

**Project title:** Understanding cardiometabolic heterogeneity in obesity: different routes for men and women?

**Project leader:** Nicole Vogelzangs

**Function:** Researcher

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**Proposal (250 words):**

**Introduction:** The obesity epidemic has spread worldwide. Obesity increases the risk of cardiometabolic diseases. However, there is large heterogeneity in cardiometabolic risk among the obese: some individuals are in good metabolic health, although a substantial proportion of them are yet at high risk of cardiovascular disease; others are metabolically unhealthy, but appear not to be at increased risk of cardiovascular disease. Striking sex differences in both body composition and cardiometabolic risk are apparent, but evidence emerges that also metabolism underlying the link between body composition and cardiometabolic risk might differ between sexes.

**Hypothesis and Objectives:** This study aims to investigate whether metabolic pathways linking body composition with cardiometabolic disease are sex-dependent and whether these sex differences could contribute to understanding cardiometabolic heterogeneity in obesity.

**Setting and Methods:** The Maastricht Study is an new population based prospective cohort study in southern Netherlands, which aims to include 10,000 individuals aged 40-75 y, with oversampling of subjects with type-2-diabetes (n=5,000). Currently app. 3500 subjects are available for data analysis. A substantial proportion of participants are (centrally) obese. Detailed information on body composition (anthropometry, bio-impedance, abdominal MRI [subcutaneous/visceral/liver fat]), metabolism (metabolomics, lipid metabolism), metabolic disease ([tissue-specific] insulin resistance, type-2-diabetes) and cardiovascular disease (history, pulse-wave-velocity, intima-media-thickness, electrocardiogram, heart ultrasound, microcirculation) is available.

**Impact:** This study contributes to understanding obesity heterogeneity, which helps to improve and personalize cardiometabolic risk classification of obese individuals. In addition, this study will provide novel targets for personalized prevention, early diagnosis and treatment of cardiometabolic diseases.

**Requirements candidate:** Highly motivated student with good English communication skills and proactive and resolute attitude. The candidate preferably has a background in Epidemiology, Health Sciences or related field with a strong interest in biology. Experience with data analysis is essential.

**Keywords:** overweight; body composition; visceral fat; liver fat; metabolomics; lipid metabolism; insulin resistance; type-2-diabetes; metabolic disease; atherosclerosis; cardiovascular disease; personalized medicine; sex-differences

**Top 5 selected publications:**

1. Prediabetes and Type 2 Diabetes Are Associated With Generalized Microvascular Dysfunction: The Maastricht Study. Sørensen BM, Houben AJ, Berendschot TT, Schouten JS, Kroon AA, **van der Kallen CJ**, Henry RM, Koster A, Sep SJ, Dagnelie PC, Schaper NC, Schram MT, **Stehouwer CD**. Circulation. 2016 Nov; 134(18): 1339-1352. **IF=19.3**

2. Distinct Longitudinal Associations of MBL, MASP-1, MASP-2, MASP-3, and MASP44 With Endothelial Dysfunction and Intima-Media Thickness: The Cohort on Diabetes and Atherosclerosis Maastricht (CODAM) Study. Hertle E, **Arts IC**, **van der Kallen CJ**, Feskens EJ, Schalkwijk CG, Hoffmann-Petersen IT, Thiel S, **Stehouwer CD**, **van Greevenbroek MM**. Arterioscler Thromb Vasc Biol. 2016 Jun; 36(6): 1278-1285. **IF=6.6**

3. Late-life depression symptom profiles are differentially associated with immunometabolic functioning. **Vogelzangs N**, Comijs HC, Oude Voshaar RC, Stek ML, Penninx BW. Brain Behav Immun. 2014 Oct; 41: 109-115. **IF=6.0**
4. Complement activation products C5a and sC5b-9 are associated with low-grade inflammation and endothelial dysfunction, but not with atherosclerosis in a cross-sectional analysis: the CODAM study. Hertle E, van **Greevenbroek MM**, **Arts IC**, **van der Kallen CJ**, Feskens EJ, Schalkwijk CG, **Stehouwer CD**. Int J Cardiol. 2014 Jun; 174(2): 400-403. **IF=6.2**
5. The association between the metabolic syndrome and alanine amino transferase is mediated by insulin resistance via related metabolic intermediates (the Cohort on Diabetes and Atherosclerosis Maastricht [CODAM] study). Jacobs M, **van Greevenbroek MM**, **van der Kallen CJ**, Ferreira I, Feskens EJ, Jansen EH, Schalkwijk CG, **Stehouwer C**. Metabolism. 2011 Jul; 60(7): 969-975. **IF=5.8**