ENGLISH SUMMARY

Background

Suboptimal nutritional status and growth during critical windows of developmental plasticity in fetal life and early childhood are key drivers of premature mortality and disability across the life-course, and the burden of undernutrition, obesity and associated cardiometabolic diseases falls disproportionately on low- and middle-income populations. Evidence from middle- and high-income countries suggests that detrimental cardiometabolic adaptations associated with growth in early life may occur already in childhood, but evidence from low-income countries is lacking. Thus, to improve our understanding of the developmental aetiology of cardiometabolic disease risk in low-income populations and to identify potential early-life targets amenable to timely interventions that promotes healthy growth, I aimed to examine the associations of growth in early life with body composition and markers of cardiometabolic risk at 60 months of age.

Methods

In a prospective birth cohort study of healthy urban preschool children from Jimma, Ethiopia, followed from birth to 60 months of age, I estimated weight velocities in the age periods 0-3, 3-6, 6-24, 24-48 and 48-60 months in 375 children using linear-spline mixed-effects (LSME) modelling (Paper 1), four distinct body mass index (BMI) trajectories from 0-60 months in 453 children using latent class trajectory modelling (Paper 2), and fat mass (FM) and fat-free mass (FFM) growth velocities in the age periods 0-3 and 3-6 months in 507 children using LSME modelling (Paper 3). FM and FFM from 0-6 months and at 60 months were assessed using air displacement plethysmography. In all three papers, I analysed associations of the derived growth exposures with height, waist-circumference, FM, FFM and markers of cardiometabolic risk at 60 months of age using multiple linear regression analyses in different adjustment models.

Findings

In this contemporary Ethiopian birth cohort, children were on average shorter at birth with deficits in weight, FM and FFM compared to international reference data. At 60 months of age, the children had increased their deficits in weight, height and in particular FFM, but had markedly higher FM which appeared to be associated with increased FM accretion in early infancy. Children who showed a higher FM and weight accretion, and accelerated BMI growth in early infancy had higher FM, greater waist circumference and higher concentrations of cardiometabolic markers related to lipid metabolism at 60 months of age. Children who showed a higher FFM and weight accretion, as well as accelerated BMI growth in early infancy were taller and had more FFM at 60 months of age. Furthermore, children who had higher weight at 60 months and higher weight accretion from 48-60 months were taller, had greater waist circumference, higher FM, higher FFM, higher blood
pressure, and higher concentrations of cardiometabolic markers related to insulin metabolism at 60 months of age. Finally, children with a slow BMI accretion through infancy and childhood were shorter, had smaller waist circumference, lower FM and FFM, and lower concentrations of cardiometabolic markers related to lipid metabolism.

**Conclusion**

In this thesis, I present the first comprehensive assessment from a low-income country on how variability in weight, BMI, FM and FFM accretion in important windows of development in early life associate with size, body composition and cardiometabolic risk markers in preschool children aged 60 months. Overall, the periods from 0-3 and 3-6 months of age appeared to be important windows for the programming of body composition in childhood. I found that higher FM accretion in infancy was strongly associated with higher FM at 60 months of age, and the same was true for FFM accretion in infancy and FFM at 60 months of age. Growth in early life was not consistently associated with the studied cardiometabolic markers. However, higher weight and FM accretion in infancy, weight accretion from 48-60 months and weight at 60 months as well as accelerated BMI growth in infancy were associated with higher concentrations of a number of cardiometabolic markers at 60 months of age. Future follow-up of this cohort is needed to examine if these relationships persist or become stronger later in childhood and adolescence.