**University of Leicester**

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| **Project Reference** | BRC Studentships |

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**Section 2 – *Project Information***

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| **Project Title** | Tracking Type 2 Diabetes Remission for Heart Health   |
| **Project Highlights:** | 1. | Interdisciplinary research project including big data, omics and imaging |
| 2. | Complex data modelling including computational biology  |
| 3. | Contributing to the evidence base of a novel patient group to help inform guidelines and/or future interventional studies  |
| **Project Summary**  |
| **Background**: Type 2 diabetes mellitus (T2D) confers an excess risk of heart failure with a propensity towards preserved ejection fraction (HFpEF).3 T2D-related cardiovascular remodelling4 (diabetic cardiomyopathy) presents early in the disease process and progresses insidiously. Exercise intolerance is an early symptom of heart failure,5 and a prognostic indicator in T2D.6 Short term favourable improvements in cardiovascular remodelling and exercise tolerance following acute weight loss with a low-calorie meal replacement plan7 or bariatric surgery8 have been demonstrated but such interventions are not feasible in all patients. The incidence of remission of T2D in routine care from the National Diabetes Audit in England is estimated to be 9.7 (95%CI 9.6 – 9.8) per 1000-person years1 and data from Scotland (SCI-Diabetes registry) indicate this to be 4.8%.2 Pilot work from our group has identified that spontaneous remission of T2D(n=25) in the community is associated with improved metabolic risk profile and ventilatory response to exercise; however there was no evidence of improvements in cardiovascular structure or function on MRI compared to those with ongoing T2D. The risk of heart failure in those in remission is unknown and there are no guidelines on treatment for prevention of heart failure. **Aim:** To describe the clinical characteristics across the diabetes journey for those in remission of Type 2 diabetes using primary care data  Research Plan: ​* **Study 1**: A systematic review of all studies reporting T2D remission excluding bariatric surgery.
* **Study 2**: Using Clinical Practice Research Datalink (CPRD) identify patients in remission of T2D (HBA1c<6.5%, ≥3months without glucose lowering therapies or surgical intervention), describe clinical characteristics and conduct a time-series analysis to describe change over time of pre-identified characteristics across the diabetes journey (pre-T2D, T2D, point of remission and post-DM).
* **Study 3**. Describe clinical characteristics by age at diagnosis, sex and by ethnic groups to identify any important phenotypic differences and determinants of relapse (non-linear modelling and cluster analysis)
* **Study 4**. Access the historical patient data for participants from our pilot study RESTORE and link data to the deep phenotypic data collected to further characterize and compare this patient group to healthy controls and active disease. This will include lipidomic data and results from a panel of 49 fibro-inflammatory markers for the entire 150 cohort.  ​

**Expected outcomes and impact**: ​Results will inform investigators on likely beneficial interventions which can be tested in phase II studies and the results will likely be incorporated into future guidelines.  ​  |
| **References**1. Holman N, Wild SH, Khunti K, et al. Incidence and Characteristics of Remission of Type 2 Diabetes in England: A Cohort Study Using the National Diabetes Audit. Diabetes Care. 2022;45(5):1151-1161. 2. Captieux M, Fleetwood K, Kennon B, et al. Epidemiology of type 2 diabetes remission in Scotland in 2019: A cross-sectional population-based study. PLoS Med. 2021;18(11):e1003828. 3. Borlaug BA. The pathophysiology of heart failure with preserved ejection fraction. Nat Rev Cardiol. 2014;11(9):507-515. 4. Athithan L, Gulsin GS, McCann GP, et al. Diabetic cardiomyopathy: Pathophysiology, theories and evidence to date. World J Diabetes. 2019;10(10):490-510. 5. Bozkurt B, Coats AJS, Tsutsui H, et al. Universal definition and classification of heart failure: a report of the Heart Failure Society of America, Heart Failure Association of the European Society of Cardiology, Japanese Heart Failure Society and Writing Committee of the Universal Definition of Heart Failure: Endorsed by the Canadian Heart Failure Society, Heart Failure Association of India, Cardiac Society of Australia and New Zealand, and Chinese Heart Failure Association. Eur J Heart Fail. 2021;23(3):352-380. 6. Seyoum B, Estacio RO, Berhanu P, et al. Exercise capacity is a predictor of cardiovascular events in patients with type 2 diabetes mellitus. Diab Vasc Dis Res. 2006;3(3):197-201. 7. Gulsin GS, Swarbrick DJ, Athithan L, et al. Effects of Low-Energy Diet or Exercise on Cardiovascular Function in Working-Age Adults With Type 2 Diabetes: A Prospective, Randomized, Open-Label, Blinded End Point Trial. Diabetes Care. 2020;43(6):1300-1310. 8. Cuspidi C, Rescaldani M, Tadic M, et al. Effects of bariatric surgery on cardiac structure and function: a systematic review and meta-analysis. Am J Hypertens. 2014;27(2):146-156.  |