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Title of project: A 20-year cardiometabolic outcome follow-up of the Inter99 cohort – The role of birth weight and prematurity

ABSTRACT

Non-communicable diseases such as type 2 diabetes (T2D) and cardiovascular disease (CVD) are among the leading causes of death and disability globally. It has been consistently shown that low birth weight is playing a significant role in the development of T2D and CVD and their associated micro- and macrovascular complications. However, previous studies have not been designed to study the timing of onset of T2D and CVD in relation to LBW and prematurity. Furthermore, it is not known how LBW and prematurity are associated with trajectories of clinical progression of cardiometabolic markers following T2D diagnosis. The Inter99 study have between 1999-2001 included a total of 6,784 Danish adults aged 30-60 years, of whom data on weight and gestational age at birth were collected from original midwife records in 4,744 participants. Using baseline cross sectional glucose tolerance tests, it was previously shown that an adverse fetal environment was strongly associated with increased risk of T2D. Now, 20 years after, with participants on average being in their mid-sixties, we aimed to examine the role of birth weight and prematurity, as proxies for the early fetal environment, on the age-specific incidence of T2D and CVD, as well as on trajectories of the clinical progression of cardiometabolic markers following T2D diagnosis. Furthermore, we aimed to study the risk of retinopathy and retinal changes in a smaller subgroup with detailed eye examinations. Data are obtained through linkage of individual-level data from the extensive Danish registers with information of T2D and CVD incidence and clinical trajectories following T2D diagnosis with data from the detailed clinical assessments and questionnaires at the Inter-99 baseline visit (1999-2001), and data on weight and gestational age at birth from midwife records. Besides the above described register-based follow-up of the Inter99 cohort, the postdoctoral fellowship will involve coordinating a comprehensive 20-year clinical follow-up of the Inter99 cohort. Using validated innovative technologies, allowing large scale measurements, subjects will be studied with respect to retinal changes, micro- and macrovascular endothelial function, coronary artery calcification, liver fat and -fibrosis, cardiac autonomic neuropathy as well as digital health wearables to monitor glucose profiles. The combined dataset will allow us to test our main hypothesis, that an adverse fetal environment reflected as low birth weight or prematurity, is associated with disproportionately increased multi-organ damage and patient relevant health outcomes in people with and without T2D.