Secondary Manifestations of ARTerial diseases in the Young with a chronic condition

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The primary objective of this study is to establish the effect of cardiovascular risk factors on preclinical atherosclerosis in children with a chronic condition, and follow this up over time.

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Arteriosclerosis, stenosis, vascular insufficiency and necrosis
Study type	Observational invasive

Summary

ID

NL-OMON56581

Source
ToetsingOnline

Brief title
SMART-Youth

Condition

- Arteriosclerosis, stenosis, vascular insufficiency and necrosis

Synonym
atherosclerosis, cardiovascular disease

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: Elisabeth von Freyburg Stichting

Intervention

Keyword: cardiovascular risk factors, children, chronic condition, preclinical atherosclerosis

Outcome measures

Primary outcome

Carotid Intima Media Thickness (cIMT) and Aortic pulse wave velocity (PWV) as preclinical atherosclerosis outcomes.

Secondary outcome

Secondary Objectives:

- Establish the development of cIMT and PWV measurements over time in children with various chronic conditions.

- Determine the relationship between dyslipidemia phenotypes and preclinical atherosclerosis in various chronic conditions.

- Compare the effect of lifestyle-related cardiovascular risk factors on preclinical atherosclerosis in children with and without a chronic condition.

- Develop a cardiovascular risk model to assess preclinical atherosclerosis in children at risk.

- Determine associations between psychosocial functioning and cardiovascular risk factors in children with a chronic condition.

The secondary parameters include: carotid artery distension using ultrasound, endothelial functioning using flow mediated dilation (FMD), inflammation using CRP levels, respiratory functioning assessed by forced expiratory volume in 1 second (FEV1) and intra-abdominal and subcutaneous fat measurements using ultrasound assessment. Besides this, lifestyle-related determinants including

nutrition (Questionnaire Eetscore Adolescents) and physical exercise (Questionnaire PAQ-A/C) are determined by validated questionnaires.

Substudy SMART-CF:

- Determine the relationship between dyslipidemia phenotypes and preclinical atherosclerosis in adults with CF.
- Determine the effect of lifestyle-related cardiovascular risk factors in adults with CF.
- Determine the association between psychosocial functioning and cardiovascular risk factors in adults with CF.
- Investigate the effect of CFTR modulators on preclinical atherosclerosis in adults with CFDetermine the relation between cardiovascular risk factors and fertility characteristics (ovarian reserve and menstrual cycle) in adult females with CF.
- Determine the relation between cardiovascular risk factors, ovarian reserve markers (AMH) and reproductive outcomes in adult females with CF.

Study description

Background summary

The Pathobiological Determinants of Atherosclerosis in Youth (PDAY) study established that atherogenesis starts in childhood, initiating in the iliac arteries and abdominal aorta and subsequently develops in higher regions of the arterial tree. Childhood and adolescence thereby provide a unique window of opportunity to prevent atherosclerotic cardiovascular disease (ASCVD) later in life, especially for pediatric groups at risk. The growing list of pediatric groups at risk includes chronic inflammatory disorders, organ transplant recipients, familial hypercholesterolemia, endocrine disorders, childhood

cancer survivors, chronic kidney diseases, congenital heart diseases, fetal growth restriction, and premature birth, next to increasing numbers of children and adolescents with traditional risk factors such as obesity, hypertension, hyperlipidemia, and hyperglycemia. The best way to assess cardiovascular health in the pediatric population is relatively uncharted territory. Multisite and multimodal assessment of early atherosclerosis emerged as the best way to capture the complexity of atherosclerosis as a systemic disease. Next to conventional carotid intima-media thickness measurements, implementation of aortic pulse wave velocity and endothelial function measurements can advance the assessment of early atherosclerosis in pediatrics.

Substudy: SMART-CF

In this substudy, we aim to expand the study to include adults within a specific subset of this cohort, namely cystic fibrosis (CF). Although the original study focuses on pediatric patients, we believe it is valuable to conduct the same measurements in adults with CF to fulfill the life course medicine perspective. By mapping cardiovascular health in both children and adults with cystic fibrosis, we aim to gain unique insights into the long-term effects of this chronic disease on the cardiovascular system. These insights become increasingly important in CF since the disease has undergone a remarkable transformation from being considered a life-threatening condition in childhood to a chronic disease due to high-quality care. More recently, through new therapeutics, known as CFTR modulators, outcomes in CF can significantly improve even more. As the life expectancy continues to increase, naturally it brings forth new challenges, one pressing population of which one is the cardiovascular health. A recent study has shown an increased risk of cardiovascular disease in pwCF making it ideal to study the atherosclerosis and the factors influencing cardiovascular risk in this group as they could also be useful for developing targeted strategies for risk stratification, allowing for more personalized and proactive management of cardiovascular health in individuals with risk factors growing into older ages.

Due to vascular impairment it may be related to the ovarian reserve. The ovarian reserve is related to fertility decline and menopausal age. The ovarian reserve can be measured via a surrogate marker which is anti-Mullerian hormone in serum. AMH declines alongside ovarian reserve during the reproductive lifespan and is associated with cardiovascular disease in young women. Female infertility and hormone levels are linked to increased risk of cardiovascular disease and outcomes later in life. However, it remains unknown if a poor cardiovascular health is the origin or consequence of diminished ovarian reserve, reduced fertility and early menopause.

Therefore, in adult women with CF ovarian reserve markers will be assessed and a questionnaire about their menstrual cycle and reproductive outcome will be inventoried to study a possible association with cardiovascular markers. It is of importance to note that since the ovarian reserve marker in the general

adult population does not carry strong predictive values for reproductive outcomes. Therefore these test are currently not used to identify women at risk for infertility in the general population.

Study objective

The primary objective of this study is to establish the effect of cardiovascular risk factors on preclinical atherosclerosis in children with a chronic condition, and follow this up over time.

Study design

The SMART-Youth study will be a prospective, longitudinal cohort study including children with various chronic conditions followed up in the Wilhelmina Children*s Hospital. In order to determine the development over time, cardiovascular risk factors and preclinical atherosclerosis measurements will be assessed every two years. For now, the study duration entails 5 years, with future plans of possible extension after this time.

Furthermore, we set up a substudy into adults with CF who are followed up in the UMC Utrecht.

Study burden and risks

The burden and associated risks with participation are low. In most patients, routine lipid blood sampling is already included in outpatient follow-up. For some patient groups, such as children with congenital heart disease, routine blood sampling is included in outpatient follow-up in the course of the SMART-Youth study. Given the atherosclerotic cardiovascular disease risk of these children, and after consultation with the treating physicians, lipid sampling will be viewed as clinical care and not solely from a research perspective for all children. We will combine the check-up visit at the outpatient clinic of the Wilhelmina Children*s Hospital with the SMART-Youth visit, to minimize the burden of traveling to the hospital. Both visits will take approximately 1 hour. There are no direct benefits for the subject when participating in this study. Participation will be completely voluntary.

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Children (2-11 years)

Inclusion criteria

Inclusion criteria for SMART-Youth consist of children aged 8 to 18 years with various chronic conditions recruited from the PROactive cohort. PROactive includes the following chronic conditions: cystic fibrosis, juvenile idiopathic arthritis, systemic autoimmune diseases, chronic kidney disease, primary immunodeficiency, autoinflammatory conditions, inflammatory bowel disease, and congenital heart disease, as well as children with unexplained medical symptoms. Children from the neonatal follow-up program for prematurity and fetal growth restriction are planned to be included in the PROactive cohort soon.
Substudy SMART-CF: Inclusion criteria for this study consist of patients with CF, 18 years of age and older.

Exclusion criteria

There are no exclusion criteria.

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	20-08-2024
Enrollment:	1350
Type:	Actual

Ethics review

Approved WMO Date:	15-02-2024
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	21-11-2024
Application type:	Amendment
Review commission:	METC NedMec

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL84874.041.23