General introduction

In 2008 a panel of experts of The Obesity Society (TOS), the leading professional obesity society in North America, wanted to provide and answer to the question whether obesity should be considered a disease (1). Since the prevalence of obesity kept increasing and obesity increases the risk of many morbidities, joint actions and aid of broad sectors of society to decrease the prevalence of obesity were needed. The TOS believed that labeling obesity as a disease would have more positive than negative consequences. They thought that it would lead to more resources being put into the prevention, treatment and research of obesity, but also to a reduction of stigma and discrimination towards obese persons. Therefore, in 2008, TOS declared obesity as a disease (1).

Obesity is defined as abnormal or excessive fat accumulation that may impair health (2). Childhood obesity is a public health problem and its prevalence has increased worldwide over the past few decades (3). In 1990, worldwide 4.2% of children up to the age of 5 were defined as overweight or obese, while in 2010 this number was already at 6.7% (4). This trend is expected to reach 9.1% in 2020 (4). For children aged 2-19 years the obesity prevalence in the United States has increased from 13.9% in 1999-2000 to 18.5% in 2015-2016 (5). In the Netherlands, between 1981 and 2015 the prevalence of overweight in children aged 4-20 years increased from 10.1% to 21.1% (6).

Children with obesity are 5 times more likely to be obese into adulthood compared to children without obesity (3, 7). Children and adults with overweight and obesity have a high risk of developing diseases targeting almost every organ system in the human body, some of which are presented in Figure 1 (8, 9, 10, 11, 12). These medical consequences can already be present during childhood and adolescence, but may also develop during adulthood (10). Furthermore, children with obesity have a greater risk of dying at a relatively young age due to comorbidities (i.e. diabetes and cardiovascular diseases) being carried over into adulthood (3, 13). Besides medical consequences, there are also psychosocial consequences of childhood obesity such as bullying, a low quality of life, fewer friends, and a low self-esteem (12, 14). Children with severe obesity report a significantly lower health-related QOL than healthy children and a similar health-related quality of life as children with cancer (14). Not only did children with obesity report a significantly lower score in total scale score for health-related QOL in comparison with healthy children, but also in all individual domains (i.e. psychical, psychosocial, emotional, social, and school functioning) (14). The social consequences of obesity may contribute to continue having difficulty in weight management, since children with overweight tend to have fewer friends which results in less interactive play and more sedentary behavior (12). Moreover, to prevent negative comments and bullying from happening, children with overweight tend to isolate themselves at home and may seek food as comfort (12).

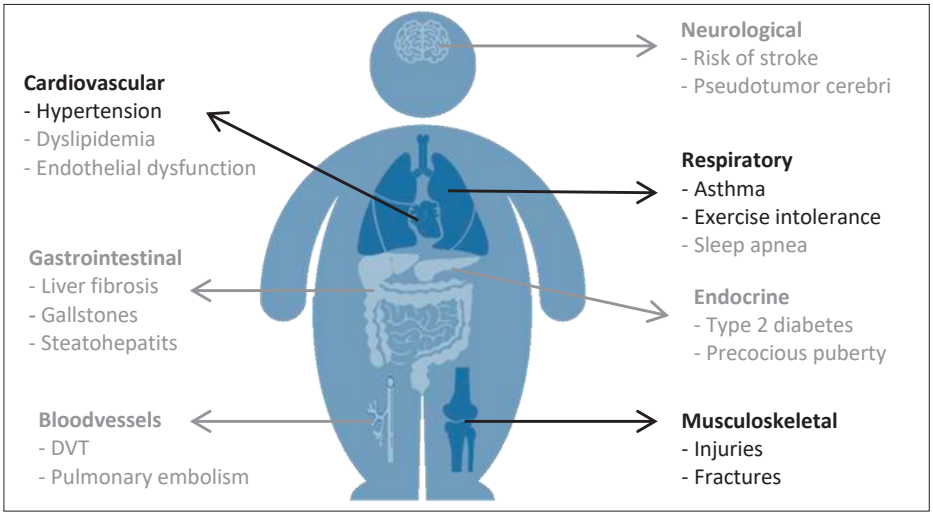

Figure 1 – Medical consequences of childhood obesity. In dark are the topics further discussed in this thesis.

Causes of obesity

The development of childhood obesity involves a complex set of factors that involve genetic, individual and environmental factors, which interact with each other (15). An overview of these factors are presented in Table 1. Weight gain results from an imbalance between energy intake and energy expenditure (15, 16). An increase in positive energy balance is often associated with dietary preferences and a more sedentary lifestyle (17, 18).

Genetics are often examined as a cause of obesity, but it is estimated that genetic factors account for less than 5% of cases of childhood obesity (19).

Individual factors that contribute to childhood obesity are, amongst others, intra-uterine exposure to maternal diabetes and having a mother or father who is overweight or obese (20, 21). Parental educational level and family income inversely correlate with the risk of childhood obesity (20). Other well-known individual risk factors for the development of childhood obesity include a decreased physical activity with increased sedentary behavior and an increased intake of energy-dense foods that are high in fat and sugars (15).

Examples of environmental factors associated with obesity include the fact that unhealthy food options are often less expensive than healthy options, recreational facilities are not accessible for all children and media and television-advertisements promote the unhealthy, sugary foods (22).

Table 1 – Factors involved in the development of childhood obesity

Genetics	Individual	Environmental
Different loci associated with BMI	Intra-uterine exposure to maternal diabetes Having a mother/father with overweight/obesity Low level of parental education Low family income Decreased physical activity Increased sedentary behavior Increased intake of high-dense food	Unhealthy food less expensive No accessible recreational facilities Media promoting unhealthy food Increased portion sizes Greater availability of sugar sweetened beverages

Treatment of childhood obesity

Since obesity is such a multifactorial problem, multidisciplinary intervention programs are the first choice of treatment in many countries including The Netherlands (23). These intervention programs should, according to the Dutch clinical guideline on obesity, focus on healthy eating with help of a dietician, the increase of physical activity with help of a physiotherapist, behavioral change with a psychologist and parenting support (23). The general practitioner can, in collaboration with the child and parents, refer the child with overweight or obesity to these intervention programs. The general practitioner decides, together with the parents, which discipline(s) the focus should be on. Furthermore, the general practitioner should meet with the child regularly to monitor the progress of the treatment.

Many studies use BMI as a primary outcome measure to measure the effectiveness of multidisciplinary intervention programs, and they have shown that these intervention programs have a beneficial effect on BMI in overweight children (24, 25). Recent studies have shown that cardiorespiratory fitness (CRF) is a stronger predictor for all-cause mortality than BMI, and therefore improving CRF with a multidisciplinary intervention program may be more important than reducing BMI (26, 27). Furthermore, childhood overweight and obesity increase the risk of high blood pressure in children, which is related to a variety of diseases in adulthood (28, 29). Thus, both CRF and blood pressure levels seem important outcome measures of multidisciplinary intervention programs.

Besides the introduction of multidisciplinary intervention programs worldwide, the WHO has issued a guideline on physical activity for children to fight the obesity epidemic (3). The guideline states that children should be moderately to vigorously active for at least 60 minutes each day (3). Since it is know that physical inactivity is a risk factor for childhood obesity, it is likely that children with overweight are less physically active than normal-weight children and that a lower percentage of children with overweight compared to normal-weight children meets the WHO physical activity guidelines (3, 21). Levels of physical activity can be measured objectively with accelerometers, but self-report can also be used to measure physical activity. However, the validity of self-reported

physical activity compared to objectively measured physical activity is controversial (30). Furthermore, it has not yet been investigated whether children themselves are able to accurately report their physical activity levels.

A multidisciplinary intervention program appears to have the best overall outcomes in the treatment of childhood obesity (31). However, pharmacological interventions, such as prescribing orlistat and sibutramine to treat childhood obesity, have also been studied. Though two recent systematic reviews found limited evidence for the use of pharmacological interventions (31, 32). Moreover, the Dutch guideline on obesity also advises against the use of medical treatment (23).

Kids4Fit

One example of a local multidisciplinary intervention program is Kids4Fit. This is an intervention program for children with overweight and obesity, living in deprived areas of Rotterdam, The Netherlands. Kids4Fit is a 12-week multidisciplinary intervention, including group session with a physiotherapist, a dietician, and a child psychologist (25). This intervention program is effective in reducing the waist circumference of obese children and analyses of this intervention also showed a non-significant trend towards a lower BMI-z up to 52 week after the intervention (25).

Role of the general practitioner

In the Netherlands, the general practitioner is responsible for primary care and therefore the first physician children and parents consult with their health related complaints. The general practitioner sees their patients regularly, since 70% of children aged 5-17 years consult the general practitioner at least once a year and on average 2 times a year (33). Since 2010 there is a clinical guideline on obesity for general practitioners in The Netherlands, issued by the Dutch College of General Practitioners (23). It provides guidance for the prevention, diagnosis, and treatment of children and adults with overweight and obesity. In short, it states that general practitioners have an signaling role for childhood obesity and should always be aware of obesity, regardless of the reason of consultation of the child (23). Self-reported weight and height are frequently used in general practice to obtain the weight status of the child in order to be able to signal obesity. However, reported values of weight and height in children have been found not to be valid in a previous study conducted in an open study population (34). The accuracy of self-reported height and weight in a study population in primary care remains unclear.

Childhood overweight and obesity is associated with medical consequences such as musculoskeletal complaints, injuries and fractures, and respiratory complaints such as asthma (Figure 1) (35, 36, 37, 38, 39). It could be expected that children with overweight consult the general practitioner more often than normal-weight children for overweight associated, medical consequences. However, up to now, no studies are available de-

scribing the relationship between childhood weight status and frequency and type of consultations at the general practice.

This thesis

The present thesis consists of three parts. In part one the accuracy of self-reported weight and-height of children are described, since these measures are needed to determine the weight status of the child. The second part describes the associations between childhood weight status and the frequency and type of consultations at the general practice. In the third part, the effect of a multidisciplinary intervention program as treatment of obesity is described and the physical activity behavior of normal-weight children and children with overweight are investigated in more depth.

PART ONE

Weight status

Body mass index (BMI) is the most common tool to classify weight status into 'underweight', 'normal-weight', 'overweight', and 'obese'. BMI is calculated by dividing a person's weight in kg by the square of the person's height in meters (kg/m^2). For adults, obesity is defined as a BMI of greater than or equal to 30 kg/m^2, while overweight is defined as a BMI great than or equal to 25 kg/m^2 (2). For children, there are age- and gender specific cut-offs of the BMI to classify them as overweight or obese. This age- and gender specific BMI is called the BMI-z. The International Obesity Task Force established these cut-offs, which are used in this dissertation (40, 41).

In order to have accurate BMI values, accurate weight and height measurements are necessary. Therefore the objective in **chapter 2** is to investigate the accuracy of self-reported weight and height compared to measured weight and height at the general practice.

PART TWO

Associations between childhood overweight and medical complications

There has been concern that childhood obesity negatively affects bone development, since childhood obesity is associated with an increased risk of bone fractures (35, 36). Previous research that has studied the differences in bone mineral density (BMD) between normal-weight children and children with overweight has been contradictory and therefore **chapter 3** describes the results of a systematic review and meta-analysis on the differences in BMD between normal-weight children and children with overweight.

Since childhood obesity increases the risk of developing musculoskeletal complaints, injuries and fractures, **chapter 4** investigates the differences in frequency and type of musculoskeletal consultations at the general practice between children with overweight and normal-weight children (35, 36).

Other frequently proposed complaints among children with underweight and- overweight are respiratory complaints, like asthma (35, 36, 37, 38, 39). **Chapter 5** therefore investigates whether childhood weight status is associated with the number and type of respiratory consultations at the general practice.

PART THREE

Treatment of obesity

Since the WHO has acknowledged obesity as a disease, people have become more aware of this health problem and several initiatives have been set up, such as the introduction of healthy fit schools. Furthermore, a clinical guideline on obesity was introduced in the Netherlands and worldwide different intervention programs for children with overweight and obesity have been set up (23). CRF and blood pressure levels are important outcome measures of intervention programs, therefore **chapter 6** evaluates the effect of a multidisciplinary intervention program (Kids4fit) for children with overweight and obesity on CRF and blood pressure.

Chapter 7 reports on the differences in physical (in)activity between normal-weight children and children with overweight. Furthermore, it is known that parents of children with overweight overestimate their child's level of physical activity (42). It has not yet been investigated whether children are able to accurately report their levels of physical activity. Therefore, this chapter also explores potential differences in self-reported and objectively measured physical activity.

Finally, in **chapter 8**, a general discussion of the main findings of this thesis will be presented.

REFERENCES

1. Allison DB, Downey M, Atkinson RL, Billington CJ, Bray GA, Eckel RH*, et al.* Obesity as a disease: a white paper on evidence and arguments commissioned by the Council of the Obesity Society. *Obesity (Silver Spring)* 2008;**16:** 1161-1177.
2. World Health Organization. Obesity and overweight factsheet. 2018 [cited 2018]. Available from: https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight.
3. World Health Organization. Childhood overweight and obesity: WHO; 2017 [cited 2017 26-10-2017]. Available from: http://www.who.int/dietphysicalactivity/childhood/en/.
4. de Onis M, Blossner M, Borghi E. Global prevalence and trends of overweight and obesity among preschool children. *Am J Clin Nutr* 2010;**92:** 1257-1264.
5. Hales CM CM, Fryar CD, Ogden CL. Prevalence of obesity among adults and youth: United States, 2015–2016. NCHS data brief, no 288. Hyattsville, MD: National Center for Health Statistics. , 2017.
6. Volksgezondheidenzorg.info. Overgewicht kinderen - trends: RIVM; [cited 2018]. Available from: https://www.volksgezondheidenzorg.info/onderwerp/overgewicht/cijfers-context/trends#node-trend-overgewicht-kinderen.
7. Simmonds M, Llewellyn A, Owen CG, Woolacott N. Predicting adult obesity from childhood obesity: a systematic review and meta-analysis. *Obes Rev* 2016;**17:** 95-107.
8. Daniels SR. Complications of obesity in children and adolescents. *Int J Obes (Lond)* 2009;**33 Suppl 1:** S60-65.
9. Krul M, van der Wouden JC, Schellevis FG, van Suijlekom-Smit LW, Koes BW. Musculoskeletal problems in overweight and obese children. *Ann Fam Med* 2009;**7:** 352-356.
10. Dietz WH. Health consequences of obesity in youth: childhood predictors of adult disease. *Pediatrics* 1998;**101:** 518-525.
11. Wallace WJ, Sheslow D, Hassink S. Obesity in children: a risk for depression. *Ann N Y Acad Sci* 1993;**699:** 301-303.
12. Niehoff V. Childhood Obesity: A Call to Action. *Bariatric Nursing and Durgical Patient Care* April 2009;**4:** 17-23.
13. Kelsey MM, Zaepfel A, Bjornstad P, Nadeau KJ. Age-related consequences of childhood obesity. *Gerontology* 2014;**60:** 222-228.
14. Schwimmer JB, Burwinkle TM, Varni JW. Health-related quality of life of severely obese children and adolescents. *Jama* 2003;**289:** 1813-1819.
15. Davison KK, Birch LL. Childhood overweight: a contextual model and recommendations for future research. *Obes Rev* 2001;**2:** 159-171.
16. Hall KD, Sacks G, Chandramohan D, Chow CC, Wang YC, Gortmaker SL*, et al.* Quantification of the effect of energy imbalance on bodyweight. *Lancet* 2011;**378:** 826-837.
17. Swinburn BA, Sacks G, Hall KD, McPherson K, Finegood DT, Moodie ML*, et al.* The global obesity pandemic: shaped by global drivers and local environments. *Lancet* 2011;**378:** 804-814.
18. Sahoo K, Sahoo B, Choudhury AK, Sofi NY, Kumar R, Bhadoria AS. Childhood obesity: causes and consequences. *J Family Med Prim Care* 2015;**4:** 187-192.
19. Anderson PM, Butcher KE. Childhood obesity: trends and potential causes. *Future Child* 2006;**16:** 19-45.
20. Freemark M. Childhood obesity in the modern age: global trends, determinants, complications, and costs. *Pediatric obesity: etiology, pathogenesis, and treatment.* Humana Press: New York, 2018, pp 3-24.

21. Brown CL, Halvorson EE, Cohen GM, Lazorick S, Skelton JA. Addressing Childhood Obesity: Opportunities for Prevention. *Pediatr Clin North Am* 2015;**62:** 1241-1261.
22. World Health Organization. Report of the Commission on ending childhood obesity 2016 [cited 2016].
23. Van Binsbergen JJ LF, Dapper ALM, Van Halteren MM, Glijsteen R, Cleyndert GA, Mekenkamp-Oei SN, Van Avendonk MJP. NHG-Standaard Obesitas. *Huisarts Wet* 2010;**53:** 609-625.
24. Snethen JA, Broome ME, Treisman P, Castro E, Kelber ST. Effective Weight Loss for Children: A Meta-analysis of Intervention Studies 2002-2015. *Worldviews Evid Based Nurs* 2016;**13:** 294-302.
25. van Middelkoop M, Ligthart KAM, Paulis WD, van Teeffelen J, Kornelisse K, Koes BW. A multidisciplinary intervention programme for overweight and obese children in deprived areas. *Fam Pract* 2017;**34:** 702-707.
26. Gaesser GA, Tucker WJ, Jarrett CL, Angadi SS. Fitness versus Fatness: Which Influences Health and Mortality Risk the Most? *Curr Sports Med Rep* 2015;**14:** 327-332.
27. Barry VW, Baruth M, Beets MW, Durstine JL, Liu J, Blair SN. Fitness vs. fatness on all-cause mortality: a meta-analysis. *Prog Cardiovasc Dis* 2014;**56:** 382-390.
28. Barlow SE, Dietz WH. Obesity evaluation and treatment: Expert Committee recommendations. The Maternal and Child Health Bureau, Health Resources and Services Administration and the Department of Health and Human Services. *Pediatrics* 1998;**102:** E29.
29. Marrodan Serrano MD, Cabanas Armesilla MD, Carmenate Moreno MM, Gonzalez-Montero de Espinosa M, Lopez-Ejeda N, Martinez Alvarez JR*, et al.* Association between adiposity and blood pressure levels between the ages of 6 and 16 years. Analysis in a student population from Madrid, Spain. *Rev Esp Cardiol (Engl Ed)* 2013;**66:** 110-115.
30. Adamo KB, Prince SA, Tricco AC, Connor-Gorber S, Tremblay M. A comparison of indirect versus direct measures for assessing physical activity in the pediatric population: a systematic review. *Int J Pediatr Obes* 2009;**4:** 2-27.
31. Rajjo T, Mohammed K, Alsawas M, Ahmed AT, Farah W, Asi N*, et al.* Treatment of Pediatric Obesity: An Umbrella Systematic Review. *J Clin Endocrinol Metab* 2017;**102:** 763-775.
32. O'Connor EA, Evans CV, Burda BU, Walsh ES, Eder M, Lozano P. Screening for Obesity and Intervention for Weight Management in Children and Adolescents: Evidence Report and Systematic Review for the US Preventive Services Task Force. *Jama* 2017;**317:** 2427-2444.
33. NIVEL. Zorg door de huisarts. Nivel Zorgregistraties eerste lijn: Jaarcijfers 2017 en trendcijfers 2011-2017. Utrecht, 2018.
34. Beck J, Schaefer CA, Nace H, Steffen AD, Nigg C, Brink L*, et al.* Accuracy of self-reported height and weight in children aged 6 to 11 years. *Prev Chronic Dis* 2012;**9:** E119.
35. Adams AL, Kessler JI, Deramerian K, Smith N, Black MH, Porter AH*, et al.* Associations between childhood obesity and upper and lower extremity injuries. *Inj Prev* 2013;**19:** 191-197.
36. Paulis WD, Silva S, Koes BW, van Middelkoop M. Overweight and obesity are associated with musculoskeletal complaints as early as childhood: a systematic review. *Obes Rev* 2014;**15:** 52-67.
37. Papoutsakis C, Priftis KN, Drakouli M, Prifti S, Konstantaki E, Chondronikola M*, et al.* Childhood overweight/obesity and asthma: is there a link? A systematic review of recent epidemiologic evidence. *J Acad Nutr Diet* 2013;**113:** 77-105.
38. Tanaka K, Miyake Y, Arakawa M, Sasaki S, Ohya Y. U-shaped association between body mass index and the prevalence of wheeze and asthma, but not eczema or rhinoconjunctivitis: the ryukyus child health study. *J Asthma* 2011;**48:** 804-810.
39. Wake M, Clifford SA, Patton GC, Waters E, Williams J, Canterford L*, et al.* Morbidity patterns among the underweight, overweight and obese between 2 and 18 years: population-based cross-sectional analyses. *Int J Obes (Lond)* 2013;**37:** 86-93.

40. Cole TJ, Bellizzi MC, Flegal KM, Dietz WH. Establishing a standard definition for child overweight and obesity worldwide: international survey. *Bmj* 2000;**320:** 1240-1243.
41. Cole TJ, Flegal KM, Nicholls D, Jackson AA. Body mass index cut offs to define thinness in children and adolescents: international survey. *Bmj* 2007;**335:** 194.
42. Small L, Bonds-McClain D, Gannon AM. Physical activity of young overweight and obese children: parent reports of child activity level compared with objective measures. *West J Nurs Res* 2013;**35:** 638-654.