SEM: 3415 ± 629.40, 0h versus 13,282 ± 3587, 10% FBS media), showing the ability of the cells to proliferate. No significant difference was observed between VC and 2.5% FBS media control using a paired t test indicating that the VC had no effect (mean ± SEM: 6160 ± 1510, VC versus 6095 ± 1278, 2.5% FBS media). Cells treated in 2.5% FBS showed no significant difference across the IGF treatment group versus VC when analysed by one-way ANOVA. In CS-FBS, as with 2.5% FBS, a paired t test showed no significant difference between VC and CS-FBS media control (mean ± SEM: 8112 ± 2048, VC versus 10,906 ± 2901, CS-FBS media). However, a one-way ANOVA showed an overall significant difference between treatment groups ($p<0.0001$) followed by Dunnett's multiple comparisons test. 0.1µg/mL and 0.3µg/mL IGF-1 significantly increased cell number relative to VC (% media, mean ± SEM: 76.40 ± 8.20 VC versus 121.30 ± 11.66, 0.1µg/mL IGF-1, 147.70 ± 14.47, 0.3µg/mL IGF-1). Cell viability, cell size (FSC) and granularity (SSC) were also assessed, however no significant differences were observed across treatment groups in either of the media conditions.

**Conclusions / Implications for practice**

Irisin and IGF1 were not cytotoxic to the cells, in fact a small increase in the MTS signal was observed, potentially due to changes in viability, cell number, or cell size. This was followed up using flow cytometry, which assessed cell number, viability and size (FSC) over a longer time course, showing that IGF-1 increased cell number, but had no effect on viability or cell size. Neither irisin or IGF-1 had an acute effect on ROS production by ASM cells, however a longer time course may capture delayed/cumulative effects on enzymes involved in ROS generation/clearance, e.g., NOXs, SODs.

Future work will further explore myokine effects on ASM cells, including confirming IGF-1 induced proliferation via CSFE assays, repeating the flow experiments with irisin, longer-term ROS assays, assessing ASM contraction/contractile protein expression, and ELISAs on supernatants to quantify inflammatory mediator release, to identify potential roles for myokines in ASM dysfunction relevant to asthma and COPD.

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## Investigating muscle-derived Specialised pro-resolving mediators as a potential treatment for muscle wasting

Jasmine Foster | BRC

**Background**

Skeletal muscle constitutes approximately 40% of the human body mass. It plays multiple key roles, including aiding in the movement of the body, aiding in metabolism and helping in homeostasis. Sarcopenia is the progressive reduction of skeletal muscle mass and muscle function, which ordinarily is related to ageing. However, it has also been seen as a co-morbidity in various groups suffering from one or multiple long-term conditions that can be subject to this sarcopenic effect much earlier in life. In both sarcopenic and patients with multiple long-term conditions, inflammation has been noted as a cross-cutting mechanism that provides a potential target. However, currently, the front-line treatment for inflammation is drugs such as NSAIDs such as aspirin or naproxen, which have been shown to inhibit muscle growth, which in turn hinders the resolution of chronic inflammation and can lead to a more considerable sarcopenic effect within -these groups. Specialised pro-resolving mediators (SPMS) are derived from polyunsaturated fatty acids (PUFAS). SPMs help activate and regulate the pro-inflammatory and pro-resolving processes, with emerging evidence that they positively affect muscle growth and repair in vitro. However, understanding the localised production of SPMs within skeletal muscle is yet to be investigated.

**Aims / Objectives**

This project aims to examine if skeletal muscle can produce SPMs and begin to identify possible molecular and cellular targets or pathways involved.

**Methodology and Main Body**

All experiments were carried out on C2C12 myotubes. Cells were exposed to TNF-α at 0ng, 10ng, 100ng, and 200ng, with cells and cell supernatants being analysed at three h, 24h, 48h and 72h. Samples were analysed for morphological change, gene expression of known SPM production indicators and inflammatory genes using qPCR. Extracellular SPM levels were analysed using solid-phase extraction followed by a bespoke LC-MS-MS assay.

**Results**

A reduction in the width of the myotubes was seen via morphological analysis (n=6) with increasing dose and exposure time ($p<0.0001$), as well as a reduction in myotube length over increasing time with high dose exposure ($p<0.0001$). mRNA analysis (n=4) showed an increase in detectable levels of both TNF-α ($P=0.0498$) and IL6 ($P=0.0111$) over both time and dose. Further, levels of COX1 ($P=0.0023$), COX2 ($P=0.0152$), and Alox5ap ($P=0.0089$) over time and dose; however, this was noticed to drop between 48h and 72h. LC-MS-MS analysis detected the presence of LXB4 and LTB4 and prostaglandins PGE2, PGD2, and PG2a increasing in response to the inflammatory state.

**Conclusions / Implications for practice**

We report here that skeletal muscle myotubes show elevated expression of markers implicated in SPM production and the detection of muscle-derived SPMs in a state of inflammatory-induced atrophy. This early optimisation data is the first step toward understanding the proper role of SPMs in skeletal muscle so we can harness their resolution properties for good in those with sarcopenia.

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## Exploring Proteomic Mechanisms Linking Sarcopenia and Cardiovascular Disease in Chronic Kidney Disease

Thivviya Sivakanthan | BRC

**Background**

Sarcopenia is an age-related syndrome characterised by the progressive loss of skeletal muscle mass, strength, and function. It is associated with adverse outcomes such as frailty, reduced quality of life, cardiovascular complications, and mortality, and frequently coexists with chronic conditions (Damluji et al., 2023). The underlying mechanisms of sarcopenia are multifactorial, involving chronic low-grade inflammation, mitochondrial dysfunction, and oxidative stress. In particular, inflammation plays a key role by disrupting muscle homeostasis and promoting muscle atrophy (Tarantino et al., 2023). Cardiovascular disease (CVD), another age-associated condition, shares overlapping risk factors with sarcopenia—including inflammation, metabolic dysfunction, and reduced physical activity (Zuo et al., 2023). This bidirectional relationship is especially relevant in individuals with chronic kidney disease (CKD), where both conditions are prevalent and inflammation is exacerbated. Despite their overlap, the mechanisms linking sarcopenia and CVD in CKD populations remain underexplored. Omics technologies, such as proteomics, offer the potential to uncover mechanistic biomarkers—particularly mitochondrial and fibro-inflammatory proteins—that could guide future risk stratification and therapeutic strategies aimed at improving kidney function, cardiac function, and mortality in CKD and kidney transplant patients. (Damluji et al., 2023).

**Aims / Objectives**

This study aims to investigate the fibro-inflammatory mechanisms and processes that link sarcopenia and cardiovascular disease in individuals with CKD, including kidney transplant recipients and patients on haemodialysis using proteomics. Specifically, we will:

1. Identify differences in the fibro-inflammatory proteome between sarcopenic and non-sarcopenic CKD patients.
2. Compare these profiles across CKD phenotypes and with healthy controls.
3. Explore associations between proteomic patterns and cardiovascular phenotypes

**Methodology and Main Body**

This study will utilise data and stored blood samples from three cohorts: 50 kidney transplant recipients from the ESCERT study (Billany et al., 2021), 50 haemodialysis patients from the CYCLE-HD study (Graham-Brown et al., 2021), and 50 healthy controls. Participants will be matched by age, gender, and ethnicity, with age prioritised to minimise confounding. Sarcopenia status in ESCERT participants will be determined using established criteria based on muscle MRI, strength tests, and physical performance assessments.

Extracellular vesicles (EVs) will be isolated from stored blood using either the Mag-Net (Wu et al., 2024) or PROSPR method (Gallart-Palau et al., 2015)—currently being optimised for automation and high-throughput use. Mass spectrometry will be used to perform exploratory proteomic analyses. The primary focus is to identify proteomic signatures of sarcopenia in kidney transplant recipients. Blood samples from these cohorts will undergo exploratory proteomic analysis, specifically targeting fibro-inflammatory protein profiles. Comparisons will also be made with healthy controls and across disease groups.

Primary outcomes include proteomic differences associated with sarcopenia and cardiovascular phenotypes. Secondary outcomes will explore links between proteomic markers and physical activity or muscle quality.

**Discussion/Implications**

This study may identify fibro-inflammatory proteomic signatures associated with sarcopenia and cardiovascular dysfunction in CKD, offering insights into underlying mechanisms and potential biomarkers. Findings could inform risk stratification and targeted therapies. Limitations include small sample sizes and the cross-sectional design, which limits causal interpretation.

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# Validation of an automated Artificial Intelligence (AI) measurement of skeletal muscle area from computed tomography (CT) of the thorax images against DXA measured soft tissue mass

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**Background**

The Global Initiative for Chronic Lung Disease (GOLD) 2025 Report (2024) conveyed an estimated global COPD prevalence of 10.3% expected to increase by 23% in those aged 25 years and over by 2050, adding to the existing socioeconomic burden of COPD. Development of biomarkers can help quantify characteristics of COPD phenotypes to better predict outcomes and facilitate the development and evaluation of improved treatment and therapy options.
Sarcopaenia is commonly observed as frailty progresses, frailty is commonly observed in advancing sarcopenia and both disease processes commonly present with decline in intrinsic capacity. Sarcopenia has been demonstrated to have a higher prevalence, appears to increase with the progression of disease severity and is associated with poorer outcomes for people with COPD. However, the impact of sarcopenia on clinically important outcomes in COPD remains unclear.
A number of imaging techniques; dual-energy X-ray absorptiometry (DXA), ultrasound, MRI and CT have been used for body composition analysis (BCA). DXA is considered the practical gold standard for BCA as the time and resource intensive manual segmentation of muscle and fat on CT and MRI imaging has been a limiting factor. Small muscle area and soft tissue truncation also present challenges for the manual segmentation of muscle in thoracic CT imaging.

**Aims / Objectives**

The emergence of automated AI algorithms may facilitate BCA in CT data sets performed for routine clinical care in respiratory disease with potential to assist prediction of adverse clinical outcomes. We aimed to validate an automated AI algorithm measuring muscle tissue segmentation from thoracic CT against DXA measures of lean mass.

**Methodology**

Initial retrospective analysis was performed on an available dataset from the PHOSP-COVID study; a national UK multicentre cohort study of patients who were hospitalized for COVID-19 and subsequently discharged (Elneima et al., 2023). A previously developed AI algorithm (Xu et al.,2023) automatically extracted skeletal muscle area at the T5, T8 and T10 levels with imputation for truncated soft tissue. Pearson correlation *r* and p-value was calculated for the CT measures at individual levels and as a total against DXA total body lean mass.

**Results**

49 participants with paired thoracic CT and DXA measures were identified. Population characteristic; N = 49, Age: median 60 (ranger: 25-91), Gender: Female 20 (41%), Male 29 (59%), Ethnicity: ASIAN 11 (22%), BLACK 3 (6.1%), WHITE 35 (71%). (baseline characteristics TBC). Very strong linear correlation between AI derived thoracic CT skeletal muscle area and DXA lean mass was seen at all measured levels though this was stronger for the T8 level. Results: T5: r=0.856, p=4.92e-15, T8: r=0.898, p=2.44e-18, T10: r = 0.856, p= 4.49e-15, All levels: r= 0.892, p = 8.39e-18. Greater imputation at the T5 level and segmentation errors at T10 associated with the adjacent liver tissue are potential reasons for poorer correlation at these levels.

**Conclusions / Implications for practice**

Our results demonstrate the potential for AI analysis of routine clinical thoracic CT imaging for BCA. Further validation including concordance of the CT and DXA measures, reproducibility in patients with emphysema, comparison to clinical outcomes and identifying cut offs indicating low muscle mass are needed.

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## Specialised Pro-RESOLVing lipid mediators in the resolution of acute Exacerbations of COPD

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**Background**

Respiratory disease is the third biggest cause of death in England and chronic obstructive pulmonary disease (COPD) is one of the leading causes of death, within respiratory disease (Gajjar and Burnett, 2024; NHS England). Frequent exacerbations accelerate disease progression and mortality. COPD is characterised by chronic and persistent inflammation in the lung, which can cause irreversible damage (Yang *et al.*, 2021). Inflammation is an active process, and resolution is initiated and moderated by specialised pro-resolving mediators (SPMs). These endogenous mediators are formed via the metabolism of polyunsaturated fatty acids (PUFAs). The pathways of SPMs reprogram the immune system to limit production of pro-inflammatory mediators and upregulate production of resolution mediators (Dalli and Serhan, 2019). Multiple studies are beginning to suggest that a key mediator in COPD may be Resolvin D1 (Finney *et al.*, 2025; Fisk *et al.*, 2025). Lower levels were associated with prolonged respiratory symptoms and Resolvin D1 was significantly increased at exacerbation onset in bacterial exacerbations (Finney *et al.*, 2025). In frequent exacerbators, levels were found to be inversely associated with the occurrence of severe exacerbations over follow-up (Fisk *et al.*, 2025). However, there is very little information on how the dynamic nature of the resolution response. Without further insight into this area, the use of SPMs within therapeutics will remain limited.

**Aims / Objectives**

The aim of the study is to investigate the effects of an acute exacerbation of COPD on resolution physiology. The primary objective is to research systemic levels of SPMs during an acute exacerbation, measured by SPM cluster analysis using liquid chromatography-mass spectrometry (LCMS). The objective of the sub-study is to describe the relationship between SPMs and the time course of the recovery of the exacerbation.

**Methodology and Main Body**

This is a single centre observational study divided into a cross-sectional main study and longitudinal sub-study. The main study will enrol 100 adult participants who have been admitted to hospital with an acute exacerbation of COPD. The surplus of the blood sample taken on admission as part of the participant's clinical care will be analysed. They will also be given the option to donate a spontaneous sputum sample. Of the 100 participants enrolled in the main study, 30 will be enrolled into the sub-study. Daily blood samples will be taken from participants from the day of enrolment until the day of discharge from hospital. They will be invited back for an optional 3-month follow up visit, where a 'recovery' sample will be obtained.

**Discussion/Implications**

Therapeutic applications of SPMs currently remain limited due to the limited bioavailability and rapid clearance of these molecules (Trilleaud *et al.*, 2021). Through the analysis techniques: proteomics, immunophenotyping and free fatty acid analysis, the results of this trial could help develop understanding surrounding resolution physiology, exploring the dynamic changes over time and the processes by which these takes place. This integrated approach has the potential to provide insight into the wider immune response in combination with the actions of SPMs, and highlight potential pathway dysregulations in the COPD population. It could also provide possible applications within other inflammatory conditions, such as the allergic response within asthma, bacterial and viral respiratory infections. Furthermore, it could reveal novel biomarkers for COPD and improve the management of COPD.

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## Beyond Home: A Novel Method to Study How Greenness and Human Movement Shape Respiratory Health Risk.

Hadiqa Tahir | BRC

**Background**

The relationship between greenness and respiratory health remains complex. Findings on the association between greenness and respiratory health are inconsistent, with studies reporting protective, null, and even adverse effects. A key reason for this may lie in how exposure is typically measured. Current epidemiological models rely on residential location as a proxy for environmental exposure, failing to account for human movement. This oversimplification can lead to exposure misclassification and biased exposure-response estimates, potentially distorting our understanding of the true health effects of greenness.

To address this, we developed a Bayesian logistic regression model that uses high-resolution, disaggregated environmental data—such as NDVI at the pixel level—and weights these based on how individuals interact with their local environment. These weighted data are then linked to individual-level health outcomes to study how greenness and human movement shape respiratory health risk.

**Aims / Objectives**

The aim of this project is to improve exposure assessment in environmental epidemiology by modelling how individual interaction with greenness affects respiratory health risk.

**Methodology and Main Body**

Using Demographic Health Survey (DHS) data from Albania, we modelled the relationship between greenness and Acute Respiratory Infection (ARI) in children under five. Greenness exposure was calculated using NDVI derived from Sentinel-2 imagery via Google Earth Engine, exported at a spatial resolution of 100 meters × 100 meters. We assigned NDVI exposure based on DHS cluster centroids within a 3,000-meter exposure radius.

Unlike traditional methods that average NDVI within a buffer, our model incorporates a distance-decay weighting function, where weights depended on the Euclidean distance between each pixel and the DHS cluster centroid. The model estimated how nearby greenery (NDVI) at the pixel level affects a person's disease risk, giving more weight to closer vegetation and less to farther areas. It accounted for local environmental influence and human movement patterns.

A simulation study was conducted to assess model performance across varying sample sizes (N = 1114, 50,000 and 100,000), effect sizes and levels of model complexity. Performance measures such as empirical standard error, mean square error, and coverage were evaluated.

**Results**

At N = 1,114, high uncertainty led to wide credible intervals and noticeable bias ($B_0$ bias = -0.19, $B_1$ bias = 0.35). Increasing the sample size to N = 50,000 and N = 100,000 substantially reduced bias (< 0.02), empirical standard error (≤ 0.3), and led to more precise and reliable effect estimates (Coverage ≥ 0.94).

**Conclusions / Implications for practice**

Current models relying on residential exposure may oversimplify environmental influences on respiratory health. By incorporating human movement, our model captures spatial variations in exposure instead of averaging across neighbourhoods. However, large sample sizes are needed to accurately detect effect direction.

We continue refining the model to enhance its ability to learn spatial weights, strengthening its epidemiological applications.

## Understanding the impact of the microbial community on *Mycobacterium tuberculosis* infection and patient outcomes

Richard Thomas | BRC

**Background**

Tuberculosis (TB) is a highly infectious airborne disease, that in 2023 returned to being the world's leading cause of death from an infectious agent (1). TB is caused by the bacterial pathogen *Mycobacterium tuberculosis*, which spreads between individuals via inhaling aerosol droplets released from an infected individual when they cough or sneeze. Despite being considered a curable disease, a combination of long treatment duration with adverse drug effects often results in low compliance and multi-drug resistance. Thus, there is a need to improve our understanding of *M. tuberculosis* biology for the development of novel and stratified therapeutic strategies (2).
The host environment can influence the physiological state of *M. tuberculosis* and susceptibility to antimicrobial treatment. One of these states *M. tuberculosis* can adopt is a drug-resistant non-replicating form known as "Differentially Culturable Tubercule Bacteria" (DCTB). Recent pilot data has demonstrated that DCTB can be formed in macrophages when activated with lipopolysaccharide (LPS), a component of the outer cell-membrane of gram-negative bacteria. This suggests that the microbiome may play a vital role in disease phenotype and influence patient and treatment outcomes. Furthermore, sequencing technologies have allowed for the exploration and characterisation of the diverse microbial communities in the lungs of pulmonary TB patients (PTB). This has provided further evidence that the respiratory microbiome can impact treatment outcomes or play a role in TB recurrence (3)

**Aims / Objectives**

This project aims to achieve a clear picture of the role that the respiratory microbiome plays in pulmonary tuberculosis and how this may influence patient outcomes. The specific breakdown of the objectives I will achieve throughout my project are:

- Using respiratory samples, this project will use culture and sequencing methodologies to explore the characteristics of the respiratory microbiota.
- Using bioinformatics and statistical analysis, this project will identify members of the microbial community associated with *Mycobacterium tuberculosis* strain phenotypes.
- Using *in vitro* models, this project will explore the impact of members of the respiratory microbiome on *Mycobacterium tuberculosis* characteristics.
- Characterise the lower airway microbiome in PTB pre- and post-treatment

**Methodology**

To quantify heterogenous *M. tuberculosis* populations, I will use previously established culture-based and culture independent methodologies. Bronchoalveolar lavage (BAL) samples will be collected and investigated for potential DCTB stimuli. Concentrations of nitrite, a stable product of nitric oxide oxidation, which will be determined using Griess reagent, while concentration of LPS will be carried out using a Limulus amoebocyte lysate assay. To characterise the microbial community and biogeography of the lower respiratory tract in PTB. Using 16S rRNA gene sequencing, gaining greater taxonomic resolution than illumina sequencing, I aim to identify microbial community characteristics associated with proximity to areas of disease and *M. tuberculosis* phenotypes.

**Expected outcome**

This project will describe the impact that the respiratory microbiome has on influencing the DCTB phenotype of *M. tuberculosis* and how this impacts patient outcomes. Quantifying the DCTB populations of patient samples will shed light onto the presence of DCTB present, therefore, providing a potential insight for predicting disease relapse. This project will also help create culture-independent based assays for the detection of DCTB in clinical samples.

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## Recovery at 1-year post Covid-19 hospitalisation in adults with pre-existing multiple long-term conditions

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**Background**

Living with multiple long-term conditions (MLTCs) (commonly defined as the co-existence of two or more long-term conditions (LTCs) in an individual) represents significant burden to an individual, their support network, healthcare systems and broader society; particularly in disadvantaged communities and settings[1].

Having pre-existing MLTCs is associated with severe SARS-CoV-2 infection[2], and non-recovery and multiorgan abnormalities 5-months post Covid-19 hospitalisation[3,4]. Whilst the presence of single pre-existing LTCs have been identified as risk factors for Long Covid[5], there is limited understanding as to how MLTCs affect longer-term recovery post Covid-19 hospitalisation, any differences according to how MLTCs are categorised, and potential implications for clinical care.

**Aims**

This study aimed to address the following research questions:

- is there a difference in recovery at one-year in those with pre-existing MLTCs to those without?
- are there differences in recovery at one-year according to how MLTCs are categorised (e.g., number or type of LTCs, bodily systems involved, 'complex' MLTCs definitions, and frequently co-occurring combinations of LTCs)?

**Methods**

Using the Post Hospitalisation COVID-19 (PHOSP-COVID) study[6], which recruited adults with an admission to a medical assessment unit or ward with confirmed or clinician-diagnosed COVID-19 between 2020-2021, adults with and without MLTCs were propensity-matched 1:1 for age, sex, ethnicity, deprivation, obesity, and smoking history. Multivariate logistic regression (with adjustment for age, sex, ethnicity, deprivation, severity of acute illness, admission duration, obesity, and smoking history) was used to model patient-perceived recovery at one-year post-discharge using complete case data. Exploratory analyses in adults with MLTCs assessed the impact on recovery according to number of LTCs, number and type of bodily systems affected, and latent-class analysis (LCA) derived MLTC clusters.

Two members of a Patient Advisory Group (comprising seven adults living with pre-existing MLTCs and Long Covid) were involved in interpretation of analyses and reporting of this study.

**Results**

1294 adults, 647 with MLTCs and 647 without MLTCs were propensity-matched: 61.9% male, 79.6% of white ethnicity, median age 59 [IQR 52-67] years. Compared with adults without MLTCs, adults with MLTCs were less likely to feel fully recovered at one-year post-discharge (odds ratio (OR) 0.66 [95% confidence interval (CI) 0.51 to 0.85], p=0.001).

In those with MLTCs, those with two or more bodily systems affected (OR 0.67 [ 95% CI 0.47-0.95], p = 0.026), respiratory, gastrointestinal or neurological/psychiatric LTCs, or co-existing mental and physical health LTCs (OR 0.64 [95% CI 0.42-0.96], p= 0.033) were less likely to feel fully recovered at one-year.

Three distinct MLTC clusters were identified using LCA: cardiovascular (n=90), depression/anxiety and asthma (n=345), and cardiometabolic (n=662). Compared with the cardiometabolic cluster, those in the depression/anxiety and asthma cluster were less likely to feel fully recovered at one-year post-discharge (OR 0.54 [95% CI 0.38-0.77], p=0.001).

**Conclusion**

Adults with pre-existing MLTCs were less likely to feel fully recovered at one-year post COVID-19 hospitalisation compared to those without MLTCs. Within those with MLTCs, number and type of

bodily systems affected and MLTC clusters were associated recovery at one-year, providing novel predictive insights for clinical care post-COVID-19 hospitalisation.

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## Sociodemographic intersections and risk of multiple long-term conditions: a systematic review

Daniel Han | BRC

**Background**
Multimorbidity, or multiple long-term conditions (MLTC), is defined as the simultaneous presence of two or more long-term conditions in an individual. Current evidence suggests unidimensional risk factors such as education, income, deprivation, ethnicity, and sex for developing MLTC. What remains unclear so far is how MLTC development differs at the intersections of sociodemographic factors.

**Aims / Objectives**
In this systematic review, we aimed to assess the current body of evidence to examine how intersecting sociodemographic factors (e.g., ethnicity x deprivation) may influence MLTC outcomes.

**Methodology and Main Body**
We searched PubMed, Medline, and Scopus on 16 April 2025 to identify studies that examined how intersecting sociodemographic factors (e.g., ethnicity x deprivation) may influence MLTC outcomes. Relevant records were summarised and study quality assessed with the Newcastle-Ottawa scale.

**Results**
We identified a total of 792 peer-reviewed studies, of which four were included in the final evidence synthesis. These studies found that MLTC outcomes can vary considerably at the intersections of unidimensional sociodemographic factors. The association of income with MLTC outcomes varied by what other sociodemographic factors it intersects with. The role of disability on MLTC outcomes varied when intersected with ethnicity. A low level of education is usually associated with MLTC, but one South African study found no clear evidence of cumulative disadvantages against the overall life expectancy and life expectancy lived with MLTC at the intersection of education and ethnicity. Sex-based morbidity-mortality paradox was partially observed in three out of four studies reviewed. The quality of the four studies was deemed limited.

**Conclusions / Implications for practice**
Despite the limited data identified from this review, this systematic review highlights the importance of applying an intersectional framework to MLTC research to better understand disparities. The reviewed studies illustrate that the associations between sociodemographic risk factors on MLTC outcomes are not uniform, but in fact vary depending on how they intersect. Future research should address gaps in longitudinal MLTC research that examines how these intersecting disadvantages accumulate onto outcome disparities over time.

**Notes**
This systematic review has been registered with PROSPERO (CRD420251006288) and conducted and reported in line with the PRISMA 2020 statement. This review has also been submitted to PLOS ONE and is currently under review.

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## ELIXIR: Examining eXercise limitation(s) and traIning Response(s) in people with multIple long-term conditions (MLTCs)

Faezeh Zangiabadi | BRC

**Background**

The number of individuals with multiple long-term conditions (MLTCs; ≥2 long-term conditions) is increasing due to the aging population and improvements in life expectancy in those with chronic conditions (1). Individuals with MLTCs experience a greater symptom burden and reduced exercise tolerance (2, 3); the strongest independent predictor of morbidity and mortality in health and disease (4, 5), which also correlates with health-related quality of life (HR-QoL; (6)). This reduction in exercise tolerance likely contributes to the poorer clinical outcomes seen in this cohort (2, 7). Exercise strategies that effectively overcome exercise limitations to increase exercise tolerance are likely to reduce morbidity, mortality, and hospitalisations, and increase health-related quality of life in individuals with MLTCs (8). However, to maximise the efficacy of exercise therapy, interventions specific to the individual and their exercise limitation(s) must be established. Currently, the mechanisms underpinning exercise tolerance in individuals with MLTCs are unknown; a key step that limits personalised exercise therapy development.

**Aims / Objectives**

This project aims to explore the mechanisms underpinning exercise tolerance in those with MLTCs and investigate the effect of an exercise-based intervention programme on exercise limitation(s).

**Methodology and Main Body**

60 participants ≥18 years old will be recruited; 20 healthy individuals and 40 patients with ≥2 long-term conditions, at least one of which has evidence of benefit from exercise. Patients will be randomly allocated into intervention group (rehabilitation + usual care) or control group (usual care). The intervention group will attend twice weekly face-to-face rehabilitation classes for 8 weeks that consist of exercise therapy and education. At baseline and 3 months post-randomisation, exercise limitations (cardiopulmonary exercise test), pulmonary function (spirometry), isometric and isokinetic muscle strength (cybex machine), muscle oxidative capacity (near infra-red spectroscopy), body composition (dual-energy x-ray absorptiometry), and physical function (sit-to-stand test and balance test) will be measured.

**Implications for practice**

Implications of this study can be divided into following categories:

**Scientific Advancement**

- This study may provide insight into how multiple organ systems (muscles, heart, lungs) interact to limit maximal dynamic whole-body exercise in people with MLTCs—an area that is poorly understood. It can also contribute to understanding whether muscle dysfunction, oxygen transport, or ventilatory issues are the main cause of limitation.

**Clinical Impact**

- If exercise limitations can be identified, exercise prescriptions can be tailored to the individual's physiological profile—improving the efficacy of rehabilitation to **better outcomes**.
- By showing that exercise improves physiological responses in people with MLTCs, the study strengthens the argument for incorporating exercise-based rehabilitation into routine care.

**Public Health & Policy**

- Demonstrating physiological improvements may convince health systems to **fund supervised rehabilitation programs** for individuals with MLTCs

**Innovation and Future Research**

- Could lead to **clinical trials** comparing different exercise modalities based on identified limitations.

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## Understanding the mechanistic effects of structured exercise interventions in long-term conditions

Faith Omoregie | LHIIP

**Background**

Long-term conditions (LTCs), also known as chronic disease, can be defined as a disease that is slow in its progress and lasts for a lengthy period (1). People with LTCs often have other chronic diseases occurring concomitantly (1), resulting in the presence of multiple long-term conditions (MLTCs). MLTCs have been progressively growing in prevalence over recent years (2). People living with MLTCs are at an increased risk of sarcopenia (2), defined as a loss of muscle mass and decline in strength and function (3).

Structured exercise interventions are potentially crucial in managing MLTCs, including any concomitant sarcopenia and resultant poor physical function (4). A recent systematic review by the *'Personalised Exercise Rehabilitation For people with multiple long-term conditions'* (PERFORM) team studied the effect of exercise-based intervention across 45 LTCs. This review identified the value of exercise in terms of exercise capacity and health-related quality of life in a wide range of LTCs. The findings of this review were used to develop an exercise-based service specifically designed to meet the needs of people with MLTCs (5).

Nonetheless, this review did not explore the biological effects of exercise interventions in LTCs. From a muscle health perspective, exercise has complex mechanistic effects in different LTCs, including the modulation of inflammation immune pathways, mitochondrial function and gene expression regulation (6,7, 8). Improving our understanding and knowledge of the biology of exercise could potentially be harnessed to improve therapeutic approaches to combat long-term diseases (4).

**Aims / Objectives**

To support the PERFORM study, this systematic review aims to understand the evidence underpinning the mechanistic effects of structured exercise targeted at LTCs. The primary outcome aims to identify the biological and mechanistic effects of structured exercise interventions across different LTCs. The secondary outcome will explore which LTCs are more likely to benefit at a biological and mechanistic level from exercise interventions.

**Methodology and Main Body**

The review was prospectively registered on PROSPERO (CRD42025639005)

**PICOD**

**Population:** Adults (age ≥18 years) with at least one LTC diagnosis.

**Interventions:** Exercise-based interventions (defined as including a structured supervised or unsupervised exercise training intervention, alone or in addition to other components, delivered in any setting, including hospital, community, or home for any duration).

**Comparator**: Any comparator group that includes either a non-exercising control group or an alternate exercise group (e.g., aerobic exercise, resistance exercise, combined exercise interventions).

**Outcomes:** Any biological and mechanistic effects (e.g., molecular and cellular mechanism, regenerative & repair mechanisms, molecular signalling pathway, metabolic effects, neuromuscular adaptations, genetics and epigenetics effects, structural adaptations).

**Design:** Pre- and post-interventional studies, including RCTs and non-RCTs. Studies must report post-intervention data.

**Search strategy and sources**

Literature search strategies were developed using MESH and keywords related to mechanisms, exercise, and chronic disease. Searches were conducted in Scopus, Medline and Web of Science. Titles and abstracts will be screened by two independent reviewers using Rayyan. Full-text screening will be undertaken by one reviewer to confirm eligibility.

**Study quality and data synthesis**

Where appropriate, a meta-analysis will explore the combined effect across all of the studies. Sensitivity analysis will be performed to explore the source of heterogeneity by omitting studies that are judged to be at high risk of bias.

**Results**

Review is in progress and currently screening the titles and abstracts.

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## Developing a pre-senescent *in vitro* model of biological ageing to reflect poor outcomes in multimorbid patients following cardiac surgery

Anab Hasan | BRC

**Background**

Multimorbidity—the presence of two or more chronic conditions—is a growing global health concern, particularly in ageing populations. These patients are often overlooked and receive fragmented care due to the healthcare system's single-disease focus. Multimorbidity is especially prevalent in the cardiovascular disease population and is associated with poorer outcomes following cardiac surgery, including acute kidney injury, stroke, and increased mortality. Although the biological mechanisms underlying multimorbidity remain poorly understood, they are thought to share processes linked to biological ageing.

Biological ageing refers to the time-dependent, cumulative decline in cellular and tissue function, often driven by mechanisms such as oxidative stress, chronic inflammation and DNA damage. Current *in vitro* models of ageing typically lead to full cellular senescence, limiting their translational relevance. Therefore, identifying early ageing phenotypes will help uncover mechanisms driving multimorbidity.

**Aims / Objectives**

This project aims to optimise a pre-senescent *in vitro* model of biological ageing using Human umbilical vein endothelial cells (HUVECs), guided by transcriptomic data from multimorbid and non-multimorbid cardiac surgery patients, to explore ageing-related mechanisms without inducing irreversible senescence.

**Methodology**

A panel of stressors was finalised based on the literature – $H_2O_2$, TNF-α, IL-1β and lipopolysaccharide (LPS) to highlight mechanisms identified in patient transcriptomic data including oxidative stress, chronic inflammation, DNA damage, nucleolar instability and mitochondrial dysfunction. Optimization is underway using pooled donor HUVECs, with plans to move to single donors. Molecular techniques used include qPCR, SA-β-Gal staining, immunofluorescence, and mitochondrial stress testing via Seahorse assay. Further plan includes treating HUVECs with Rapamycin- found to promote longevity. Subsequent validation will involve comparison of further bulk RNA and single nuclei RNA sequencing analysis of the clinical data and the optimised *in vitro* model focusing on pathways dysregulated in multimorbid patients.

**Preliminary findings and ongoing optimisations**

Further bulk RNA sequencing analysis comparing conditions of multimorbid and non-multimorbid patients revealed dysregulation in pathways relating to immune response, oxidative stress and mitochondrial function. These key pathways will be reflected in the biological ageing *in vitro* model currently being optimised. For the oxidative stress model, concentration–response curves were generated to identify optimal $H_2O_2$ dosages for inducing pre-senescent oxidative stress using SA-β-Gal assays for validation. Ageing-related markers (p16, p21, IL-6, and IL-8) showed increased expression in treated cells compared to untreated controls, as assessed by qPCR and immunofluorescence. Mitochondrial dysfunction is anticipated; however, optimisation of the Seahorse assay is ongoing. For the inflammatory model preliminary data indicate that TNF-α-treated cells exhibit elevated IL-8 and CCL2 expression, consistent with an inflammatory phenotype. Further optimisation is currently underway for IL-1β and LPS treatments.

**Implications for practice**

This model aims to offer a reproducible and accessible system for exploring the molecular underpinnings of biological ageing linked to multimorbidity. In the long term, it may serve as a platform to identify biomarkers or therapeutic targets, ultimately contributing to improved surgical outcomes and develop personalised risk stratification for multimorbid patients.

## Exercise as an anti - inflammatory treatment in Axial Spondyloarthritis (axSpA) for patients taking biologic therapy: a proof of concept study (ExTASI-B).

Sepehr Qooja | BRC

**Background**

Over 200,000 people in the UK have axial spondyloarthritis[1]. In 80% of cases the condition begins in the second or third decade of life. Exercise is encouraged as an essential treatment of axial spondyloarthritis (axSpA), with the potential to both promote well-being, increase flexibility and range of movement, improve posture and reduce stiffness and pain. axSpA is an inflammatory arthritis and raised levels of indicators ('markers') of this inflammatory process (e.g. CRP) can be detected in the blood of patients [2]. Despite axSpA being an inflammatory condition with prescribed medication focused on reducing inflammation there are no studies that have assessed the potential of exercise to act as an anti-inflammatory adjuvant to biologic therapy in axSpA. This research will investigate the effect of 12 weeks of a home-based walking exercise intervention on measures of systemic inflammation and body composition, well-being and measures of disease activity using established and validated methods in 20 axSpA patients on regular biologic therapy and compare this group with 20 patients on regular biologic therapy who carry on with their standard care and normal levels of activity.

**Aims / Objectives**

The aim of this study is to determine the potential for aerobic exercise to act as an additional anti-inflammatory treatment for patients with axSpA taking regular biologic medication.

The primary objective is:

- To determine the effect of 12 weeks of a structured home-based aerobic exercise intervention on markers of immune-mediated inflammation.

Secondary Objectives are:

- To determine the acceptability of the home-based intervention, using quantitative questionnaires.
- To determine the effect of the home-based intervention on established non-invasive markers of disease activity.
- To assess the effect of the home-based intervention on circulating markers of cardiometabolic health, blood pressure and anthropometrical measures and immune markers that associate with systemic inflammation
- To assess the effect of the home-based intervention on objective measures of physical function and exercise tolerance

**Methodology and Main Body**

In this proof-of-concept study, 40 patients with diagnosed axSpA and taking biologics will be initially assessed to provide baseline data and characterisation of usual activity over a 7-day period, quantified using tri-axial activity monitors. This 7-day objective physical activity monitoring will be repeated for all participants after 12 weeks of study involvement.

Patients will then continue to take their regular biologic therapy and will be randomly allocated (n=20 in each group) to either a 12-week home-based walking exercise programme or standard care incorporating recommended daily stretching exercises. For all patients, at baseline and after approximately 4, 8 and 12 weeks of the exercise programme or standard care, a variety of assessments will be performed to measure disease activity, markers of inflammation, cardio-metabolic health and anthropometry. At baseline and 12 weeks additional non-invasive assessments to assess quality of life, self-reported physical activity and medication adherence will be performed.

**Results**

This project is now in its first phases, with anticipated results by June 2026.

**Conclusions / Implications for practice**

This proof-of-concept study will determine the potential of exercise as an adjuvant anti-inflammatory treatment for patients with axSpA taking biologic medication.

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## Exploring Stigma and Patient Perceptions in Chronic Breathlessness: A study protocol

Saul Lovatt | BRC

**Background**

Breathlessness is a common and distressing symptom, associated with a poorer physical and mental health related quality of life. It is commonly caused by diseases such as chronic obstructive pulmonary disease and heart failure. However, causes are often multifactorial, with mental health disorders and obesity also frequent contributors.

Health related stigma is an adverse social judgment, relating to an identity associated with a health condition. It can result in cognitive, behavioural, and physiological responses that lead to deteriorating outcomes. This includes being less likely to access care, and experience delays in diagnosis.

For people with breathlessness, internalised stigma may result from feelings of blame, shame or guilt associated with a smoking history or obesity. The attitudes of health care professionals (HCPs) may also contribute to stigma. Complexity associated with the management of breathlessness may create uncertainty for both patients and HCPs, creating differences in how people access or engage with services. Understanding this may help to improve access or engagement with services.

For people with breathlessness little is known about the extent of stigma and the experience of health care services and how this may impact care. This includes the perspectives of diverse ethnic groups where differences in health outcomes exist. Understanding this may help to improve access or engagement with services.

**Aims / Objectives**

1. To investigate the presence, contributing factors and effect of stigma in individuals with chronic breathlessness.
2. To explore patient perceptions of accessing health care services with breathlessness in a diverse population.

**Methodology and Main Body**

A cross-sectional survey of a bespoke questionnaire will explore the extent of stigma in people with breathlessness. Additionally, a concurrent qualitative study will explore the experience of accessing health care services including perceptions, explanatory diagnoses and/or related stigma across diverse patient groups.

**Conclusions / Implications for practice**

Anticipated outcomes of this study are a better understanding of stigma and the perceptions of those accessing healthcare services with breathlessness. This may lead to the design of services that improve access and engagement; as a result, reducing symptom burden, hospital admissions and improving health related quality of life.

# Content and usability testing of the MyHealthMapp programme to improve communication around the 24-hour movement behaviours between people with long-term conditions and health care professionals: a qualitative think aloud study.

Martha Thomas | BRC

**Background**

There are high levels of physical inactivity in people living with multiple long-term conditions (MLTCs) [1]. Barriers for physical activity in this population include low physical capacity, symptom burden, fear of injury and lack of time and specific physical activity guidelines [2,3]. Physical inactivity increases the risk of: frailty, sarcopenia, reduced physical function, poorer quality of life and increases the risk of hospitalisation and cost to the National Health Service [4,5,6]. Consideration of all the 24-hour movement behaviours, including the 5S's (sleep, sitting, stepping, sweating and strengthening activities) gives people a wider range of opportunities to improve their physical activity and health [7] and promotes a person-centred care approach to care, as recommended by NICE guidelines [8]. A shared decision-making (SDM) approach should be utilised to guide care towards goals most meaningful to the individual [9]. Digital tools can be used to promote SDM as the use of digital interventions has been shown to improve understanding of health, self-care behaviours and patient engagement as well as physical activity outcomes [10,11,12]. MyHealthMapp is an online tool that has been developed by the Leicester Diabetes Centre for people living with Type 2 Diabetes to facilitate conversations around the 24-hour movement behaviours and personal health outcomes during an appointment with a health care professional. MyHealthMapp collects participant data using a smart watch or mobile phone to display results and generate personalised targets using an algorithm developed by researchers at the Leicester Diabetes Centre. MyHealthMapp uses red, amber, green (RAG) ratings to compare participant data with general population guidelines and educational animations to improve knowledge, engagement and ability for participants to understand their results and be involved in their own care.

**Aims / Objectives**

Investigate the refinements that need to be made to MyHealthMapp to improve the content and usability for people living with MLTCs and frailty by conducting a series of think aloud interviews.

**Methodology and Main Body**

Think aloud interviews are a type of qualitative interview, developed in line with the person-based approach [13]. Twenty people (n=10 living MLTCs and frailty and n=10 living with MLTCs without frailty) were asked to 'think aloud' while using MyHealthMapp, followed by a number of semi-structured questions. Interviews were transcribed, analysed using reflexive thematic analysis (grouped by theme) and mapped to the APEASE criteria and the MoSCoW framework to identify potential refinements.

**Results**

Three themes, consistent among frail and non-frail participants, were constructed from the interviews: (1) users thought it would be useful in a real-life setting; (2) the use of jargon and abbreviations were raised as a concern; and (3) some participants were unsure about the use of RAG ratings within MyHealthMapp.

**Conclusions / Implications for practice**

The 24-hour movement behaviours (5Ss) should be considered in the management of MLTCs to improve outcomes and promote person centred care [14]. Digital tools, such as MyHealthMapp can be used to facilitate communication and SDM around the 24-hour movements behaviours. The results from this 'think aloud' study are being used to make refinements to MyHealthMapp for people living with MLTCs and frailty. MyHealthMapp will be used and tested in a person-centred feasibility randomised controlled trial (the personal-agility study) looking to improve the 24-hour movement behaviours in people living with MLTCs and frailty.

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## Multimodal Artificial Intelligence Driven Cancer Clinical Decision Support

Xueting Liu | BRC

**Background**

Cancer remains a major global health challenge, with cases projected to rise significantly over the next few decades (Chang et al., 2025). Precision oncology, which leverages molecular profiling to tailor treatments, is key to improving cancer outcomes(Schott, Perou and Hayes, 2015). Artificial intelligence (AI) and machine learning (ML) have transformative potential in clinical decision support (CDS) for cancer care by integrating multimodal data, including multi-omics, histopathology whole-slide images (WSIs), and electronic health records (EHRs) (Dlamini et al., 2020).

However, the adoption of AI-CDS tools in oncology is limited by sociotechnical barriers, such as lack of trust, poor usability, and misalignment with clinical workflows; and technical challenges, including ineffective multimodal data integration, limited generalizability for rare cancers, and insufficient interpretability of AI models (Sutton et al., 2020). Addressing these barriers is critical to realizing the full potential of AI-CDS in transforming cancer care.

**Aims / Objectives**

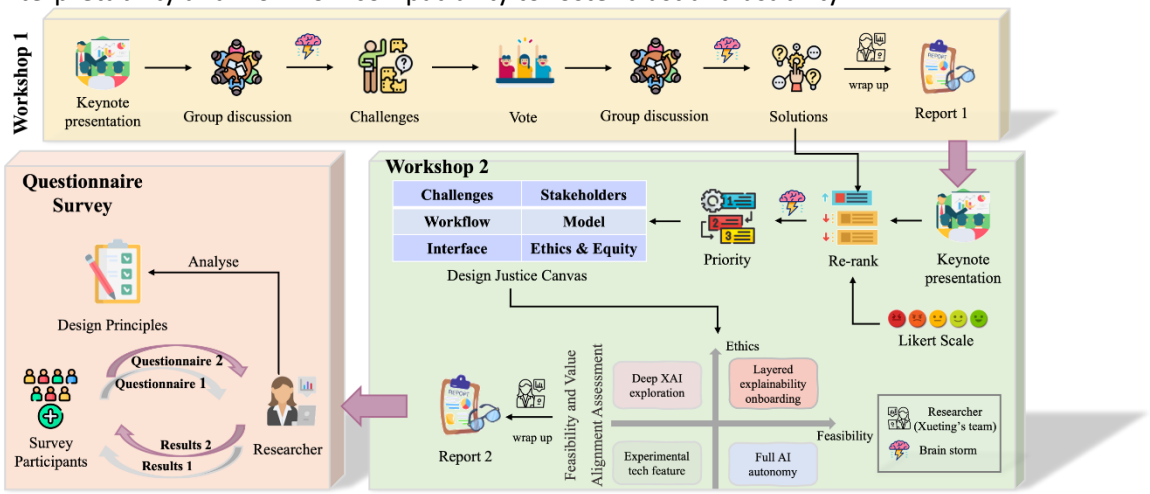
This PhD project aims to develop trustworthy, interpretable, and user-centred multimodal ML-driven AI-CDS tools for oncology through sociotechnical co-design and advanced ML methods. The project has two primary objectives:

(1) Co-Designing Trustworthy and Sociotechnical Design Principles for Multimodal Artificial Intelligence Driven Cancer Clinical Decision Support Tools.

(2) Develop advanced multimodal machine learning models for Cancer Clinical Decision Support which aiming to tackle three main challenges including multimodal data alignment, low-resource data adaption, explainability.

**Methodology and Main Body**

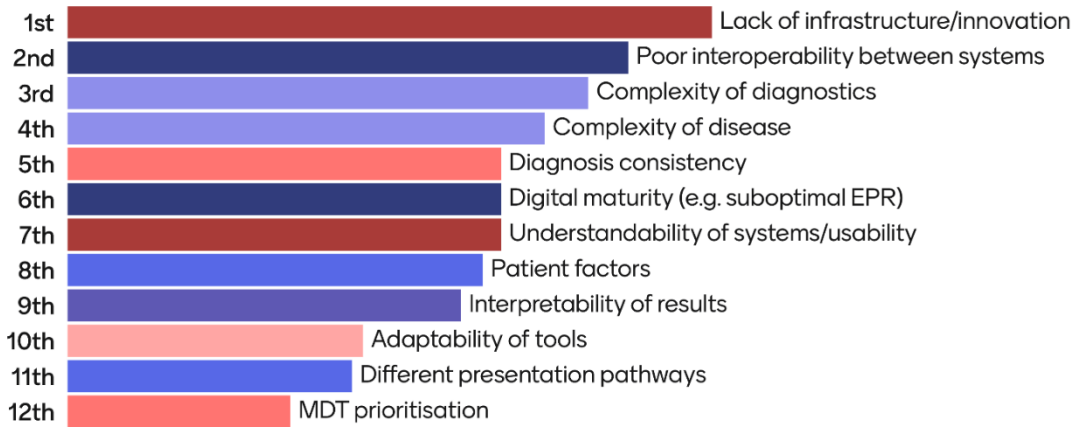
For Objective 1, a hybrid approach will combine participatory workshops, a modified Delphi process, and structured validation surveys to engage stakeholders in identifying barriers, onboarding needs, and context-sensitive design principles for AI-CDS tools. This co-design process will prioritize interpretability and workflow compatibility to foster trust and usability.




For Objective 2, a robust ML framework will be developed to integrate multi-omics and histopathology whole slide images (WSIs) from existing data sources, employing novel methods for cross-modal feature alignment to address data heterogeneity, self-supervised learning for low-resource adaptation, and explainable AI techniques to enhance transparency.

**Results**

Workshop 1 results: sociotechnical barrier mapping




**Conclusions / Implications for practice**

This research will advance precision oncology by designing AI-CDS tools that are trusted, interpretable, and have the potential to be seamlessly integrated into clinical workflows. By addressing sociotechnical and technical barriers, the project will enhance existing diagnostic and prognostic accuracy and treatment decision-making, particularly for rare cancers and low-resource settings. The co-designed tools and ML framework will empower clinicians with transparent, data-driven insights, fostering adoption and improving patient outcomes. Furthermore, the context-sensitive design principles and interpretable ML methods developed here will have broader applicability to other AI-driven healthcare innovations, contributing to the global effort to reduce disease burden and advance equitable, person-centred healthcare.

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## Life after endometrial cancer: Exploring the survivorship-related psychosocial needs of survivors

Humairaa Daud | BRC

**Background**

The incidence of endometrial cancer (EC) is increasing, most notable in pre-menopausal women. Although long-term cure rates are high, many patients experience survivorship challenges, including health anxiety and fear of recurrence. Current research targets physical health and lifestyle factors contributing to recovery and survivorship whereas research into the psychosocial and emotional needs of EC survivors is minimal.

**Aims / Objectives**

This research aims to investigate the survivorship challenges and psychosocial impact of living with and beyond endometrial cancer amongst woman who have undergone treatment for endometrial cancer.

**Methodology and Main Body**

Women who had completed curative primary treatment for an EC with no clinical suspicion of recurrence were recruited to participate in a semi-structured telephone or virtual interview. The discussion focused on their experience from diagnosis, undergoing treatment, and their recovery and survivorship concerns. Interviews were analysed using reflexive thematic qualitative analysis to identify themes and trends.

**Results**

In total 21 women participated in an interview. The median age of participants was 56 years, range 43 to 71 years; seventeen were of White British ethnicity, two were other White, one was Asian British and one was mixed White and Asian. The transcripts provided substantial data of which the psychosocial and physical impact post-treatment will be discussed here. The analysis produced five themes which focus on the physical recovery and lasting effects of treatment, surgical menopause and the implications, social and familial support, psychological impact, and concerns about future health, particularly regarding fear of recurrence.

**Conclusions / Implications for practice**

Despite the generally good prognosis associated with EC, the experience of diagnosis and treatment are physically and emotionally impactful on participants. The impact of treatment and surgical menopause contribute to the quality of survivorship. The influence of support and lack thereof is similarly notable as a direct form of reducing the concerns and mental strain on EC survivors. Finally, the complex psychological needs are important considerations as participants experience long-lasting effects that impact their quality of life; symptoms of Fear of Recurrence also suggest EC survivors may benefit from psychological intervention. This suggests that the survivorship concerns of people living beyond EC extend beyond the lifestyle and physical health factors that dominate current research and the emotional and psychosocial concerns need to be considered in future research.

# Enhancing Representation of Black ethnic minority groups in Public and Patient Involvement and Engagement (PPIE) Biomedical and Healthcare Research: Strategies for Overcoming Inclusion Barriers and Establishing Trustful Partnership

Koby Achaempong | BRC

**Background**

Healthcare research is instrumental in mitigating health inequalities, with PPIE being one of the key windows of opportunity for mitigating such inequalities, considering that the purpose of PPIE is to give the public a voice within healthcare research while ensuring that the most relevant questions are answered (Robinson, 2014). However, a pronounced representation gap of underserved groups, especially those experiencing health inequalities in domains like cancer (Wan et al., 2016), diabetes, and cardiovascular diseases, is evident within PPIE. This deficit not only exacerbates health inequalities but also restricts the depth and applicability of research outcomes, neglecting insights on the implications of diseases and treatments on marginalised communities and sidelining their perspectives in research design and execution. This can lead to considerable voids in healthcare research, potentially reinforcing racial and ethnic health disparities (Salas et al., 2022) while defeating the purpose of PPIE (Pratt, 2019). Due to various barriers, including power inequities, lack of diversity (Ocloo et al., 2021) and mistrust between black communities and healthcare systems (Rajakumar et al., 2009), black ethnic minorities remain the least represented in PPIE in the global West, with anecdotal evidence suggesting similar patterns in the UK, and within the Leicester BRC (Gafari et al., 2024). This PhD Project, therefore, aims to enhance the representation of Black ethnic minority groups in Leicestershire healthcare research, foster community relationships, address access barriers, evaluate PPIE strategy effectiveness, and collaboratively refine approaches to ensure inclusion and trust in the BRC research processes.

**Methods**

The study will be conducted in three phases: a scoping review, a qualitative phase, and an impact measurement phase. The scoping review will aim to assess the current level of black representation in PPIE and what strategies have been used in literature to improve black representation. Based on findings from this review and engagement with PPIE coordinators and researchers, qualitative research will be designed to collect data from black ethnic minorities on barriers to access and how these barriers might be removed to increase trust between these communities and the BRC's research. A PPIE group will be set up for this project, and the design and implementation of the entire research will be based on cocreation. The study will use outreach methods like community visits, clinic events, and social media to foster community ties and gather diverse views on PPIE barriers, facilitators to access and PPI strategy effectiveness. Interviews and focus groups will be conducted with black African, British and Caribbean community members. At the same time, cross-sectional surveys will be done across the clinics of the three themes. Data will be analysed thematically, collaborating with these communities to gather insights, co-create PPI strategies, and refine approaches for an impact measurement model. The final phase will involve co-hosting events with black communities to disseminate the research findings and implement the impact measurement model.

Discussion: The study aims to develop a locally relevant understanding of the historical mistrust between black ethnic minorities and healthcare research systems in LLR, as well as strategies to increase the involvement and engagement of black communities with PPIE and the entire research process. Hopefully, some of these findings will also be relevant for improving research participation as well. Finally, it aims to create a locally pertinent impact measurement model for interventions that aim to enhance black ethnic minorities' representation in PPIE and research within the Leicester BRC and the LLR healthcare system as a whole.

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# Informing inclusion training for health research professionals: A systematic review with thematic narrative synthesis of cultural competency and diversity training in healthcare and research

Emma Beeston | BRC

**Background**

We live in a world where migration has always occurred, but currently, increasing numbers of people are leaving their countries of birth due to economic instability, political conflict, violence, persecution, or climate change (1). As the UK becomes more diverse, it is vital for healthcare professionals to be as culturally competent as possible to meet the needs of the populations they serve and to recruit representative cohorts into health research (2, 3).

The importance of cultural sensitivity in healthcare is not a new phenomenon. In the 1950s, Madeleine Leininger developed transcultural nursing theory, which emphasised the need to provide culturally appropriate care in order to reduce health inequalities and poor health outcomes (4). Since then, various models of cultural competence, such as those by Camphina-Bacote (1991), Betancourt (2000), Papadopoulos *et al*., (1998) and Sue & Sue (1981) have informed many training programmes (5). The term 'cultural competence' remains widely used in training and education interventions, but it is now widely accepted that it is not possible to be competent in all cultures. This has led to a shift toward concepts like cultural humility, cultural sensitivity and cultural safety emphasising an on-going journey of personal and professional development (6, 7).

**Aims / Objectives**

This systematic review aims to map and synthesise literature on cultural competence and diversity and inclusion training for healthcare professionals working in primary, secondary, or social care and for health researcher professionals working in any healthcare field or related area. The review seeks to identify existing training programmes, their design and delivery, how they are evaluated for effectiveness and if they can be adapted or utilised to inform the development of a tailored inclusion training package for health research professionals (8).

**Methodology and Main Body**

This systematic review will follow PRISMA guidelines (9). Searches will be conducted using Web of Science, SCOPUS, Ovid Medline and CINAHL, focusing on literature published in English. Inclusion criteria will cover any type of cultural competence, inclusion or diversity training for healthcare or health research professionals that includes an evaluation or outcome measure. A thematic narrative synthesis will be conducted using the approach outlined by Popay *et al*., (2006) (10).

**Conclusions / Implications for practice**

Although cultural competence training for healthcare providers is widely available, there is limited evidence of training specifically designed for research professionals. This review will examine existing literature and explore whether current healthcare training programs can be adapted to support the development of tailored inclusion training for health research. The findings will be valuable for inclusion leads, research managers, partners and others in health and care research. Such training could ultimately enhance study design, participant recruitment, retention and patient benefit (11).

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## Ischaemic lesions in acute intracerebral haemorrhage: pathophysiological investigation using novel multimodal cerebral and systemic haemodynamic assessments (CHALLENGE-ICH)

Sarah Matuja | BRC

**Background**

The Cerebral Haemodynamics in Ageing and Stroke Medicine (CHiASM) Research Group bridge the gap between technical studies in cerebrovascular physiology in the context of intracerebral haemorrhage, and delivery of clinical stroke care and research. This is a vital but uncommon niche, and exactly what is required to deliver translational programmes of research with the potential to deliver significant improvements in stroke care, in reasonable time frames. We hypothesise that the burden of ischaemic lesions in intracerebral haemorrhage is greatest in those with the most affected cerebral haemodynamic phenotype (determined by degree of BP lowering, dynamic cerebral autoregulation status, lowest achieved resting end-tidal carbon dioxide and burden of pre-existing small vessel disease).

**Aims / Objectives**

To determine the relationship between cerebral haemodynamic variables and ischaemic lesions on magnetic resonance imaging (MRI) post intracerebral haemorrhage in the first multi-modality study combining real-time dynamic assessment, radiological and clinical end-points.

**Methodology and Main Body**

This will be a multi-modality prospective observational cohort study at the University Hospitals of Leicester (UHL) NHS Trust. Patients with acute intracerebral haemorrhage will be recruited within 24 hours of onset at University Hospitals of Leicester NHS Trust. Transcranial Doppler ultrasound will be conducted during supine rest. Beat-to-beat non-invasive blood pressure will be recorded continuously using the Finometer cuff device attached to the middle finger of the non-dominant hand (non-hemiparetic hand in stroke patients). R-R interval will be recorded using a 3-lead ECG. Respiratory rate will be recorded, and end-tidal partial pressure of carbon dioxide ($EtCO_2$) monitored using small nasal cannulae placed at the base of the nose (Salter Labs, ref 4000) attached to a capnograph (Capnocheck Plus) to monitor respiration. Simultaneous bilateral insonation of the middle cerebral arteries (MCAs) will be performed with the subject lying supine on a couch using TCD (DWL Dopplerbox 10.5.1 software version) to measure cerebral blood velocity as the most widely accepted surrogate of cerebral blood flow in dynamic cerebral autoregulation studies. The candidate will develop expertise in real time data collection of multiple variables, advanced methods of modelling cerebral blood velocity regulation, leading to parameters that will be subjected to multivariable logistic regression in order to evaluate determinants of ischaemic lesions.

**Conclusions / Implications for practice**

This study will deliver new data on the role of carbon dioxide change in the development of ischaemic lesions post intracerebral hamerrohage, investigate the interaction with blood pressure lowering post intracerebral hamerrohage and develop functional MRI data to inform greater understanding of the relationship between cerebral vasomotor reactivity and ischaemic lesions. The risk of ischaemic stroke after a haemorrhage remains a concern, however, more pressingly the potential that existing treatments we deliver may contribute to this risk is important to discern. Through this PhD studentship, there will be data generated that will either confirm or refute the contribution of haemodynamic change on ischaemic stroke risk – something post-hoc trial data (does not assess aspects such as dynamic cerebral autoregulation) has not been able to convincingly clarify. This will enable more informed decision making for clinicians and consequently opportunities for patients to understand the risks associated with commonly delivered treatments including blood pressure lowering.

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# Are Sedentary Behaviour and Physical Activity linked to Markers of Inflammation in Healthy 18-to-50-year olds?

Orla McGinty | BRC

**Background**

Cardiovascular Diseases (CVDs) are the leading cause of death globally, accounting for 32% of deaths in 2019.[1] Sedentary behaviour (SED) is an independent risk factor for CVD, with elevated SED linked to increased CVD incidence and mortality risk.[2,3,4,5] Inflammation represents a potential mechanism by which SED and CVD are linked as inflammation plays a large role in the development, progression and prognosis of CVDs[6,7] and several studies have found a link between SED and inflammation.[8,9,10] However, many of these studies relied on subjective measurement of movement behaviour (i.e. self-report, questionnaires), which may yield inaccurate quantification of SED and physical activity (PA).[11,12] Device-based SED and PA measurement (i.e. accelerometers, inclinometers) provide objective results with high reliability and validity[11,13] that overcome inaccuracies of subjective methods.[11,12]

**Aims / Objectives**

This study aims to investigate:

1. The relationships between device-assessed SED and PA with circulating inflammatory markers.
2. To investigate if these relationships differ based on characteristics such as sex and ethnicity.
3. The effects of compositionally modelled changes in movement behaviours on circulating inflammatory markers.

**Methodology**

This study involves 2 sessions at the National Centre for Sport and Exercise Medicine (NCSEM) at Loughborough University. Session 1 will assess eligibility, with participants eligible if they are normotensive, without any long-term pre-existing conditions, not taking medication regularly, non-obese, non-smokers or vapers, and not regularly consuming excessive amounts of alcohol. Once eligibility is confirmed, anthropometric measures of body composition (e.g., body fat, waist circumference) will be taken before completion of a questionnaire pack assessing psychosocial and lifestyle factors such as PA, SED, stress and sleep. Participants will be fitted with two activity monitors to measure PA (ActiGraph GT3XBT+ (ActiGraph, Pensacola, FL, USA), wrist worn) and SED (ActivPAL (PAL Technologies Ltd., Glasgow, UK), thigh worn) and will be given an activity log. They will wear these devices and complete their normal activities for 8 days to measure habitual movement behaviours. Following this monitoring period, a venous blood sample will be taken for analysis of circulating inflammatory markers (e.g. monocytes subsets, interleukin-6). Activity monitor data will be analysed to determine movement behaviours including minutes of SED, light intensity PA (LPA), and moderate-vigorous PA (MVPA). Generalised linear models will be used to determine relationships between movement behaviours and markers of inflammatory-immune activity and will be adjusted for *a priori* determined covariates.

**Hypotheses**

We hypothesise that those spending higher amounts of time engaging in SED and those with more prolonged bouts of sedentary time will have higher markers of inflammation. We hypothesise that those with higher amounts of PA and those who break up sedentary bouts more frequently will have lower markers of inflammation. We also hypothesise that theoretically modelled reductions and reallocations of sedentary time and will have a beneficial influence on inflammatory markers.

**Future directions**

From this study, we hope to identify associations between movement behaviours and inflammatory markers, and use this information to develop personalised interventions to reduce sedentary behaviour and assess its impact on inflammation. Our study will add to existing evidence using a gold-standard measurement approach in a diverse and representative sample.

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## Loop Diuretic Use as a Marker of Hidden Heart Failure in Cardio-Renal-Metabolic Disease: Insights from Clinical Trials, Real-World Data, and Health Economic Modelling

Riaz Alaei Kalajahi | BRC

**Background**

Heart failure (HF) is a complex clinical condition that marked by elevated intracardiac pressures or reduced cardiac output (1, 2) often arising from cardiorenal metabolic (CRM) disorders. It is associated with high mortality, morbidity and reduced health related quality of life.

Timely diagnosis is vital, but in primary care limited access to testing can delay recognition. In a study of 36,748 patients with newly diagnosed HF patients, 79% of patients were diagnosed in hospital. Notably, 41% had presented with key HF symptoms in primary care up to 5 years earlier, yet only 24% followed NICE HF guideline recommended pathways, and 44% received no diagnostic testing or referral.(3, 4).

Loop diuretics (LD) are widely used to treat congestion in HF. However, many CRM patients are prescribed LD in primary care without a HF diagnosis. These patients show similar mortality and hospitalisation rates to those diagnosed with HF, and often share similar clinical profiles (3).

This suggests that LD use may indicate elevated HF risk and supports the hypothesis that some CRM patients on LD without an HF diagnosis may have undetected or masked HF.

**Aims / Objectives**

The **overall aim** of the thesis is to investigate whether loop diuretic use in individuals with cardio-renal-metabolic conditions is a marker of hidden heart failure, by evaluating its reporting in clinical trials, describing its epidemiology in routine care, assessing its association with adverse outcomes, and estimating the potential health and economic impact of earlier recognition and treatment.

In **four linked phases** the **objectives** are:

(i) To evaluate how and whether loop diuretic use is reported and addressed in the analyses of cardio-renal-metabolic trials and identify whether **loop diuretic use** is associated with higher **risk of adverse outcomes (phase 1)**

**(ii)** To describe the epidemiology of loop diuretic prescribing in primary care in patients with or without future heart failure diagnosis and to phenotype patients with potentially missed diagnosis (phase 2)

(iii) To investigate whether loop diuretic use in patients with cardio-renal-metabolic conditions is associated with an increased risk of adverse outcomes, suggestive of hidden heart failure using real world data

(iv) To estimate the healthcare costs and resource utilisation associated with loop diuretic use in patients with cardio-renal-metabolic conditions, and to model the potential economic impact of earlier recognition and treatment of hidden heart failure in this population

**Methodology and Main Body**

(i) Systematic review of RCTs to evaluate how and whether loop diuretic use is reported and addressed in the analyses of Cardio-renal-metabolic (CRM) trials and identify whether **loop diuretic use** is associated with higher **risk of adverse outcomes.**

(ii) CPRD study to describe the epidemiology of loop diuretic prescribing in primary care in patients with or without future heart failure diagnosis, to investigate the predicitors of future HF diagnosis and outcomes and to phenotype patients with potentially missed diagnosis. Methods: descriptive, dose and dose change measurement, logistic regression and survival analysis

(iii) CPRD study to investigate whether loop diuretic use in patients with CRM conditions is associated with an increased risk of adverse outcomes, suggestive of hidden heart failure using real world data. Methods: propensity matching, survival analysis

(iv) CPRD study to estimate the healthcare costs and resource utilisation associated with loop diuretic use in patients with cardio-renal-metabolic conditions, and to model the potential economic

impact of earlier recognition and treatment of hidden heart failure in this population. Methods: Incremental cost difference and cost trajectories, multi-state modelling

**Conclusions / Implications for practice**
Recognition of patients with CRM conditions at higher risk of future events of HF will be important for:

- designing future CRM trials
- developing tailored HF screening strategies
- designing cost saving strategies.

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## Utilizing LifeMap to investigate malignant arrhythmia therapeutic efficacy in athletes (Ultimate-Athlete)

Abdulmalik Idris Koya | BRC

**Background**

Although exercise is associated with an increase in overall health and quality of life[1], sudden cardiac death (SCD) remains a major cause of death among exercise enthusiasts. Implantable cardioverter defibrillators (ICDs) are preventative when the right candidate is selected for implantation [2]. Previous guidelines have advised against sports participation for athletes at risk [3]. While expert consensus and emerging data show the promise of safe sport participation for athletes with ICDs [4], there is a need to investigate who will truly benefit. Intrinsic markers of cardiac action potential duration have been promising in identifying those at greatest risk of SCD [5].

**Aims / Objectives**

We aim to measure cardiac action potential markers in healthy athletes using UoL's patented LifeMap and compare them with athletes identified as at risk of SCD.

**Methodology and Main Body**

In a case-control design, we will compare markers of cardiac action potential duration using the UoL patented LifeMap. LifeMap utilizes two markers of action potential duration, regional restitution instability index, and peak electrocardiogram restitution slope to detect myocardial electrical instability during exercise and non-invasive electrophysiology testing.

**Implications for practice**

We anticipate the findings from this study will imply that the invasive LifeMap technique will be equal to non-invasive exercise recording, and recreational and competitive sports enthusiasts at risk of SCD will be correctly identified, which will translate to safe sports participation.

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## Integrative approach to understand the gut and circulatory viral association in heart failure

Mohammad Hossein Razizadeh | BRC

**Background**

Heart failure is a chronic and progressive disease in which the heart is unable to pump enough blood to meet the body's needs. It is usually caused by damage to the heart muscle (for example, after a heart attack), uncontrolled blood pressure, valvular disease, or structural heart disease. Patients often present with symptoms such as shortness of breath, chronic fatigue, swelling of the extremities, and decreased tolerance to daily activities.

It has been suggested that the virome (the collection of viruses in the body) may play an important role in the pathophysiology of heart failure. Viral infections have been associated with myocardial injury, chronic inflammation, and impaired heart function. Also, the gut virome (including bacteriophages) may influence the progression of heart failure through microbiome-dependent immune and metabolic mechanisms.

**Aims / Objectives**

The aim of this study is to explore the link between gut and blood viromes in the pathophysiology of HF and investigate past and current viral exposures through serum antibody repertoire epitope sequencing. Our objectives are to develop methodologies, sequencing strategies, and data integration protocols to unravel the role of the human virome in heart failure.

**Methodology and Main Body**

This research is going to be accomplished by analysis of gut and circulatory viromes in faecal and blood samples, respectively, using virus-enriched long-read metagenomics (Nanopore). The serum antibody repertoire of the patients will be analyzed by an M13 phage-based random peptide display system and short-read sequencing (Illumina) to identify epitopes recognised by immunoglobulins. Data from the different systems will be integrated at the genome level. Selection processes will be explored. All biological samples have been obtained from the same patients in the University Hospital Heidelberg (Dr. Ashraf Yusuf Rangrez).

**Conclusions / Implications for practice**

This research can extend our understanding of the human virome associated with heart failure and the role of the adaptive immune system in shaping the structure of the virome. This knowledge will deepen our understanding of viral signatures at the system level and provide the basis for hypothesis-driven research. The analytical pipelines that will be established can be used to unravel the mysteries of other human diseases (e.g., chronic infections, microbiome/virome dysbiosis, and autoimmunity).

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## Establishing normative ranges for cardiopulmonary function and physiology for transgender people: a pilot, feasibility study

Naila Niaz | BRC

**Background**

Transgender individuals face significant disparities in cardiovascular health, with studies reporting altered lipid profiles, increased insulin resistance, elevated blood pressure, and a potentially higher incidence of cardiovascular events such as myocardial infarction and venous thromboembolism following gender-affirming hormone therapy (GAHT) (1–3). Despite these risks, reference values for cardiac volumetry and function in transgender people remain undefined. Cardiovascular Magnetic Resonance Imaging (CMR) is the gold standard for assessing cardiac structure and function (4-5), yet normative values have not been established for those on long-term GAHT. Quantitative measures—such as ejection fraction, end-diastolic and end-systolic volumes, stroke volume, and myocardial mass—are essential for diagnosing cardiac conditions, guiding treatment decisions, and predicting patient outcomes. Moreover, GAHT has been shown to influence vascular stiffness and endothelial function, particularly in transgender men (6-7). Understanding these physiological changes is essential to inform inclusive, evidence-based cardiopulmonary assessment and care. However, research participation barriers—like stigma and concerns about safety—limit transgender inclusion and slow progress toward inclusive clinical guidance.

**Objectives**

Primary objective

- To assess the feasibility of measuring cardiac volumetric indices in transgender people who have been on cross-gender hormone treatment for over 2 years.

Secondary/exploratory objectives

- To measure cardiopulmonary fitness in transgender people who have been on cross-gender hormone treatment for over 2 years
- To explore potential barriers to research participation by transgender people

**Methods**

This single-center, observational, cross-sectional pilot study will recruit 50 transgender adults (25 transmasculine and 25 transfeminine), aged ≥18 years, with over 2 years of GAHT. Participants will undergo:

1. CMR will be used to measure left ventricular (LV) end-diastolic and systolic volumes, LV mass, and ejection fraction. The protocol will include late gadolinium enhancement (LGE) sequences to assess myocardial fibrosis or scarring, which may reflect subclinical myocardial damage or remodelling related to long-term hormone therapy.
2. Cardiopulmonary Exercise Testing (CPET) will be conducted to determine peak oxygen uptake ($VO_2$ max) and other ventilatory parameters. VO2 serves as a key indicator of aerobic capacity and overall cardiopulmonary fitness.
3. Quadriceps strength testing using isometric dynamometry to assess peak torque in the dominant leg.
4. Qualitative interviews to explore perceived barriers to research participation, analysed using the Framework Method (8).

Quantitative data will be analysed descriptively, and normative ranges defined as mean ± 2 standard deviations. Statistical comparisons will use t-tests or non-parametric equivalents, with $p < 0.05$ considered significant. Thematic analysis will be applied to qualitative data, providing contextual understanding and highlighting participant-reported barriers and enablers.

**Discussion/Implications**

This study addresses a critical gap in the literature by establishing baseline physiological data for transgender individuals on long-term GAHT. Integrating CMR, CPET, and strength testing provides a

comprehensive assessment of cardiopulmonary and musculoskeletal function. The qualitative component offers insight into research participation barriers, supporting the development of more inclusive and accessible study designs. Although limited by its cross-sectional nature and single-site setting, findings will guide future longitudinal research and promote gender-affirming clinical practice. Ultimately, this work lays the foundation for reference values that can improve diagnosis, risk stratification, and care planning in transgender health.

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## Epidemiology of Cardiometabolic Disease

Lauren Anderson | BRC

**Background**

Cardiometabolic disease rates are growing globally (1). Cardiovascular disease (CVD), chronic kidney disease (CKD) and type 2 diabetes mellitus (T2DM) are recognized as being frequently co-occurring cardiometabolic conditions (2), and are shown to be leading causes of death worldwide (3).

CVD, CKD and T2DM can all be described as long-term conditions. The presence of multiple long-term conditions (MLTCs), defined as two or more long term conditions, leads to a reduced quality of life, greater healthcare demands and higher mortality rates (4). The number of individuals with MLTCs has increased as interventions improve and with ageing populations (5). T2DM, CVD and CKD are all linked to having comorbidities, and an increased risk of MLTCs (5-7).

**Aims / Objectives**

Aim 1: To determine the prevalence and incidence of CVD, CKD (stages 3a to 5) and T2DM, individually and in combination.

Aim 2: To investigate the ordering and timing of CMD events in the general population, individually and in combination.

Aim 3: Risk factors associated with the development of CMD conditions, and their combinations.

Aim 4: Associations with all-cause and cause-specific mortality.

**Methodology and Main Body**

This is a retrospective cohort study that will use a random sample of 1 million individuals (age ≥18) from the CPRD dataset. Incidence and prevalence rates will be determined for each of the conditions individually and in combination. Stratification by age groups and ethnicity will also be considered. Investigation into whether there are any patterns in the ordering and timing of development for CMD conditions will be conducted. To visualise timings of occurrence, a stacked area plot will be used. We will also assess whether any risk factors predict the onset of CMD conditions. This includes whether any are driving the development of a second or third condition. Sankey plots will be used to visualise the flow of individuals through the development of each condition and the associations with mortality.

Throughout, there may be missing data, where some variables were not recorded or collected. These will be imputed using MICE methods, where appropriate.

**Discussion/ Implications for practice**

The results of this project could increase early detection and targeted interventions, preventing or delaying the onset of CMD. This would reduce the burden of CMD and MLTCs and improve long-term health outcomes. Furthermore, understanding of how these conditions interact could lead to improved prediction models, and more accurate risk predictions.

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## Weight changes adversely affect markers of glycaemic control and insulin resistance in a South Asian and White cohort living with obesity at high risk of type 2 diabetes

Frank Arsenyadis | LHIIP

**Background**

Weight gain can impact cardiometabolic health and increase the risk of chronic conditions linked to excess adiposity such as Type 2 Diabetes (T2D).

**Aims / Objectives**

The aim of this analysis was to investigate the ethnicity interaction (White European, South Asian) between changes in body weight and markers of glycaemia (following Oral Glucose Tolerance Test (OGTT) in a cohort living with obesity at high risk of T2D.

**Methodology and Main Body**

This analysis reports cohort data from the PROPELS (ISRCTN: 83465245) 3-arm randomised controlled trial which recruited people from primary care at high risk of type 2 diabetes. Measures of weight and markers of glycaemia were obtained at Baseline, 1-year and 4-years across all randomised groups including demographic, medical characteristics and lifestyle behaviours. All three trial arms were analysed as a single cohort to investigate the ethnicity interaction between changes in body weight and changes in markers of glycaemia (2-hour post-prandial glucose and insulin, Homeostatic Model Assessment for Insulin Resistance (HOMA-IR) and Matsuda Index). Generalised estimating equation models adjusted for randomisation group, sex, age, occupation, deprivation, smoking, statin or blood pressure medication status, baseline OGTT parameters and baseline bodyweight were used to analyse associations between change in body weight and change in 2-hour post-prandial glucose (Model 1), 2-hour post-prandial insulin (Model 2), HOMA-IR (Model 3) or Matsuda Index (Model 4).

**Results**

467 participants had ≥2 weight observations and formed the sub-cohort that undertook OGTT; 318 (50.2% female) were White European (WE) and 149 (42.2 % female) were South Asian (SA). An ethnicity interaction was observed for 2-hour post-prandial glucose (p=.003), where each kilogram increase in weight was associated with a 0.2mmol/mol (95% CI: 0.1mmol/mol to 0.3mmol/mol) increase in 2-hour post-prandial glucose in SA compared to 0.1mmol/mol (0.04mmol/mol to 0.1mmol/mol) in WE, a 2.6pmol/l (0.5pmol/l to 4.7pmol/l) increase in 2-hour post-prandial insulin in SA compared to a 1.6pmol/l, (0.7pmol/l to 2.4pmol/l) in WE, a 0.03 (0.01 to 0.05) increase in HOMA-IR in SA compared to a 0.02 (0.01 to 0.03) in WE, and a -18.2 (-28.6 to -7.8) decrease in Matsuda Index in SA compared to a -14.6 (-24.6 to -4.6) in WE. Associations were linear in each model.

**Conclusions / Implications for practice**

Weight increase had a greater adverse impact in 2-hour post-prandial glucose and insulin during OGTT, HOMA-IR, Matsuda Index in SA compared to WE ethnic groups living with obesity. These results require replication but highlight the need for a personalised and targeted approach for T2D prevention in high risk populations.

# Metabolic score for insulin resistance (METS-IR) and visceral fat (METS-VF): exploring their predictive utility for insulin sensitivity and adiposity in White European and Black African populations

Farid Salimi Shojaei | BRC

**Introduction**

Reduced insulin sensitivity (IS) and increased visceral adipose tissue (VAT) are critical determinants of the metabolic complications of obesity. Nevertheless, their accurate assessment remains complex, expensive, and limited in accessibility. The Metabolic Score for Insulin Resistance (METS-IR) and the Metabolic Score for Visceral Fat (METS-VF) are emerging as inexpensive, practical indices for addressing this gap. Although these metrics have been applied in White European (WE) populations, their performance in Black African (BA) populations—who develop impaired IS and type 2 diabetes (T2D) at lower levels of VAT—remains insufficiently explored. This study aims to evaluate the utility of METS-IR in estimating IS and METS-VF in predicting VAT across both WE and BA populations with varying degrees of glucose tolerance (GT).

**Methodology**

Data were collected from 96 men across a spectrum of GT, including 49 WE (23 normal GT, 9 impaired GT and 17 with T2D) and 47 BA (19 normal GT, 10 impaired GT, 18 with T2D). Participants underwent a 2-step hyperinsulinaemic-euglycaemic clamp and Dixon magnetic resonance imaging (MRI) to assess IS and VAT, respectively. Fasting venous blood samples were collected to measure serum triglycerides, high-density lipoprotein cholesterol, and plasma glucose. These variables, together with body mass index, were subsequently used to derive METS-IR and METS-VF scores using established formulae. Regression analyses were conducted in R Statistical Software (v4.2.1; R Core Team 2021) to assess the relationship between METS-IR and IS, as well as METS-VF and VAT. Ethnicity and glucose tolerance status were considered as covariates.

**Results**

METS-IR was significantly associated with IS across the entire sample ($\beta = -0.0189$, $R2 = 0.43$, $p<0.001$), with similar predictive strength observed in BA ($\beta = -0.0154$, $R2 = 0.36$, $p<0.001$), and WE ($\beta = -0.0215$, $R2 = 0.49$, $p<0.001$). Interaction analysis indicated no significant moderation by ethnicity ($p = 0.18$). METS-VF demonstrated strong associations with VAT in the overall sample ($\beta = 39.35$, $R2 = 0.56$, $p<0.001$), with predictive differences between BA ($\beta = 27.87$, $R2= 0.53$, $p<0.001$) and WE ($\beta = 43.57$, $R2= 0.63$, $p<0.001$). The overall predictive utility of both scores for IS and VAT remained significant across GT categories.

**Conclusions**

METS-IR and METS-VF accurately predicted insulin sensitivity and visceral adiposity in BA and WE populations. While METS-VF demonstrated slightly reduced predictive strength in BA compared with WE, it remained a robust predictor in both groups. Both scores also demonstrated consistent predictive utility for IS and VAT across all GT categories. Further studies are needed to investigate the role of these indices in metabolic disease prevention.

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# Chrono nutrition, a potential dietary treatment to support glycaemic control in pregnant women with diabetes: a systematic review and meta-analysis

Cerys Deakin | BRC

**Background**

The increasing prevalence of diabetes, particularly with an earlier age of onset, presents new challenges, especially regarding the co-occurrence of diabetes in pregnant women. Key guidelines emphasize lifestyle interventions as the cornerstone of care, yet there is a significant lack of clarity on what the optimal interventions are. The global diabetes burden continues to rise, with an estimated 838 million people affected, marking a 31% increase since 1990. This trend poses significant health risks for both mothers and babies, impacting immediate health and long-term outcomes. Chrono-nutrition, an emerging field, may offer a promising treatment approach for pregnant women with diabetes. By identifying optimal times for food intake and restricting eating to those periods, chrono-nutrition could potentially enhance glucose control and prevent adverse pregnancy outcomes.

**Aims / Objectives**

Hypothesis: it is anticipated that this systematic review will identify the following

1. Consuming proportionally more energy and/or carbohydrates earlier on in the day is beneficial to glucose control and/or pregnancy outcomes in pregnant women with/without diabetes
2. More or larger RCT's with pregnant women and diabetes are required to reliably conclude the former and implement into care practices

Aims:

Primary aim-

- To identify if chrono nutrition can improve glycemic control during pregnancy for both healthy pregnant women and pregnant women with diabetes

Secondary aim-

- To identify if chrono nutrition has potential to be a beneficial treatment strategy for DIP.
- To identify if there is an ideal approach to chrono-nutrition.

Questions:

1. What are the effects of chrono nutrition on glycaemia in pregnant women with diabetes?
2. What are the effects of chrono nutrition on pregnancy outcomes in pregnant women with diabetes?
3. What were the techniques, and was there an ideal approach to chrono nutrition?
4. If deemed beneficial, to what extent can chrono nutrition be practically applied to clinical care?

**Methodology and Main Body**

A comprehensive literature search was conducted using Medline, Cochrane Library, EMBASE, SCOPUS, and CINAHL. Boolean operators linked terms related to pregnancy, diabetes, and chrono-nutrition. The search was limited to human studies and covered dates from the earliest available time until March 3, 2025. Predefined inclusion and exclusion criteria were discussed among reviewers. Studies included pregnant women at risk for gestational diabetes or other diabetes types, focusing on chrono-nutrition interventions. Exclusion criteria covered animal studies, unrelated interventions/outcomes/population, qualitative study designs, and reviews. 4 reviewers conducted the screening using Endnote and Rayaan, with disagreements resolved by discussion.
Data extraction and analysis Is yet to be done.

**Results**

All 6055 resulting records were exported into EndNote where 961 duplicates were removed. In endnote, title screening was undertaken by 1 reviewer (CD) whereby 4807 articles were excluded.

The 287 remaining records were then exported to Rayaan for further screening. Abstract screening was conducted by 4 reviewers and disagreements were resolved by discussion
Full text screening, data extraction, and analysis is yet to be done.

**Conclusions / Implications for practice**
It is anticipated that the results will highlight specific times of day when glucose control may be weaker. However, it is expected that there will be insufficient evidence to draw reliable conclusions or provide definitive guidance for care providers regarding optimal eating times. Further research into the identified time points may be necessary to develop evidence-based guidelines for using eating timing as a strategy to optimize blood glucose control in pregnant individuals with diabetes. If this approach proves beneficial, it is expected to have minimal time, cost, and burden implications for healthcare workers, patients, and the NHS, given its low cost and ease of implementation.

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## Mitochondrial Adaptations to GLP-1RA, GLP-1RA/GIP, and Amylin Analog Therapy in Skeletal Muscle

Victoria Old | BRC

**Background**

The increasing prevalence of obesity and type 2 diabetes mellitus (T2DM) has led to greater use of pharmaceutical weight management interventions. GLP-1 receptor agonists (GLP-1RAs) like semaglutide have demonstrated weight reductions of up to 15%, while the dual GLP-1RA/GIP agonist tirzepatide has achieved losses of approximately 20%. Amylin analogs (AAs) such as cagrilinitide show more modest reductions (~10%) but may be combined with GLP-1RAs. However, concerns have emerged regarding skeletal muscle loss, with studies indicating up to 40% of total weight loss comes from muscle loss. Given skeletal muscle's significant mitochondrial content and the role of mitochondrial dysfunction in obesity-related diseases, evaluating the effects of these therapies on mitochondrial function is crucial.

**Aims / Objectives**

This study examines mitochondrial respiration following exposure to these pharmacological agents.

**Methodology and Main Body**

C2C12 myotubes were cultured and treated with low and high doses of GLP-1RA (semaglutide), GLP-1RA/GIP (tirzepatide), or AA (cagrilinitide) for 48 hours and 5 days to model short- and long-term effects (n=6). Mitochondrial respiration was assessed using the Seahorse Mito Stress Test.

**Results**

Basal respiration was significantly reduced in semaglutide- and cagrilinitide-treated cells at 48 hours compared to control ($P<0.05$). Tirzepatide caused a significant reduction between 48 hours and 5 days ($P<0.0001$). ATP production declined significantly at 48 hours in semaglutide and cagrilinitide groups ($P<0.05$) and at 5 days for tirzepatide ($P<0.05$). However, maximal respiration increased significantly in tirzepatide-treated cells at 5 days ($P<0.005$). Proton leak was significantly reduced in tirzepatide-treated cells between 48 hours and 5 days ($P<0.005$). Spare respiratory capacity increased significantly at 48 hours in the high-dose semaglutide group ($P<0.005$) and at 5 days in tirzepatide-treated cells ($P<0.005$). Non-mitochondrial oxygen consumption was significantly reduced at 48 hours in semaglutide ($P<0.05$) and high-dose cagrilinitide groups ($P<0.05$).

**Conclusions / Implications for practice**

These findings indicate that pharmacological weight loss interventions impact mitochondrial respiration in skeletal muscle. Early reductions in basal respiration and ATP production, particularly in semaglutide and cagrilinitide, suggest mitochondrial downregulation in the initial phase. Tirzepatide demonstrated a distinct pattern, with reduced ATP production but increased maximal respiration and spare capacity at 5 days, suggesting mitochondrial adaptation. The reduction in proton leak with tirzepatide may reflect improved mitochondrial efficiency. Further studies are needed to assess the clinical relevance of these findings.

## Association Between Type 2 Diabetes and Fracture Risk: Site-Specific Differences – A Systematic Review and Meta-Analysis of Cohort Studies

Sara Naderpour | BRC

**Background**
Type 2 diabetes is associated with an increased risk of fracture; however, the impact of T2D and subsequent fracture at different sites remains inconclusive.

**Aims / Objectives**
This systematic review and meta-analysis aimed to quantify the association between T2D and the risk of fracture at different sites by synthesising findings from prospective and retrospective cohort studies.

**Methodology and Main Body**
A thorough systematic literature search was performed across the Medline, Embase, CINAHL, and Web of Science databases to identify observational studies comparing fracture risk between patients with and without diabetes, up to June 7, 2024.
Based on the variation in fracture sites reported in the studies, we classified fractures according to anatomical criteria into seven main groups: 1- Axial (Vertebral + Pelvic), 2- Axial (Cranial), 3- Appendicular (Upper Limb), 4- Appendicular (Lower Limb), 5- Appendicular unspecified, 6- Osteoporotic or Fragility fracture, 7- Any Fracture. To evaluate the strength of association with T2D, we used pooled Hazard Ratios (HR) with corresponding 95% confidence intervals (95% CI) through a random-effects model. This study is registered in PROSPERO (CRD42024548795).

**Results**
Out of 5,533 studies, 21 cohort studies comprising 12,153,334 individuals were included in the meta-analysis. The included studies included a total of 2,470,199 individuals with T2D, among whom 44,174 fractures were reported. In addition, 9,683,135 individuals without T2D were included, with 109,431 fractures recorded. The pooled hazard ratio (HR) for total fractures among individuals with T2D compared to non-diabetic individuals was 1.27 (95% CI: 1.22–1.32), indicating a 27% increased risk. T2D was significantly associated with an increased risk of appendicular lower limb fractures (HR: 1.43), upper limb fractures (HR: 1.29), osteoporotic/fragility fractures (HR: 1.14), appendicular unspecified fractures (HR: 1.20), and any fracture (HR: 1.17). No significant association was found for vertebral + pelvic (HR: 1.06) or cranial fractures (HR: 1.56; wide CI). Meta-regression analyses showed that male percentage and diabetes duration significantly modified fracture risk, particularly for lower limb fractures.

**Conclusions / Implications for practice**
Type 2 diabetes is associated with an increased risk of fractures, particularly in the appendicular skeleton and osteoporotic sites, despite often normal or elevated bone mineral density. These findings highlight the importance of targeted fracture prevention strategies and site-specific risk assessment in individuals with T2D.

**Keywords**
Type 2 diabetes, fragility fracture, Hip fracture, fracture risk

## SGLT2I reduces obesity associated cancers in people living with type two diabetes

Testimony Ipaye | BRC

**Background**

Obesity is a well-established risk factor for 13 specific malignancies collectively referred to as obesity-associated cancers (OAC) (1). Weight-reducing interventions such as bariatric surgery and glucagon-like peptide-1 receptor agonists (GLP-1 RAs) have been associated with a reduced risk of OAC (2-4). However, the scalability of bariatric surgery is limited, and access to GLP1 RAs remains a challenge (5,6). Sodium-glucose co-transporter 2 inhibitors (SGLT2i), a class of antidiabetic agents commonly used as second-line therapy for type 2 diabetes (T2D), promote weight loss, yet their impact on OAC incidence remains unclear.

**Aims / Objectives**

To compare the incidence rates of all cancers as a composite outcome, all OAC as a second composite outcome, and individual OAC among patients with T2D prescribed SGLT2i versus dipeptidyl peptidase-4 inhibitors (DPP4i).

**Design, Setting, and Participants**

This retrospective cohort study was based on a us collaborative network in the TriNetX federated research database. The study population included patients from 141 health care organizations with T2D who had no prior diagnosis of cancer and were prescribed SGLT2i or DPP4i. Exposures is the prescription of SGLT2i or DPP4i. The incidence of all cancers collectively, OAC collectively, and individual OAC was assessed using cox proportional hazards models and Kaplan-Meier survival analyses. Hazard ratios (HRs), cumulative incidence, and 95% confidence intervals (CIs) were calculated. All models were adjusted for baseline confounders through propensity score matching.

**Results**

In a study population of 105,857 patients with T2D, with or without obesity, SGLT2i use compared to DPP4i was associated with a significant reduction in the incidence of composite all cancers (HR = 0.787; 95% CI, 0.754–0.823) and composite OAC (HR = 0.837; 95% CI, 0.783–0.896). A significant risk reduction was also observed for 5 of 12 individual OAC, including colorectal cancer (HR = 0.768; 95% CI, 0.652–0.905), gallbladder cancer (HR = 0.335; 95% CI, 0.122–0.923), renal cancer (HR = 0.804; 95% CI, 0.662–0.976), liver cancer (HR = 0.764; 95% CI, 0.637–0.917), and thyroid cancer (HR = 0.726; 95% CI, 0.531–0.992). Among 83,921 patients with both T2D and obesity, SGLT2i was associated with a significant reduction in composite all cancers (HR = 0.752; 95% CI, 0.717–0.788), composite OAC (HR = 0.796; 95% CI, 0.739–0.857), and three individual OAC: breast cancer (HR = 0.816; 95% CI, 0.704–0.946), colorectal cancer (HR = 0.750; 95% CI, 0.628–0.896), and liver cancer (HR = 0.675; 95% CI, 0.549–0.830). In 12,092 patients with T2D but without obesity, SGLT2i was associated with a reduction in composite all cancers, composite OAC, and 8 individual OAC; however, these findings did not reach statistical significance.

**Conclusions / Implications for practice**

In this study, SGLT2i use was associated with a lower incidence of all cancers collectively, OAC, and specific individual OAC compared to dpp4i in patients with T2D. These findings suggest that SGLT2i may have weight-independent effects in reducing cancer risk. Our results provide preliminary evidence of the potential role of SGLT2i in cancer prevention, particularly in high-risk populations.

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## The effect of exercise induced dehydration on post prandial glycemic response

Emma McClelland | BRC

**Background**

Certain populations, including occupational, recreational and competitive exercisers, as well as manual workers and emergency services, are susceptible to dehydration, particularly when activity is undertaken in warm/hot environments (Kingma *et al*., 2014; Hannan *et al*., 2024). The physical and cognitive consequences of dehydration are well documented (James *et al*., 2017; Wittbrodt and Millard-Stafford, 2018); however, effects on metabolic health are less understood with a paucity of data on exercise-induced dehydration and metabolic health. With climate change greatly increasing heat exposure and potential for dehydration, the effects of dehydration on glucose regulation and metabolic health needs attention to inform recommendations in relevant populations.

**Aims / Objectives**

This study aims to investigate the effect of exercise-induced dehydration on postprandial glycaemia in healthy adults. Secondary aims will investigate postprandial insulin concentrations, other metabolic responses, cognitive function, and use in-vitro methods to understand potential molecular events explaining findings. It is hypothesised that dehydration will increase postprandial glycemia vs euhydration.

**Methodology and Main Body**

*Study design*

This is a randomised crossover trial involving active (≥150 min moderate intensity activity per week), healthy adults aged 18-45 years. Power analysis (GPower) determined a minimum sample size of 14 for a statistical power of 0.95, alpha of 0.05 and effect size of 1.05. To account for dropouts, 16- 20 participants will be recruited.

*Preliminary Trial*

After consenting, cycling V̇O2peak will be determined, before participants will be familiarised with the cognitive tests and exercise used in experimental trials.

*Experimental Days*

Participants will complete two trials, where they will undertake moderate-intensity intermittent exercise (10 min cycling at ~50% V̇O2peak, 5 min rest) in a hot environment (~36°C, ~50% relative humidity) to produce sweat losses of ~2.5% body mass. Water intake of ~100% (EUH trial) or ~2% (DEH trial) sweat losses will be provided. Post-exercise, participants will complete cognitive testing, a cannula will be inserted, and they will consume a standardised liquid meal (30% estimated daily energy requirement; CHO: 65%, Protein: 15%, Fat: 20%) 1 h post-exercise to explore glycaemic and other relevant metabolic outcomes. Venous blood samples will be collected pre-exercise (venepuncture), pre-meal, and 20, 40, 60, 90, 120, 150 and 180 min postprandial. Serum collected pre-meal will be used for in-vitro experiments.

**Results**

To date, the effects of dehydration on glycaemic responses are mixed (Johnson *et* al., 2017; Carroll *et al*., 2019; Jansen *et al*., 2019; Vanhaecke *et al*., 2020), likely due to different methodologies and populations. As intracellular dehydration caused by hypertonic saline infusion impaired glycaemic control (Jansen et al., 2019), it is expected that the substantial intracellular dehydration caused by exercise-induced sweating will produce similar effects. This may impair insulin signalling and likely increase hepatic glucose output due to a greater stress response (Vanhaecke *et al*., 2020).

**Conclusions / Implications for practice**

These results will help establish recommendations for those undertaking occupational/recreational activity in hot environments given that changes in water intake represent a simple, cheap and accessible modifiable lifestyle behaviour. The results will be used to inform the design of future studies in populations that regularly experience dehydration, including older adults.

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# Using the isotemporal substitution model to examine longitudinal associations between 24-hour movement behaviours and cardiometabolic health in adults at high risk of type 2 diabetes.

Jialin Li | BRC

**Background**

Type 2 diabetes mellitus (T2DM) is a leading global health concern, with prevalence expected to rise from 8.8% in 2017 to 9.9% by 2045 (Standl et al., 2019). In the UK, over 5.8 million people are estimated to be living with diabetes, with type 2 accounting for around 90% of cases (Diabetes UK, 2024). Individuals with T2DM face increased risk of complications such as cardiovascular disease, kidney failure, visual impairment, depression, and amputation (WHO, 2009; Einarson et al., 2018; Alicic et al., 2017).

T2DM is strongly influenced by modifiable lifestyle behaviours. Physical inactivity, prolonged sedentary time, and poor sleep are all independently associated with greater risk of developing diabetes and related complications (Hamilton et al., 2014; Knutson & Van Cauter, 2008). These behaviours are increasingly studied together using a 24-hour movement behaviour framework, which acknowledges the interdependent nature of daily time use (Kracht et al., 2024).

The isotemporal substitution model (ISM) enables researchers to estimate the impact of reallocating time between behaviours. While previous research has often been cross-sectional, recent prospective studies suggest that healthier 24-hour movement patterns are linked to reduced metabolic risk (Zhu et al., 2023; García-Hermoso et al., 2023). However, more longitudinal evidence is needed in high-risk populations.

**Aims / Objectives**

This study aims to examine longitudinal associations between 24-hour movement behaviours (physical activity, sedentary behaviour, and sleep) and cardiometabolic health outcomes in adults at high risk of type 2 diabetes, using the ISM to estimate the effects of reallocating time between behaviours.

**Methodology and Main Body**

This study used longitudinal accelerometer data collected via thigh-worn devices (activPAL) at baseline, 12 months, and 48 months from participants in the PROPELS trial (n = 1125 with valid baseline data). Physical behaviours were processed using ActiPASS, which applied the validated Acti4 algorithm to classify daily time spent in sleep, sedentary behaviour, standing, moving, and exercise-like activities (e.g., running, stair climbing, cycling).

To investigate longitudinal associations between changes in 24-hour movement behaviours and cardiometabolic health outcomes (e.g., HbA1c, fasting glucose, insulin), the ISM was applied. The ISM estimated the effect of reallocating time from one behaviour to another while holding total time constant, enabling meaningful interpretation of behavioural trade-offs. Longitudinal analyses were conducted to assess the impact of within-person changes in movement behaviours on metabolic markers over the 48-month follow-up period.

**Results**

The average 24-hour movement composition at baseline was sleeping (6.8 ± 1.3 hours), sedentary behaviour (10.9 ± 1.9 hours), standing (3.4 ± 1.3 hours), Move (1.3 ± 0.5 hours), walking (1.3 ± 0.5 hours), and exercise-like activity (8.8 ± 8.1 minutes). At 48 months, the composition remained broadly similar: sleeping (6.9 ± 1.4 hours), sedentary behaviour (10.9 ± 1.9 hours), standing (3.4 ± 1.3 hours), move (1.2 ± 0.5 hours), walking (1.3 ± 0.5 hours), and exercise-like activity (9.4 ± 8.5 minutes).

ISM was applied to examine the prospective associations between changes in time-use composition and cardiometabolic health outcomes.

**Conclusions / Implications for practice**

This research contributes to the field of time-use epidemiology by applying the ISM to longitudinal data. The findings offer valuable insights into the health impacts of reallocating time between daily behaviours and may inform targeted prevention strategies and the development of 24-hour movement behaviour guidelines for individuals at high risk of type 2 diabetes.

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## The relationship between physical activity and exercise capacity in adults after COVID-19: One-Year outcomes post-hospital

Lin Wang | BRC

**Background**

We have previously reported that the majority of patients do not feel fully recovered one year after hospital discharge for COVID-19. Understanding the relationship between exercise capacity and daily physical activity (PA) is crucial for developing effective rehabilitation interventions for this population.

**Aims / Objectives**

We therefore aimed to investigate the relationship between exercise capacity and moderate-to-vigorous physical activity (MVPA) in patients post-hospitalisation for COVID-19.

**Methodology and Main Body**

One-year follow-up data from the Post-hospital COVID-19 (PHOSP-COVID) study was used including objective accelerometer data for 14 days and exercise capacity by the Incremental Shuttle Walk Test distance. The relationship between weekly minutes of MVPA and ISWT distance was assessed by Spearman Correlation Coefficient. Quadrant analysis categorised participants into four quadrants based on WHO PA guideline(150 minutes cut-off) and median ISWT scores: Quadrant I (High MVPA, High ISWT), II (Low MVPA, High ISWT), III (Low MVPA, Low ISWT), IV (High MVPA, Low ISWT)

**Results**

640 patients had both measurements at one-year post-hospitalisation for COVID-19: 37% female, mean (SD) age 60.4 (11.5) years, ISWT distance 378 (305), MVPA minutes per day 25.9(24.4). There was a moderate association between ISWT distance and MVPA: 0.52, $p<0.01$. Numbers of participants in each quadrant were I n=206, II n=114, III n=230, and IV n=90.

**Conclusions / Implications for practice**

We report only a moderate positive correlation between MVPA and ISWT performance one year post-hospitalisation for COVID-19, and our data highlights individual treatable traits for physical activity and exercise capacity. Personalised rehabilitation programmes are therefore needed to promote recovery and improve health-related quality of life.

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## Age at diagnosis of type 2 diabetes and accelerometer-assessed physical activity

Jonathan Goldney | LHIIP

**Background**

Physical inactivity is associated with an increased risk of mortality and morbidity. It is therefore essential to understand the association between physical activity and age at diagnosis of type 2 diabetes to inform preventative efforts in individuals with early-onset type 2 diabetes (diagnosis <40 years) who are at a higher risk of complications.

**Methodology**

This cross-sectional study utilised pooled data from studies undertaken at the Leicester Diabetes Centre, England. Physical activity was measured via wrist-worn accelerometery for 7-14 days and type-2 diabetes status and demographic information were self-reported. Using generalised linear models, we predicted differences in moderate-to-vigorous physical activity (MVPA) and likelihood of meeting physical activity guidelines (150mins MVPA/week) between individuals with newly-diagnosed type 2 diabetes vs individuals without diabetes, across age categories (<40, 40-59 and ≥60 years), adjusted for sex, season of accelerometer wear and number of valid wear days.

**Results**

In total, 1,817 individuals were included (49.3% women; 62.9% with type 2 diabetes; mean age [SD] 55.3 years [13.7]). In individuals without diabetes, an older age was associated with lower MVPA. In individuals with newly-diagnosed type 2 diabetes, MVPA was more stable with age, but consistently lower than in individuals without diabetes: -21.0 minutes/day (95% CI: -33.8, -8.3) at age <40 years, -15.0 minutes/day (-22.6, -7.4) at age 40-59 years, and -17.7 minutes/day (-29.6, -5.9) at age ≥60 years. Individuals with newly-diagnosed type 2 diabetes were similarly less likely to achieve recommended levels of MVPA than individuals without type 2 diabetes across all age categories: relative risk with vs without diabetes= 0.62 (0.40, 0.95) at age <40 years; 0.75 (0.61, 0.93) at age 40-59 years; 0.63 (0.44, 0.90) at age ≥60 years.

**Conclusions**

Newly-diagnosed type 2 diabetes is associated with low physical activity regardless of age at diagnosis. This is of particular concern for individuals with early-onset type 2 diabetes who are at higher risk of complications as compared to individuals with later-onset.

## Inequalities in influenza vaccine performance: The role of obesity, dietary and sociodemographic factors: a scoping review protocol

Stanislava Katsarova | LHIIP

**Background**

Influenza causes millions of infections annually, leading to high levels of hospitalisation and mortality ([1,2]). Vaccination is the best way to prevent and improve infection outcomes ([3]). Vaccine efficacy and effectiveness are measures of how well a vaccine works to protect individuals from infection in controlled and real-world settings, respectively ([4,5]). For the purpose of this review, we will use the combined term vaccine performance. However, variation exists between individuals' vaccine responses, leading to disparities in protection against influenza and other viruses across the population ([6]). It has been suggested that this variation is influenced by many factors including age, comorbidities, pre-existing immunity, nutritional status and more ([7,8]). However, the role of other factors, such as obesity, dietary and sociodemographic factors is still not fully understood ([6,9]). These could be contributing to health inequalities in vaccine performance across individuals and the population.

**Aims / Objectives**

Our aim with this scoping review is to highlight potential sources of health inequalities in influenza vaccine responses. This would highlight the groups of the population who may be at risk of having suboptimal influenza vaccine responses which could be valuable information to policy makers. The objective of this scoping review is to summarise the available evidence on the relationship between obesity, dietary and sociodemographic factors and their effect on influenza vaccine performance. To our knowledge, this is the first scoping review exploring this topic. A preliminary search of PubMed, the Cochrane Database of Systematic Reviews and JBI Evidence Synthesis was conducted and no current or ongoing systematic or scoping reviews on the topic were identified.

**Methodology and Main Body**

The proposed scoping review will follow JBI's methodology for conducting scoping reviews and the inclusion criteria will be guided by the Population, Concept, Context (PCC) framework ([10]):

- Population: children and adults (all ages).
- Concept: Quantitative intervention and observational studies investigating obesity, sociodemographic or dietary factors, and their effect on influenza vaccine performance.
- Context: any region or country, English language only

Methods**:** Searches will be conducted in Scopus, Embase, PubMed and Web of Science, using a defined search strategy. No regional or publication date restrictions will be applied. Titles and abstracts will be screened according to the inclusion criteria above, by two independent reviewers, using Covidence software. Included studies will be screened in full to confirm eligibility. The reference lists of included studies will be manually screened for additional eligible studies. After screening is completed, data will be extracted, charted and presented in a tabular format in the review paper alongside a narrative summary.

**Results**

This scoping review is estimated to be completed by August 2025 and results will be disseminated through publication in a suitable journal.

**Conclusions / Implications for practice**

The findings of this review will help inform researchers on important factors contributing to inequalities in influenza vaccine performance. This knowledge could serve to inspire further interventions aimed at improving individual vaccine responses, considering the ongoing challenges posed by influenza outbreaks worldwide.

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# Multilevel Analysis of Individual Heterogeneity and Discriminatory Accuracy (MAIHDA) to understand how obesity risk varies according to multiple lifestyle behavior recommendations

Ansuman Swain | BRC

**Background**

Obesity is a major public health concern and a risk factor for various chronic diseases, including type 2 diabetes, cardiovascular conditions, and several cancers [1]. Lifestyle behaviours such as physical activity, diet, sleep, alcohol intake, and smoking are well-established contributors to obesity. While the individual associations between these behaviours and obesity risk are well documented, their combined and interactive effects on obesity risk remain poorly understood. MAIHDA is a novel approach that allows investigation of high-order interactions through multilevel analysis of individuals nested within intersectional groups or "strata" [2].

**Aims / Objectives**

This study aimed to use MAIHDA to examine the combined and interactive effects of meeting vs. not meeting the public health recommendations of five key lifestyle behaviors on obesity risk.

**Methodology and Main Body**

The study sample comprised of 139,540 men and 125,455 women aged 40-69 years from the UK Biobank study. Five self-reported lifestyle behaviours—physical activity, fruit and vegetable consumption, sleep duration, alcohol intake, and smoking status—were re-categorized as meeting vs. not meeting public health guidelines (e.g. consuming 5 portions of fruit and vegetables daily) and combined to create 48 unique strata. The outcomes were BMI and obesity status (Obesity vs. normal weight). MAIHDA models—linear for BMI and logistic for obesity status—were fit with individuals (level 1) nested within strata (level 2). Three models were employed: Model 1 (null random-intercept model with no predictor variables), Model 2 (with fixed effects for lifestyle behaviors), and Model 3 (with confounders and fixed effects). For each model, the Variance Partition Coefficient (VPC) was computed to describe the proportion of variance in BMI and obesity status due to differences between strata. The Proportional Change in Variance (PCV) between model 1 and models 2 and 3 were also calculated to assess the amount of between stratum variance in the outcome due to additive effects. Strata-specific predicted BMI and obesity probabilities were also estimated.

**Results**

17% of men and 23% of women had obesity. For both sexes, strata with the lowest BMI and obesity risk were associated with meeting most recommendations, while strata with the highest BMI and obesity risk were linked to meeting few. Logistic Model 1 VPCs showed that 7% of variance in obesity risk among males and 5% among females was explained by differences between strata (as opposed to between individuals within strata). After adjusting for main effects and confounders (Model 3), VPCs attenuated to 0.5% among males and 0.1% among females, suggesting differences in obesity risk were largely additive effects. PCVs from Model 3 also indicated primarily additive rather than interactive effects. Results were similar for BMI in the linear models.

**Conclusions / Implications for practice**

Using a novel statistical approach (MAIHDA), this study highlights that additive effects of multiple lifestyle behaviours predominantly explain differences in BMI and obesity risk. Therefore, meeting a greater number of individual public health lifestyle recommendations is important in mitigating obesity risk.

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## Elevated Obesity Rates in UK HGV Drivers: Insights from a Socio-Economically Matched Population Analysis

Ellie Gunner | BRC

**Background**

Heavy goods vehicle (HGV) drivers face unique barriers that prevent them from living healthy lifestyles, contributing to an elevated risk of obesity. Yet no studies have directly compared obesity prevalence in this group to the general UK population.

**Aim**

This study aimed to address this gap by comparing obesity rates between HGV drivers and the general population, adjusting for socio-demographic factors, to inform targeted interventions and policies.

**Methodology**

The present study used male HGV driver data (n= 625) from existing research, including baseline data from the SHIFT UK randomised controlled trial, and survey data. Obesity prevalence in HGV drivers across four age groups (25-34, 35-44, 45-54 and 55-64 years) were compared to that of male respondents from the 2019 Health Survey for England (HSfE), but only those from the same socio-economic group as HGV drivers (categorised by occupational group) were included (n=485).

**Results**

After adjusting self-reported BMIs within the driver dataset for consistency with HSfE methods, HGV drivers were significantly more likely to have obesity in comparison to the male respondents of the 2019 Health Survey for England (51.52% vs 34.02%, $p<0.001$), with a particularly large difference present in the 25-34 age group (45.83% vs 21.98%, $p<0.001$).

**Conclusions / Implications for practice**

These results demonstrate that obesity prevalence is greater in UK HGV drivers than members of the general population, independent of socioeconomic status, highlighting the urgent need for more robust approaches to tackle obesity in this occupational group. The high obesity prevalence in younger drivers is a particular concern, due to the obesogenic environments that drivers work within and the risk for this to be exacerbated over time. In addition, there are well-established links between obesity, chronic disease and accident risk so this could have catastrophic implications on the health and safety of HGV drivers, along with other road users.

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## Intersectional inequality in general and central obesity: a cross-sectional UK Biobank study using multilevel analysis of individual heterogeneity and discriminatory accuracy

Joseph Hutchinson | LHIIP

**Background**
People exist at a combination of different individual and neighbourhood deprivations as well as demographics. However, little is known about the intersectional inequality of these combinations on obesity. This study aims to analyse the intersectional inequality of these variables on obesity and central obesity using the Multilevel Analysis of Individual Heterogeneity and Discriminatory Accuracy (MAIHDA) technique.

**Methods**
The sample comprised 452,499 participants from England and Scotland in the UK Biobank study. Individuals were grouped into 320 intersectional strata according to their household income, neighbourhood deprivation, sex, ethnicity and age. MAIHDA was used to establish how body mass index (BMI), fat mass index (FMI), and waist circumference (and their associated obesity classifications) differ between versus within the intersectional strata. We then calculated the proportion of between variation (inequality due to our strata) that is additive or multiplicative.

**Results**
6.5%, 25.2% and 19.5% of variation in BMI, FMI and Waist circumference respectively is between the strata. Of this, 26.6%, 3.5% and 12.0% is multiplicative as opposed to additive. There are 77, 59 and 99 strata for BMI, FMI and waist circumference demonstrate a significant multiplicative effect. There are some patterns. One example is the different multiplicative effect between black and white men and women. In general, white women have a privileged multiplicative effect, whilst black women have a disadvantaged effect. Meanwhile men of the same ethnicities experience the inverse relationship. The relationship between individual and neighbourhood deprivation is not universally experienced by all strata. For example, black men living in areas of high deprivation have higher BMIs as their household income increases.

**Conclusions**
A large proportion of variation in general and central obesity is due to inequality, of which up to 33.3% is multiplicative in nature. It is important that these intersectional effects are considered when designing policy interventions to avoid policy failure. For example, regarding obesity, deprived black women experience both additive and multiplicative disadvantage. Therefore, interventions focussed on this group may be more effective than modelled from an additive perspective.

**Conflicts of Interest**
None disclosed

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