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General introduction

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BACKGROUND

Early childhood is a critical period for the development of eating habits, because taste preferences and dietary behaviors are shaped during this period and are suggested to track into adulthood [1,2]. In addition, adequate dietary intake in all phases of childhood is essential for optimal growth, development, and health, not only in childhood, but also in later life [3-5]. It has been shown that the origins of several chronic diseases, including type 2 diabetes and cardiovascular diseases, which are nowadays the leading causes of mortality worldwide, lies in childhood [6,7]. Several studies have shown that potential risk factors for these diseases, including obesity, hyperlipidemia, and high blood pressure, already occur in childhood [6-9], and may track into adulthood [10-12]. Also other diseases with a high burden in the general population, including osteoporosis, and atopic diseases, have been shown to originate in childhood [6,13,14]. Early-life nutrition has been suggested to play an important role in setting the risk of several health outcomes in later life, including coronary heart disease, type 2 diabetes, osteoporosis, and asthma [3-5]. Therefore, nutrition in early life should be a key target in the prevention of chronic diseases and maintenance of health throughout the life course.

This thesis focuses on the relation of diet with health conditions that are highly prevalent already in childhood, including adiposity, other cardiometabolic markers, and atopic diseases. These health conditions are important public health problems, with a large increase in prevalence in recent decades. Also, these problems already occur in childhood and are suggested to track into adulthood. Hence, it is of high importance to identify modifiable risk factors – such as diet – in order to start prevention at an early stage.

DIETARY PATTERNS

Although intake of several single nutrients or foods in childhood has been linked to health, children consume a variety of nutrients and foods combined in meals rather than single nutrients or foods. The combination of nutrients and foods in meals may capture complex synergistic or interaction effects of nutrients and foods, food structure, or preparation methods on health. Over the past few decades, analysis of dietary patterns has emerged as an important research field, complementary to studies focusing on single dietary compounds [15,16]. Well-known dietary patterns include the Mediterranean diet, characterized by high intakes of fruit, vegetables, and fish, and low intakes of red meat; and the Western diet, characterized by high intakes of energy-dense, high-processed foods, and low intakes of fruit and vegetables. Dietary patterns may better capture the

complex interactions between nutrients and foods, which may give better insights on the effects of overall diet on health.

Two main approaches to study dietary patterns can be distinguished, namely data-driven or predefined. Data-driven dietary patterns are identified based on the variation of dietary intake data within a study population, whereas predefined dietary patterns are constructed based on specific dietary guidelines or recommendations [15]. Dietary guidelines are often country specific because of different eating habits [17]. Most dietary guidelines combine recommendations for both foods and individual nutrients. The current dietary guidelines in the Netherlands are unique in the sense that they are completely food-based, which might be easier to link to real-life foods for the general population. Although the Dutch dietary guidelines are based on extensive previous research on nutrients, foods, and dietary patterns in relation to specific diseases, the association of adherence to these overall dietary guidelines with health outcomes has not yet been evaluated. In addition, these dietary guidelines were developed to prevent the most common diseases in the general population, and the effects of adherence to these guidelines on health in childhood has not yet been studied.

BODY COMPOSITION AND CARDIOMETABOLIC HEALTH

Childhood obesity is a rising public health problem worldwide, which causes serious health problems both in childhood as well as later in life [18,19]. Estimates suggest that currently, 15% of children in the Netherlands has overweight or obesity [20]; in South-European countries, estimates of childhood overweight and obesity prevalence even reach 40% [21]. Childhood obesity impacts children's health and quality of life, by causing for example fractures, asthma, and poor self-esteem. In addition, children with obesity are likely to remain obese as adults and are at risk of chronic diseases. Obesity is also strongly related to cardiometabolic health in childhood; e.g., variations in blood lipids, blood pressure, and insulin resistance are already influence by obesity in childhood [19]. These cardiometabolic risk factors have been shown to track from childhood to adulthood [14,22] and thereby increasing the risk of coronary heart diseases, type 2 diabetes, and premature death [7,18,23]. Poor diet in childhood is one of the fundamental causes of childhood obesity and other cardiometabolic markers[24], and should therefore be a key target in the prevention of developing these cardiometabolic risk factors in childhood and later life. Hence, it is essential to gain knowledge about dietary factors that may influence obesity and cardiometabolic health in childhood, which is of high importance for early prevention of chronic diseases. Previous studies that examined the associations of dietary intake with obesity in children mainly focused on body mass index (BMI) as an outcome measure. However, especially in growing children, the use of a general mea-

sure like BMI is not an adequate measure of body fatness, as body mass includes both fat mass as well as lean mass and bone mass [25,26]. Increased BMI may be caused by increased fat mass or increased lean mass, or both [27]. Therefore, it is important to consider both of these as potential obesity-related outcomes.

ATOPIC DISEASES

Another disease that is already highly prevalent in childhood are atopic diseases, such as eczema, asthma, and food allergy. The prevalence of childhood atopic diseases has rapidly increased in recent decades [28-30]. These diseases have a substantial impact on the quality of life of those affected. Genetic background is one of the factors associated with risk of atopic diseases, but given the rapid increase in prevalence, environmental risk factors, including geographic area and lifestyle factors may play a substantial role in the development of allergies and other atopic diseases [30,31]. Early-life nutrition is an important modifiable lifestyle factor that affects the maturation process of a child's immune system, and has therefore often been hypothesized to influence the development of atopic diseases.

There has been great interest in the role of early-life dietary exposures in the development of atopic diseases. Previous studies have examined several nutritional aspects, including the avoidance of several allergenic foods during pregnancy or lactation [32], timing of introduction of highly allergenic foods [33], exclusive and/or longer duration of breastfeeding [34,35], probiotics and prebiotics [36-38], and supplements such as fatty acids [39,40] or vitamin D [41]. However, evidence for an effect of these nutritional interventions remain inconsistent. In addition, these nutritional factors may also represent an overall dietary pattern. Nevertheless, the role of overall diet quality in childhood in the development of atopic diseases remains unclear.

THIS THESIS

Objectives

The aims of this thesis were to evaluate overall diet quality in childhood, to study its determinants, and to examine its associations with body composition, cardiometabolic health, and atopic diseases (**Figure 1.1**).

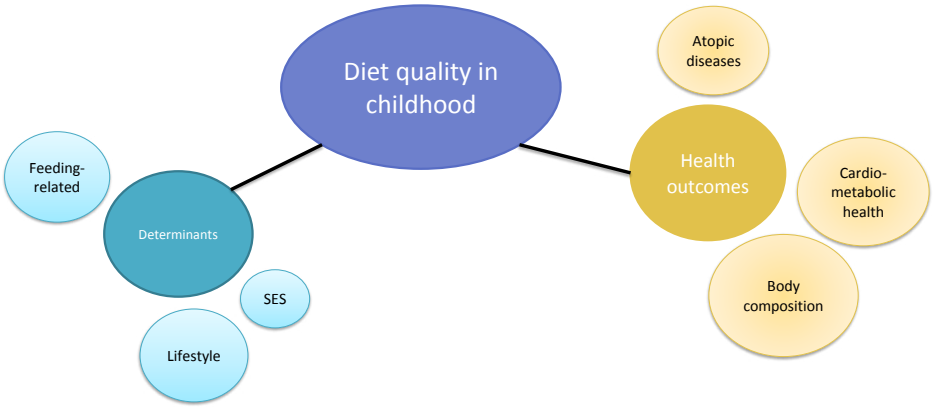

Figure 1.1. Aims of this thesis

Study populations

The studies in this thesis were embedded in three population-based cohort studies: the Generation R Study, the ABCD Study, and the Rhea Study.

Generation R Study

The Generation R Study is an ongoing population-based prospective cohort from fetal life onward in Rotterdam, the Netherlands [42]. Pregnant women with a delivery date between April 2002 and January 2006 were invited to participate in the study. The Generation R Study is designed to identify early environmental and genetic causes of normal and abnormal growth, development, and health from fetal life until young adulthood. In total, 9,778 women were included in the study and 7,893 children were enrolled in early childhood. During pregnancy, physical examinations were performed and questionnaires were used to obtain information on several sociodemographic and lifestyle factors, including diet. From birth onward, we obtained information on health and growth of the children from Child Health Centers and with questionnaires. Child food intake was assessed at two moments in childhood using food-frequency questionnaires (FFQ) which were specifically designed for that age group. At child's ages of 6 and 10 years, they were invited to our dedicated research center at Erasmus University Medical Center for a detailed physical examination. We measured height and weight; and fat mass, fat-

free mass, and bone mass were assessed using dual-energy X-ray absorptiometry (DXA). Additionally, blood pressure and serum concentrations of triacylglycerol, cholesterol, and insulin were measured. At the age of 10 years, skin prick tests were performed to examine sensitization to several inhalant and food allergens.

ABCD Study

The Amsterdam Born Children and their Development (ABCD) Study is an ongoing prospective population-based cohort study in Amsterdam, the Netherlands [43]. Between January 2003 and March 2004, all pregnant women living in Amsterdam were invited to participate. This large prospective population-based cohort study examines the associations between maternal lifestyle, medical, psychosocial and environmental conditions during pregnancy and children's health at birth as well as in later life. Of the 12,373 women approached, 8,266 women were enrolled in the study, and 7,995 children participated at birth. Around the children's age of 6 years, an FFQ was used to assess diet in childhood. In addition, questionnaires were used to obtain information on socioeconomic and lifestyle factors of the participants. Growth of the children were measured at their ages of 6 and 12 years at our research center. In addition, detailed measures of body composition were assessed using bioelectrical impedance analysis (BIA).

Rhea Study

The Rhea Study (The Mother-Child Cohort) is an ongoing prospective population-based cohort on the island of Crete, Greece [44]. This cohort included a representative sample of mother-child pairs from early pregnancy and aims to follow them up to young adulthood. One of the general objectives of the study is to characterize nutritional, environmental, and psychosocial determinants of children's growth and development. A total of 1,610 pregnant women were enrolled in the study between 2007 and 2008 and 1,363 live born children were available for follow-up. Dietary data was collected at child's age of 4 years using an FFQ. Information of sociodemographic and lifestyle factors was obtained using questionnaires. Data on height, weight, and waist circumference were repeatedly collected in early childhood. Blood samples were obtained to determine concentrations of leptin and adiponectin at the age of 4 years and of total, LDL, and HDL-cholesterol, and triglycerides at the ages of 4 and 6 years. Systolic and diastolic blood pressure of the children were measured at both time points. In addition, at the age of 6 years, body composition of the children was measured using BIA.

Outline

Chapter 2 of this thesis focuses on overall diet in early childhood. **Chapters 2.1** and **2.2** describe parental feeding-related determinants of diet quality in early childhood, including maternal history of eating disorders (Chapter 2.1) and feeding practices (Chap-

ter 2.2). **Chapter 2.3** focuses on dietary taste patterns in the diet of young children. In **chapter 2.4**, we evaluated overall diet quality in school-age children in the Generation R Study, its socioeconomic and lifestyle determinants, and its relation with diet quality in early childhood.

Chapter 3 focuses on diet quality in childhood in relation to children's body composition and cardiometabolic health. **Chapters 3.1** and **3.2** describe our research on diet quality in relation to growth and body composition in the Generation R Study (Chapter 3.1) and the ABCD Study (Chapter 3.2). **Chapter 3.3** presents results on the associations of diet quality with bone health in childhood. **Chapters 3.4** and **3.5** describe associations of diet quality with cardiometabolic health in children in the Generation R Study (Chapter 3.4) and the Rhea Study (Chapter 3.5).

Chapter 4 focuses on diet and atopic diseases in childhood. In Chapter 4.1, associations of diet quality at different time points in childhood with allergic sensitization and atopic diseases in the Generation R Study are presented. **Chapter 4.2** provides an overview of the current scientific literature on the effects of dietary interventions in the first 2 years of life on the development of atopic diseases.

Chapter 5 provides on overview of the main findings from all studies described in this thesis. In this chapter, major strengths and limitations as well as implications and recommendations for future studies are discussed.

REFERENCES

1. Nicklaus S. The role of dietary experience in the development of eating behavior during the first years of life. *Annals of Nutrition and Metabolism.* 2017;70(3):241-245.
2. Schwartz C, Scholtens PAMJ, Lalanne A, Weenen H, Nicklaus S. Development of healthy eating habits early in life. Review of recent evidence and selected guidelines. *Appetite.* 2011;57(3):796-807.
3. Zalewski BM, Patro B, Veldhorst M, et al. Nutrition of infants and young children (one to three years) and its effect on later health: A systematic review of current recommendations (EarlyNutrition project). *Critical reviews in food science and nutrition.* 2017;57(3):489-500.
4. Langley-Evans SC. Nutrition in early life and the programming of adult disease: a review. *Journal of Human Nutrition and Dietetics.* 2015;28:1-14.
5. Robinson S, Fall C. Infant nutrition and later health: a review of current evidence. *Nutrients.* 2012;4(8):859-874.
6. Reilly JJ, Kelly J. Long-term impact of overweight and obesity in childhood and adolescence on morbidity and premature mortality in adulthood: systematic review. *International journal of obesity.* 2011;35(7):891.
7. Morrison JA, Glueck CJ, Wang P. Childhood risk factors predict cardiovascular disease, impaired fasting glucose plus type 2 diabetes mellitus, and high blood pressure 26 years later at a mean age of 38 years: the Princeton-lipid research clinics follow-up study. *Metabolism.* 2012;61(4):531-541.
8. Morrison JA, Glueck CJ, Horn PS, Yeramaneni S, Wang P. Pediatric triglycerides predict cardiovascular disease events in the fourth to fifth decade of life. *Metabolism.* 2009;58(9):1277-1284.
9. Baker JL, Olsen LW, Sorensen TI. Childhood body-mass index and the risk of coronary heart disease in adulthood. *N Engl J Med.* 2007;357(23):2329-2337.
10. Chen X, Wang Y. Tracking of blood pressure from childhood to adulthood: a systematic review and meta-regression analysis. *Circulation.* 2008;117(25):3171-3180.
11. Juhola J, Magnussen CG, Viikari JS, et al. Tracking of serum lipid levels, blood pressure, and body mass index from childhood to adulthood: the Cardiovascular Risk in Young Finns Study. *J Pediatr.* 2011;159(4):584-590.
12. Camhi SM, Katzmarzyk PT. Tracking of cardiometabolic risk factor clustering from childhood to adulthood. *Int J Pediatr Obes.* 2010;5(2):122-129.
13. Craigie AM, Lake AA, Kelly SA, Adamson AJ, Mathers JC. Tracking of obesity-related behaviours from childhood to adulthood: a systematic review. *Maturitas.* 2011;70(3):266-284.
14. Singh AS, Mulder C, Twisk JWR, Van Mechelen W, Chinapaw MJM. Tracking of childhood overweight into adulthood: a systematic review of the literature. *Obesity reviews.* 2008;9(5):474-488.
15. Hu FB. Dietary pattern analysis: a new direction in nutritional epidemiology. *Current opinion in lipidology.* 2002;13(1):3-9.
16. Ocké MC. Evaluation of methodologies for assessing the overall diet: dietary quality scores and dietary pattern analysis. *Proceedings of the Nutrition Society.* 2013;72(2):191-199.
17. Montagnese C, Santarpia L, Buonifacio M, et al. European food-based dietary guidelines: A comparison and update. *Nutrition.* 2015;31(7-8):908-915.
18. Ebbeling CB, Pawlak DB, Ludwig DS. Childhood obesity: public-health crisis, common sense cure. *The lancet.* 2002;360(9331):473-482.

19. Friedemann C, Heneghan C, Mahtani K, Thompson M, Perera R, Ward AM. Cardiovascular disease risk in healthy children and its association with body mass index: systematic review and meta-analysis. *Bmj.* 2012;345:e4759.
20. Statistics Netherlands (CBS). Lengte en gewicht van personen, ondergewicht en overgewicht; vanaf 1981 *https://opendata.cbs.nl/statline/#/CBS/nl/dataset/81565NED/table?ts=1553851467369.* Retrieved 11-11-2019.
21. Spinelli A, Buoncristiano M, Kovacs VA, et al. Prevalence of Severe Obesity among Primary School Children in 21 European Countries. *Obes Facts.* 2019;12(2):244-258.
22. Simmonds M, Llewellyn A, Owen CG, Woolacott N. Predicting adult obesity from childhood obesity: a systematic review and meta-analysis. *Obes Rev.* 2016;17(2):95-107.
23. Park MH, Falconer C, Viner RM, Kinra S. The impact of childhood obesity on morbidity and mortality in adulthood: a systematic review. *Obes Rev.* 2012;13(11):985-1000.
24. Ambrosini GL. Childhood dietary patterns and later obesity: a review of the evidence. *Proceedings of the Nutrition Society.* 2014;73(1):137-146.
25. Freedman DS, Sherry B. The validity of BMI as an indicator of body fatness and risk among children. *Pediatrics.* 2009;124(Supplement 1):S23-S34.
26. Wilkes M, Thornton J, Horlick M, et al. Relationship of BMI z score to fat percent and fat mass in multiethnic prepubertal children. *Pediatric obesity.* 2019;14(1):e12463.
27. Freedman DS, Wang J, Maynard LM, et al. Relation of BMI to fat and fat-free mass among children and adolescents. *International journal of obesity.* 2005;29(1):1.
28. Thomsen SF. Epidemiology and natural history of atopic diseases. *European clinical respiratory journal.* 2015;2(1):24642.
29. Nwaru BI, Hickstein L, Panesar SS, et al. The epidemiology of food allergy in Europe: a systematic review and meta-analysis. *Allergy.* 2014;69(1):62-75.
30. Nutten S. Atopic dermatitis: global epidemiology and risk factors. *Annals of Nutrition and Metabolism.* 2015;66(Suppl. 1):8-16.
31. Sicherer SH, Sampson HA. Food allergy: a review and update on epidemiology, pathogenesis, diagnosis, prevention, and management. *Journal of Allergy and Clinical Immunology.* 2018;141(1):41-58.
32. Kramer MS, Kakuma R. Maternal dietary antigen avoidance during pregnancy or lactation, or both, for preventing or treating atopic disease in the child. *Evidence-Based Child Health: A Cochrane Review Journal.* 2014;9(2):447-483.
33. Zutavern A, Brockow I, Schaaf B, et al. Timing of solid food introduction in relation to eczema, asthma, allergic rhinitis, and food and inhalant sensitization at the age of 6 years: results from the prospective birth cohort study LISA. *Pediatrics.* 2008;121(1):e44-e52.
34. Yang YW, Tsai CL, Lu CY. Exclusive breastfeeding and incident atopic dermatitis in childhood: a systematic review and meta-analysis of prospective cohort studies. *British journal of dermatology.* 2009;161(2):373-383.
35. Kramer MS, Matush L, Vanilovich I, et al. Effect of prolonged and exclusive breast feeding on risk of allergy and asthma: cluster randomised trial. *Bmj.* 2007;335(7624):815.
36. van der Aa LB, Heymans HS, van Aalderen WM, Sprikkelman AB. Probiotics and prebiotics in atopic dermatitis: review of the theoretical background and clinical evidence. *Pediatr Allergy Immunol.* 2010;21(2 Pt 2):e355-367.
37. Cuello-Garcia CA, Brozek JL, Fiocchi A, et al. Probiotics for the prevention of allergy: A systematic review and meta-analysis of randomized controlled trials. *J Allergy Clin Immunol.* 2015;136(4):952-961.

38. Cuello-Garcia C, Fiocchi A, Pawankar R, et al. Prebiotics for the prevention of allergies: A systematic review and meta-analysis of randomized controlled trials. *Clin Exp Allergy.* 2017;47(11):1468-1477.
39. Miles EA, Calder PC. Can Early Omega-3 Fatty Acid Exposure Reduce Risk of Childhood Allergic Disease? *Nutrients.* 2017;9(7).
40. Palmer DJ, Sullivan T, Gold MS, et al. Effect of n-3 long chain polyunsaturated fatty acid supplementation in pregnancy on infants' allergies in first year of life: randomised controlled trial. *Bmj.* 2012;344:e184.
41. Yepes-Nunez JJ, Brozek JL, Fiocchi A, et al. Vitamin D supplementation in primary allergy prevention: Systematic review of randomized and non-randomized studies. *Allergy.* 2018;73(1):37-49.
42. Kooijman MN, Kruithof CJ, van Duijn CM, et al. The Generation R Study: design and cohort update 2017. *European Journal of Epidemiology.* 2016;31(12):1243-1264.
43. Van Eijsden M, Vrijkotte TGM, Gemke RJBJ, van der Wal MF. Cohort profile: the Amsterdam Born Children and their Development (ABCD) study. *International journal of epidemiology.* 2010;40(5):1176-1186.
44. Chatzi L, Leventakou V, Vafeiadi M, et al. Cohort profile: the mother-child cohort in Crete, Greece (Rhea study). *International journal of epidemiology.* 2017;46(5):1392-1393k.