Publications and scientific contributions

List of included papers

Paper I Megersa BS, Zinab B, Ali R, Kedir E, Girma T, Berhane M, Admassu B, Friis H, Abera M, Olsen MF, Filteau S, Nitsch D, Yilma D, Wells JCK, Andersen GS, Wibaek R. Associations of weight and body composition at birth with body composition and cardiometabolic markers in children aged 10 y: the Ethiopian infant anthropometry and body composition birth cohort study. *The American Journal of Clinical Nutrition. 2023. DOI: 10.1016/j.ajcnut.2023.06.010*

Paper II Megersa BS, Andersen GS, Abera M, Abdissa A, Zinab B, Ali R, Admassu B, Kedir E, Nitsch D, Filteau S, Girma T, Yilma D, Wells JCK, Friis H, Wibaek R. Associations of early childhood body mass index trajectories with body composition and cardiometabolic markers at age 10 years: the Ethiopian infant anthropometry and body composition (iABC) birth cohort study. *The American Journal of Clinical Nutrition. 2024. DOI: 10.1016/j.ajcnut.2024.03.004*

Paper III Megersa BS, Andersen GS, Abera M, Abdissa A, Zinab B, Ali R, Admassu B, Kedir E, Nitsch D, Filteau S, Girma T, Yilma D, Wells JCK, Friis H, Wibaek R. Associations of fat mass and fat-free mass accretion in early childhood with body composition and cardiometabolic markers at age 10 years: the Ethiopian iABC birth cohort. In preparation for journal submission.

Co-authorships

Zinab B, Ali R, Megersa BS, Belachew T, Kedir E, Girma T, Abdisa A, Berhane M, Admasu B, Friis H, Abera M, Olsen MF, Andersen GS, Wells JCK, Filteau S, Wibaek R, Nitsch D, Yilma D. Association of linear growth velocities between 0 and 6 years with kidney function and size at 10 years: A birth cohort study in Ethiopia. *The American Journal of Clinical Nutrition. 2023*. DOI: 10.1016/j.ajcnut.2023.09.014

Contribution to section and international conferences

56th Annual Meeting of the European Diabetes Epidemiology Group (EDEG), Crete, Greece, April 2022. Associations of birth weight and birth body composition with later body composition and cardiometabolic risk markers at age 10 years: the Ethiopian iABC birth cohort study (Poster).

Seminar at the Department of Nutrition, Exercise and Sports (2022): Early childhood growth with body composition and cardiometabolic risk at age 10 years: the Ethiopian iABC birth cohort study (Oral).

TABLE OF CONTENTS

ABBREVIATIONS

ADP	Air displacement plethysmograph
BFFM	Birth fat-free mass
BFM	Birth fat mass
BIC	Bayesian information criteria
BMI	Body mass index
BW	Birth weight
CI	Confidence interval
CVD	Cardiovascular disease
DOHaD	Developmental origins of health and disease
FFM	Fat-free mass
FFMI	Fat-free mass index
FM	Fat mass
FMI	Fat mass index
HDL	High-density lipoprotein
HOMA-IR	Homeostasis model assessment of insulin resistance
HPA	Hypothalamic pituitary adrenal axis
iABC	infant Anthropometry and Body Composition
IQR	Inter-quartile range
IWI	International Wealth Index
JUSH	Jimma University Specialized Hospital
LDL	Low-density lipoprotein
LMICs	Low- and middle-income countries
LSMEM	Linear spline mixed-effects modeling
NCDs	Noncommunicable diseases
OGTT	Oral glucose tolerance test
PAR	Predictive adaptive response
SAT	Subcutaneous adipose tissue
SD	Standard deviation
SDG	Sustainable Development Goals
T2D	Type 2 diabetes
VAT	Visceral adipose tissue
WHO	World Health Organization

SUMMARY

Background: Birth weight and rapid weight gain during early childhood have been associated with childhood overweight and cardiometabolic diseases such as cardiovascular diseases and type 2 diabetes in adulthood. However, evidence of the relative importance of birth fat mass (FM), birth fat-free mass (FFM), and their accretion in early childhood on later adiposity and cardiometabolic health is limited. Furthermore, little is known about how associations of growth in early childhood with body composition, and cardiometabolic markers are tracking throughout childhood. Despite an increasing burden of childhood overweight and cardiometabolic diseases in sub-Saharan African countries, there is limited evidence from longitudinal studies on how birth size and early childhood growth are related to adiposity and cardiometabolic risk in later childhood.

Objective: The overall objective of this PhD thesis was to examine associations of weight and body composition at birth and early childhood growth from 0-5 years with anthropometry, body composition, abdominal fat, and cardiometabolic markers at age 10 years.

Methods: This thesis is based on data from the Ethiopian infant Anthropometry and Body Composition (iABC) birth cohort study. Body composition from birth to 10 years of age was assessed using air-displacement plethysmography. The exposure variables included in the thesis were weight, FM, and FFM at birth (**Paper I**), previously identified body mass index (BMI) trajectories from 0-5 years (**Paper II**), as well as FM and FFM accretion in selected periods from 0-5 years (0-3, 3-6, 6-48, and 48-60 months) (**Paper III**). Linear spline mixed-effects modeling was applied to estimate FM and FFM from 0-5 years (**Paper III**). Outcomes were obtained from 355 children who attended the 10-year follow-up and included anthropometry (height, waist circumference, and BMI), body composition (fat mass index [FMI] and fat-free mass index [FFMI]), abdominal subcutaneous- and visceral fat, cardiometabolic markers including blood pressure (systolic and diastolic), markers of glucose homeostasis (glucose, insulin, C-peptide, and homeostasis model assessment of insulin resistance [HOMA-IR]), and lipid profile (total-, LDL-, HDL-cholesterol, and triglycerides). Associations between exposure variables and the 10-year outcomes were assessed using multiple linear regression analysis.

Results: At 10 years, the mean (SD) age of the children was 9.8 (1.0) years, mean height z-score and BMI z-score were -0.76 (0.94) and -0.77 (1.15), respectively. Higher birth weight and FFM were associated with greater height, FFMI, and higher insulin, C-peptide, and HOMA-IR, whereas

higher birth FM was associated with greater FMI and abdominal subcutaneous fat, but not visceral fat (**Paper I**). FM accretion from 0-3 months and 3-6 months, but not FFM, was linked to higher blood pressure and glucose concentrations. Furthermore, FM and FFM accretion between 6-48 months predicted higher insulin and HOMA-IR, whereas FFM accretion during the same period was associated with lower total and LDL cholesterol concentrations (**Paper III**). Children with rapid growth to high BMI trajectories had greater waist circumference, and those with slow to high BMI trajectories had higher FM and abdominal subcutaneous fat, whereas children with stable low BMI had lower FFMI compared to those with normal BMI trajectories (**Paper II**). Additionally, children with slow growth to high BMI trajectories showed higher insulin and HOMA-IR, whereas those with rapid BMI trajectories showed higher C-peptide and lower total cholesterol concentrations at 10 years of age.

Conclusion: Overall, based on the children included in this cohort, Ethiopian children were on average shorter and thinner compared with standard reference and showed lower FM and FFM than UK children at 10 years of age. In this cohort, prenatal environment, as indicated by proxy measures of birth weight and birth body composition and early childhood growth trajectories, and FM and FFM accretions were associated with adiposity, body composition, and cardiometabolic markers in later childhood. Children with higher FFM accretion in early childhood may have a lower risk of dyslipidemia later in life. Conversely, those with higher FM accretion and who experienced rapid or slow growth to high BMI growth patterns in early childhood might have an increased risk of adiposity and increased cardiometabolic markers later in life, given that these children are exposed to an obesogenic environment and have sedentary lifestyles.

RESUMÉ (SUMMARY IN DANISH)

Baggrund: Fødselsvægt og hurtig vægtøgning i den tidlige barndom har været forbundet med overvægt i barndommen og kardiometaboliske sygdomme som hjerte-kar-sygdomme og type 2-diabetes i voksenalderen. Imidlertid er der begrænset viden om den relative betydning af fedtmasse (FM) og fedtfri masse (FFM) ved fødslen, og tilvæksten i den tidlige barndom på senere fedme og kardiometabolisk sundhed. Desuden vides kun lidt om, i hvilket omfangt sammenhængen mellem vækst i den tidlige barndom og kropssammensætning og kardiometaboliske markører fortsætter gennem hele barndommen. På trods af en stigende byrde af overvægt i barndommen og kardiometaboliske sygdomme i de afrikanske lande syd for Sahara, er der begrænset evidens fra longitudinelle undersøgelser om, hvordan fødselsstørrelse og tidlig barndomsvækst er relateret til fedme og kardiometabolisk risiko i senere barndom.

Formål: Det overordnede formål med denne Ph.D.-afhandling var at undersøge sammenhænge mellem vægt og kropssammensætning ved fødslen, samt vækst fra 0-5 år, med antropometri, kropssammensætning, abdominalt fedt og kardiometaboliske markører ved 10-årsalderen.

Metoder: Afhandlingen er baseret på data fra den etiopiske fødselskohortestudie, *Infant Anthropometry and Body Composition* (iABC). Kropssammensætning fra fødslen til 10-årsalderen blev vurderet ved hjælp af luftfortrængningsspletysmografi. Eksponeringsvariablerne inkluderet i afhandlingen var vægt, FM og FFM ved fødslen (**Artikel I**), tidligere identificerede *body mass index* (BMI) *trajectories* fra 0-5 år (**Artikel II**), samt FM- og FFM-tilvækst i udvalgte perioder fra 0-5 år (0-3, 3-6, 6-48 og 48-60 måneder) **(Artikel III)**. *Linear spline mixed-effects* modellering blev anvendt til at estimere FM og FFM fra 0-5 år **(Artikel III)**. Resultaterne var baseret på 355 børn, som deltog i 10-års opfølgningen og inkluderede antropometri (højde, taljeomkreds og BMI), kropssammensætning (fedtmasseindeks [FMI] og fedtfrit masseindeks [FFMI]), abdominalt subkutant og visceralt fedt, kardiometaboliske markører inklusive blodtryk (systolisk og diastolisk), markører for glukosehomeostase (glukose, insulin, C-peptid og homeostasemodel for insulinresistens [HOMA-IR]) og lipidprofil (total-, LDL -, HDL-kolesterol og triglycerider). Forbindelser mellem eksponeringsvariabler og de 10-årige resultater blev vurderet ved hjælp af multipel lineær regressionsanalyse.

Resultater: Efter 10 år var den gennemsnitlige (SD) alder for børnene 9,8 (1,0) år, gennemsnitlig højde z-score og BMI z-score var henholdsvis -0,76 (0,94) og -0,77 (1,15). Højere vægt og FFM

ved fødslen var forbundet med større højde, FFMI og højere insulin, C-peptid og HOMA-IR, hvorimod højere FM ved fødslen var forbundet med større FMI og abdominalt subkutant fedt, men ikke visceralt fedt (**Artikel I**). FM-tilvækst fra 0-3 måneder og 3-6 måneder, men ikke FFM, var forbundet med højere blodtryk og glukosekoncentrationer. Ydermere forudsagde FM- og FFM-tilvækst mellem 6-48 måneder højere insulin og HOMA-IR, hvorimod FFM-tilvækst i samme periode var forbundet med lavere total- og LDL-kolesterolkoncentrationer (**Artikel III**). Børn med hurtig vækst til højt BMI-*trajectories* havde større taljeomkreds, og børn med langsom vækst til højt BMI-*trajectories* havde højere FM og abdominalt subkutant fedt, hvorimod børn med stabilt lavt BMI-*trajectories* havde lavere FFMI sammenlignet med dem med normal BMI-*trajectories* (**Artikel II)**. Derudover viste børn med langsom vækst til højt BMI-*trajectories* højere insulin og HOMA-IR, mens børn med hurtige BMI-*trajectories* viste højere C-peptid og lavere total kolesterol ved 10-årsalderen.

Konklusion: Samlet set var etiopiske børn, baseret på denne kohorte, kortere og tyndere sammenlignet med en reference, og havde lavere FM og FFM end børn i Storbritannien i 10-årsalderen. I denne kohorte var prænatalt miljø, baseret på vægt og kropssammensætning ved fødslen, og BMI-*trajectories* i tidlig barndom, samt FM- og FFM-tilvækst forbundet med fedme, kropssammensætning og kardiometaboliske markører senere i barndommen. Børn med højere FFM-tilvækst i den tidlige barndom kan have en lavere risiko for dyslipidæmi senere i livet. Omvendt kan de med højere FM-tilvækst og de med hurtig eller langsom vækst til højt BMI-*trajectories* i den tidlige barndom have en øget risiko for fedme og øgede kardiometaboliske markører senere i livet, da disse børn er udsat for et obesogent miljø og har stillesiddende livsstil.