Application number/Title: 32743 : Thyroid signalling and common age-related diseases: a Mendelian Randomisation study and thyroid pathway analysis

Applicant PI: Dr Diana van Heemst

Applicant institution: Leiden University Medical Centre, Leiden, Noord-Holland, Netherlands

Keywords provided by the Applicant PI to describe the research project:

age-related, disease, mendelian randomisation, thyroid

Application Lay Summary:

In the coming decades, human ageing will be one of the biggest challenges faced by our health care systems. A better understanding of causal pathways that are common to several age-related diseases, in particular of those leading to co-morbidities, constitutes an important challenge. We hypothesise that inappropriate thyroid hormone action is a common mechanism underlying susceptibility to age-related degenerative diseases. In this project, we will employ genetic methods to investigate the causal role of the thyroid hormone pathway in diseases of the cardiovascular system, bone, joints, brain, muscle and blood. Methods include Mendelian randomisation and association analysis. UK Biobank aims to improve the prevention, diagnosis and treatment of a wide range of serious and life-threatening illnesses ? including cardiovascular diseases, arthritis, osteoporosis, and forms of dementia. Achievement of this aim is dependent on improved understanding of the pathophysiology of diseases. The proposed work will result in a better understanding of the causal role of thyroid hormone in the pathophysiology of cardiovascular disease, osteoporosis, osteoarthritis, neuropsychological disorders, sarcopenia and anaemia. We will conduct a Mendelian Randomisation study and a genetic association study to investigate the causal association of thyroid status with clinical and subclinical measures of age-related diseases of the following domains:

1. Cardiovascular system (e.g. blood pressure, stroke)
2. Bones and joints (e.g. osteoporosis, osteoarthritis)
3. Brain (e.g. cognitive function, depression)
4. Muscles (e.g. hand grip strength, body composition)
5. Blood (e.g. haemoglobin concentration, anaemia) Because genetics explain only 5.64% of variation in TSH levels and 2.30% of variation in fT4 levels,

we need a large sample size to answer our research question. Therefore we will need information on the maximum number of participants for which the outcomes specified below are available for this study.