**LEICESTER LIFESTYLE AND HEALTH RESEARCH GROUP**

**Optimising the measurement of muscle and physical function in clinical trials of people living with obesity**

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**Section 2 – *Project Information***

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| **Project Title** | **Optimising the measurement of muscle and physical function in clinical trials of people living with obesity** |
| **Project Summary** | |
| *Aim:*  To optimise the measurement of muscle and physical function in clinical trials of people living with obesity.  *Background:*  Obesity is a complex global health concern, impacting morbidity and mortality1,2. Along with delirious effects on mental and physical health, obesity significantly impacts muscle and physical functioning, which can profoundly reduce quality of life and the ability to complete activities of daily living3,4.  Despite significant weight loss and improvements in metabolic health, the effect of weight loss interventions, with and without additional lifestyle changes, on muscle and physical function is unclear, partly due to the heterogeneity and potentially unsuitable choice of assessment tools (e.g., use of subjective measures)5.  Obesity may impact the psychometric properties of common physical function tests6,7, reducing our ability to detect and interpret changes following an intervention by distorting our understanding of true functional ability and invalidating cut-offs for conditions such as sarcopenia8. As well as standardising the choice of outcomes, there is also a need to better understand what changes in functional tests are clinically (e.g., important to health) and statistically (e.g., not due to error) meaningful in people with obesity.  Choosing correct and psychometrically sound functional assessments for obesity is critical, especially as the effect of (e.g., drug-lifestyle) interventions on physical function becomes prominent in trial design and outcome preference.  *Methods:*  Year 1/2  A comprehensive COSMIN9 evaluation of measurement properties of self-report and performance-based muscle and physical function measures in people with obesity. This will determine which measures of function are psychometrically superior/inferior across different socio- and clinical-characteristics, make recommendations (supported by a Delphi survey of key stakeholders) for tests to use in the future, and identify further research gaps.  Year 2/3  Using prospective and retrospective data from LDC/BRC studies to explore as yet unidentified psychometric properties of physical functional measures in people with obesity. This analysis could focus (depending on the COSMIN analysis) on constructs such as validity and reliability, determining the minimal clinically important differences and minimal detectable changes, etc.  *Expected outcomes and impact:*  Based on a rigorous psychometric evaluation and consensus exercise with key stakeholders, this PhD would identify and recommend assessments for physical function in people with obesity. This would assist measurement selection by clinicians and researchers interested in evaluating and interpreting physical function in obesity. Using prospective and retrospective data, the PhD will explore as yet unidentified properties of physical function to further support outcome measure choice, interpretation, and implementation.  *Aim:* To explore the 24-hour movement behaviours before and after metabolic and bariatric surgery (MBS) and evaluate a post-operative physical activity and pharmacotherapy intervention (18 months post-MBS) to optimise physical function and MBS related long-term health outcomes.  *Background:* The increasing incidence of severe obesity (body mass index [BMI] ≥35kg.m2) represents a major public health concern1,2. Despite the advancement of new anti-obesity medications (AOMs) which have instigated a revolution in obesity treatment, metabolic bariatric surgery (MBS) continues to be the most effective and durable treatment for individuals living with severe obesity3,4. AOM could however exist in synergy with MBS and lifestyle modification to optimise and maintain MBS related health outcomes long-term5,6.  MBS, like AOM induced weight loss, does not eliminate the need for accompanying changes in key lifestyle behaviours, such as physical activity, as these behaviours are essential and recommended to optimise long-term MBS related outcomes and physical function7,8,9. As research evolves, the importance of physical activity for optimising MBS outcomes is gaining greater recognition 7,9,10,11. While a strong evidence base highlights that moderate-to-vigorous intensity physical activity (MVPA) is essential for optimising long-term MBS related health outcomes12; it is important to note that MVPA only accounts for a small proportion of daily activity, thus neglecting the largest proportion of individuals’ movement across a 24-hour day. A holistic approach recognising all of the movement behaviours, sleep, sedentary behaviour and light activity in addition to MVPA, and their co-dependent relationship is therefore essential to inform and optimise future MBS care.  *Methods:* This programme of work will encompass evidence synthesis, observational and experimental methodologies.  WP1-Evidence Synthesis (years 1)  To explore existing literature to provide a comprehensive summary of what is currently known about the 24 hour movement behaviours in MBS to inform future MBS research and physical activity recommendations.  WP2-Observational (years 1-3)  To measure the 24-hour movement behaviours both before and at multiple time points after MBS to characterise this clinical populations’ 24-hour movement behaviours in standard care and understand the impact of MBS on these behaviours.  WP3-Experimental (Year 2-3)  A randomised controlled trial study will be undertaken as part of an on-going platform trial to investigate whether physical activity support plus AOM >18 months after MBS (the point of weight-loss plateau) can optimise physical function, MBS outcomes and support the prevention of recurrent weight gain.  *Expected outcomes and impact:* At least 3 high quality research outputs will be produced, complimented by focused knowledge exchange activities (e.g., conference attendance). This cross-cutting research will inform future MBS clinical care and support the development of 24-hour movement behaviour guidelines in MBS. | |
| **References** | |
| 1. Phelps NH, Singleton RK, Zhou B, et al. Worldwide trends in underweight and obesity from 1990 to 2022: a pooled analysis of 3663 population-representative studies with 222 million children, adolescents, and adults. *The Lancet* 2024; **403**(10431): 1027-50.  2. Haslam DW, James WP. Obesity. *Lancet* 2005; **366**(9492): 1197-209.  3. Norris T, Blodgett JM, Rogers NT, Hamer M, Pinto Pereira SM. Obesity in early adulthood and physical functioning in mid-life: Investigating the mediating role of c-reactive protein. *Brain Behav Immun* 2022; **102**: 325-32.  4. Lang IA, Llewellyn DJ, Alexander K, Melzer D. Obesity, Physical Function, and Mortality in Older Adults. *Journal of the American Geriatrics Society* 2008; **56**(8): 1474-8.  5. Ahmad E, Arsenyadis F, Almaqhawi A, et al. Impact of novel glucose-lowering therapies on physical function in people with type 2 diabetes: A systematic review and meta-analysis of randomised placebo-controlled trials. *Diabet Med* 2023; **40**(6): e15083.  6. Mahaffey R, Morrison SC, Stephensen D, Drechsler WI. Clinical outcome measures for monitoring physical function in pediatric obesity: An integrative review. *Obesity* 2016; **24**(5): 993-1017.  7. Kroman SL, Roos EM, Bennell KL, Hinman RS, Dobson F. Measurement properties of performance-based outcome measures to assess physical function in young and middle-aged people known to be at high risk of hip and/or knee osteoarthritis: a systematic review. *Osteoarthritis Cartilage* 2014; **22**(1): 26-39.  8. Belfield AE, Wilkinson TJ, Henson J, et al. Sarcopenia prevalence using handgrip strength or chair stand performance in adults living with type 2 diabetes mellitus. *Age Ageing* 2024; **53**(5).  9. MacRae JM, Harasemiw O, Lightfoot CJ, et al. Measurement properties of performance-based measures to assess physical function in chronic kidney disease: recommendations from a COSMIN systematic review. *Clin Kidney J* 2023; **16**(11): 2108-28. | |