Children with Overweight in Primary Care

Janneke van Leeuwen

Department of General Practice
Erasmus MC University Medical Center Rotterdam

This thesis is mainly based on data from the DOERAK study. The DOERAK study was funded by the Department of General Practice, Erasmus MC University Medical Center, Rotterdam. One chapter of this thesis was based on data from the Kids4Fit study. This study was funded by Fonds Achterstandswijken Rotterdam.

Financial support for the publication of this thesis was kindly provided by the SBOH, employer of GP trainees, and by the Erasmus University, Rotterdam, The Netherlands.

ISBN: 978-94-6361-248-7
Illustration cover: Marieke van Leeuwen
Lay-out and printing by Optima Grafische Communicatie

Children with Overweight in Primary Care

Kinderen met overgewicht in de huisartsenpraktijk

Proefschrift

ter verkrijging van de graad van doctor aan de
Erasmus Universiteit Rotterdam
op gezag van de
rector magnificus

Prof.dr. R.C.M.E. Engels

en volgens besluit van het College voor Promoties.
De openbare verdediging zal plaatsvinden op

woensdag 18 september om 13:30 uur

door

Janneke van Leeuwen
geboren te Hilversum

Erasmus University Rotterdam

PROMOTIECOMMISSIE

Promotoren:	Prof. dr. B.W. Koes
	Prof. dr. P.J.E. Bindels
Overige leden:	Prof. dr. H. Raat
	Prof. dr. E.F.C. van Rossum
	Prof. dr. N.J. de Wit
Copromotor:	Dr. M. van Middelkoop

CONTENTS

Chapter 1

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).

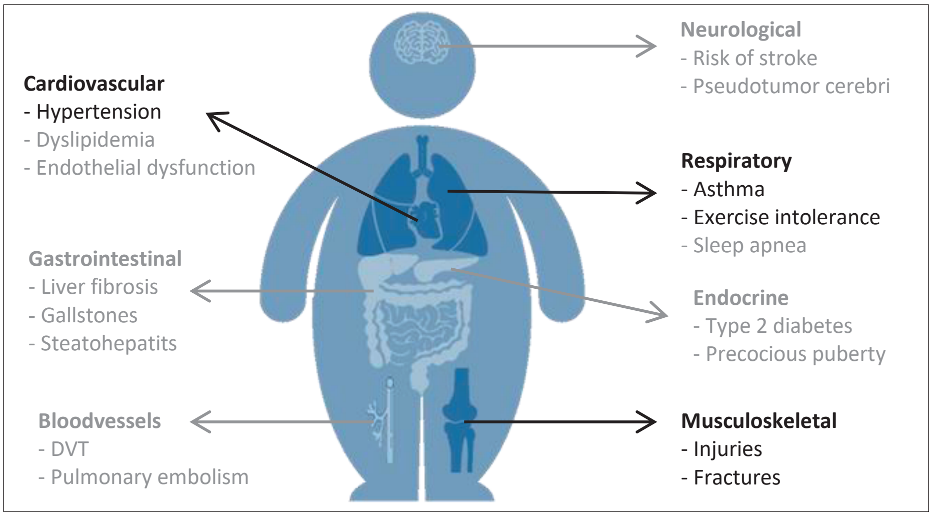


Figure 1 – Medical consequences of childhood obesity. In dark are the topics further discussed in this thesis.

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 un-healthy 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 describing 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.

Part I

Self-reported measures

Chapter 2

General practitioners cannot rely on reported weight and height of children

Janneke van Leeuwen, Marienke van Middelkoop, Winifred D. Paulis, Herman J. Bueving, Patrick J.E. Bindels, Bart W. Koes

Prim Health Care Res Dev. 2018. 8: 1-6

ABSTRACT

Background

Screening, signaling and treatment of childhood obesity by the general practitioner depends on accurate weight and height measurements.

Aim

The aim of this study is to investigate the differences between reported and measured weight and height for underweight, normal-weight, and overweight children, particularly in a GP setting.

Methods

Data on reported and measured weight and height from a cohort including 715 normal-weight and overweight children aged 2-17 were used. Means of reported and measured weight and height were compared using the paired T-test.

Results

Of the 715 included children, 17.5% were defined as being underweight, 63.2% normal-weight and 19.3% overweight according to direct measured height and weight.

In the age group 2-8 years, parents of underweight children reported a significantly higher weight than measured weight (MD 0.32kg (0.02, 0.62)), while parents of overweight young children reported a significantly lower weight (MD-1.08kg (-1.77,-0.39)). In the age group 9-17 years, normal-weight (MD-0.51kg (-0.79 ,-0.23)) and overweight children (MD-1.28kg (-2.08,-0.47)) reported a significantly lower weight than measured weight.

Conclusions

General practitioners cannot rely on reported weight and height measures from parents and children. In case of suspected under- or overweight in children, it should be advised to measure weight and height in general practice.

INTRODUCTION

Childhood obesity is a public health problem and its prevalence is increasing worldwide (1).

Reported, rather than measured weight and height are often used to calculate body mass index (BMI) and to classify the child as being underweight, normal-weight or overweight (2). This method of data collection is quicker, easier and cheaper and therefor often performed in both clinical practice and research. However, parents presenting to health care providers may give inaccurate information on the child's weight and height, since it has been shown that parents are likely to misperceive the weight status of their overweight child (3). As a result, children could be misclassified as being normal-weight rather than overweight or obese, which could lead to children missing out on proper and necessary treatment. Though, direct measurements of height and weight by a clinician are more-time consuming and more expensive.

General practitioners (GP) in the Netherlands are often the first health care provider of children and therefore play an important role in screening and signaling childhood obesity (4). The question arises whether the GP can rely on reported measurements by parents and children themselves or should children be measured during consultation at the GP? Therefore this study aims to investigate the accuracy of reported weight and height in children aged 2-17 compared to direct measurements by the GP.

METHODS

Study design

This study is a cross-sectional study using data from the DOERAK ("Determinants of (sustained) Overweight and complaints; Epidemiological Research among Adolescents and Kids in general practice") cohort study. The study protocol has been published previously (5). The study has been approved by the Institutional Review Board of the Erasmus University Medical Center, Erasmus MC.

Participants

Children aged 2-18 visiting their GP (or GP-trainee) between December 2010 and April 2013 were asked, during consultation, to participate in the study. This age range was used, since BMI-z scores can be calculated for children starting at age two and parents are legally responsible for their child up to the age of 18. Children were eligible to participate in the study if they/their parents had a basic understanding of the Dutch language, i.e. to be able to give informed consent and fill out Dutch questionnaires. Children with mental or physical disabilities, with comorbidities affecting weight, and children visiting their GP with emergency problems were not eligible. If child and parent showed interest after receiving verbal information during consultation, the child's weight and height were measured and recorded in the medical file, and contact information was sent to the research team. Study information and informed consent forms (and informed assent forms for children aged 12 and older) were then sent to the participants, where after the researcher contacted the family to answer possible questions and to investigate the willingness to participate. Both parents had to sign the informed consent (for children of all ages), and children aged 12 and older also had to sign the informed assent form. Children were formally included when informed consent forms (and if needed informed assent forms) were received.

Data collection and measurements

After formal inclusion, the GP or GP trainee were approached to collect data on the child's weight and height which was measured during consultation using calibrated scales and stadiometers. Measurements were performed by the GP or GP trainee who both followed the same study protocol (5).

The GP questionnaire was used to extract the participant's gender and age. Baseline BMI-z scores were calculated from the measured weight and height, and weight status was determined using the international age and gender specific cut-off points (6, 7). Children were then categorized in three different weight status groups: underweight, normal-weight, overweight/obese (from here on referred to as the overweight group).

Reported weight and height measures were collected from the baseline questionnaires which were filled out by parents of children aged 2-8, or children themselves (age 9 and older). From these reported weight and height measures, BMI-z scores, and corresponding weight status, were also calculated. The parent's questionnaires were used to extract information on socio-economic status (ses) (based on net household income (<2000 euros/month, ≥2000 euros/month)), ethnicity (both parents born in the Netherlands, at least one parent born in another country) and marital status reported by parents (parents living together, parents separated). Highest level of education in the household was categorized into three levels (up to lower secondary level, upper secondary level, at least bachelor level), based on the international standard classification of education (8).

Statistical analysis

Baseline demographics were described for underweight, normal-weight, and overweight children using means (sd) for continuous variables and frequencies (%) for dichotomous or categorical variables. Potential differences in baseline demographics between underweight and normal-weight, and overweight and normal-weight children were analyzed using the independent-samples T-test. Additionally, potential differences in measured and reported height, weight and BMI-z in the subgroups young (2-8 year) and older children (9-17 year), and boys and girls were analyzed using the paired T-test. The magnitude of the differences was determined using mean differences (MD) with 95% Confidence Intervals (CI). Complete case analysis was used. P-values <0.05 were considered statistically significant. IBM SPSS statistics 12.0 was used for statistical analyses.

RESULTS

Of the 1109 children that showed interest in study participation, 733 were included. Measured and/or reported weight and/or height was not available of 139 children who were excluded, and therefore 594 children were included in the present study (Figure 1). There were no significant differences in baseline characteristics between the excluded and included children.

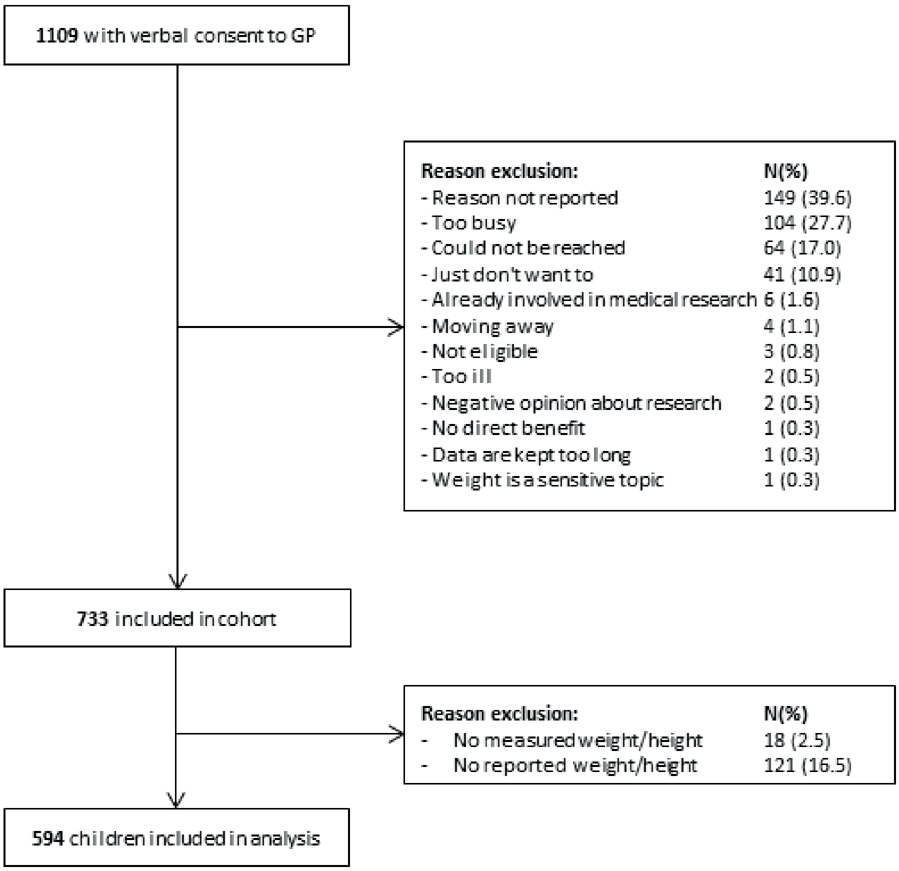


Figure 1 – Flowchart of inclusion

At baseline, 18.2% of the children were defined as being underweight, 62.3% normal-weight and 19.5% overweight according to direct measured height and weight (Table 1). The children in the underweight group were significantly younger than the normal-weight children (6.8 versus 8.3 years), while the overweight children were significantly older than the normal-weight children (9.3 versus 8.3 years).

Table 1 – Baseline characteristics.

Patient characteristics	**Study population N=594**	**Underweight* N=108**	**Normal weight* N=370**	**Overweight/ obese* N=116**
	N=594	**N=108**	**N=370**	**N=116**
Gender female, N (%)	316 (53.2)	57 (52.8)	196 (53.0)	63 (54.3)
	N=594	**N=108**	**N=370**	**N=138**
Age (years), mean (SD)	8.2 (4.0)	6.8 (3.9)‡	8.3 (4.1)	9.3 (3.7)‡
	N=541	**N=98**	**N=340**	**N=103**
SES, N (%)				
Low (<2000 euros)	121 (22.4)	20 (20.4)	75 (22.1)	26 (25.2)
Middle/High (>=2000 euros†)	420 (77.6)	78 (79.6)	265 (77.9)	77 (74.8)
	N=585	**N=107**	**N=363**	**N=115**
Highest education in household, N (%)				
Low (up to lower secondary level)	99 (19.9)	19 (17.7)	61 (16.8)	19 (16.5)
Middle (upper secondary level)	238 (40.7)	37 (34.6)	147 (40.5)	54 (47.0)
High (at least bachelor level)	248 (42.4)	51 (47.7)	155 (42.7)	42 (36.5)
	N=569	**N=107**	**N=351**	**N=111**
Ethnicity, N (%)				
Both parents born in Netherlands	483 (84.9)	91 (85.0)	303 (86.3)	89 (80.2)
At least one parent born in another country	86 (14.5)	16 (15.0)	48 (13.7)	22 (19.8)
	N=582	**N=107**	**N=362**	**N=113**
Marital status, N (%)				
Parents separated	93 (16.0)	16 (15.0)	56 (15.5)	21 (18.6)
Parents together	489 (84.0)	91 (85.0)	306 (84.5)	92 (81.4)

*weight status based on weight and height measures from general practitioner; †more than 2000 euros monthly net income per household; ‡significantly different from normal weight.

Analyses among the three weight groups showed that underweight children reported a significantly higher weight than measured (MD 0.58kg (0.11, 1.05)) while overweight children reported a significantly lower weight than measured (MD-1.20kg (-1.75,-0.65)). In the normal-weight group, no significant differences were found. For height, no significant differences between reported and measured height were found for all weight groups.

Tablte 2 – Mean differences between reported and measured weight, height and BMI-z according to weight status and age group

Weight status* Age group	Weight (kg)				Height (cm)				BMI-z			
	Reported Mean(sd)	Measured Mean(sd)	MD (95% CI)	P-value	Reported Mean(sd)	Measured Mean(sd)	MD (95% CI)	P-value	Reported Mean(sd)	Measured Mean(sd)	MD (95% CI)	P-value
Underweight*												
2-8 years	17.68	17.36	0.32	0.03†	112.13	113.19	-1.06	0.01†	-1.06	-1.67	0.60	0.001†
	(3.99)	(4.06)	(0.02 – 0.62)		(13.96)	(13.31)	(-1.87 –-0.25)		(1.56)	(0.88)	(0.25 – 0.97)	
9-17 years	34.82	33.65	1.17	0.10	150.35	149.46	0.90	0.50	-1.72	-2.06	0.34	0.08
	(8.42)	(9.58)	(-0.25 – 2.59)		(14.21)	(15.38)	(-1.78 – 3.58)		(1.10)	0.84)	(-0.04 – 0.71)	
Normalweight*												
2-8 years	21.87	21.76	0.11	0.66	117.05	117.12	-0.07	0.87	0.01	0.10	-0.09	0.12
	(6.23)	(5.16)	(-0.38 – 0.60)		(14.53)	(13.84)	(-0.83 – 0.70)		(1.02)	(0.63)	(-0.21 – 0.03)	
9-17 years	45.64	46.15	-0.51	<0.001†	157.26	157.14	0.12	0.48	-0.14	-0.05	-0.10	0.001†
	(11.40)	(11.64)	(-0.79 –-0.23)		(13.39)	(13.20)	(-0.22 – 0.47)		(0.71)	(0.67)	(-0.15 –-0.04)	
Overweight*												
2-8 years	29.13	30.21	-1.08	0.003†	124.45	123.36	1.09	0.03†	1.41	1.98	-0.57	0.001†
	(9.02)	(8.89)	(-1.77 –-0.39)		(15.44)	(15.48)	(0.14 – 2.04)		(1.27)	(0.62)	(-0.90 –-0.24)	
9-17 years	59.51	60.78	-1.28	0.002†	156.88	156.87	0.01	0.99	1.77	1.92	-0.15	0.03†
	(16.08)	(15.65)	(-2.08 –-0.47)		(12.80)	(12.47)	(-0.67 – 0.68)		(0.73)	(0.57)	(-0.29 –-0.01)	

*weight status based on weight and height measures from the general practitioner; †P-value < 0.05

The subgroup analyses among age groups showed that parents of underweight children aged 2-8 years, reported a significantly higher weight (MD 0.32kg (0.02, 0.62)) and lower height (MD -1.01cm (-1.69, -0.34)) than measured weight and height (Table 2). Parents of overweight children aged 2-8 reported a significantly lower weight (MD -1.08kg (-1.77,-0.39)) and larger height (MD 1.09 (0.14, 2.04)) than measured weight and height. There were no significant differences between reported and measured weight and height for normal weight children aged 2-8.

Normal-weight (MD -0.51kg (-0.79 ,-0.23)) and overweight children aged 9-17 reported a significantly lower weight than measured weight (MD-1.28kg (-2.08,-0.47)).

When looking at boys and girls separately, both overweight boys (MD-1.03kg (-1.74, -0.31)) and overweight girls (MD -1.34kg (-2.17, -0.51)) reported a significantly lower weight than measured. Boys aged 9-17 of normal-weight (MD-0.43kg (-0.87,-0.001)) and overweight (MD-1.06kg (-1.94,-0.18)), and girls aged 9-17 of normal-weight (MD-0.57kg (-0.95, -0.19)) and overweight (MD -1.46kg (-2.80, -0.12)) reported a significantly lower weight than measured. Parents of overweight girls aged 2-8 years reported a significantly lower weight than measured (MD-1.17kg,-1.94,-0.40)).

Of the 109 children who were classified as underweight by the GP, 33 would be misclassified into the normal-weight group when using reported measurements, and one child into the overweight group. Of the children who were classified as overweight by the GP (total 116), 20 would be misclassified as normal-weight and four as underweight using self-reported measurements (Table 3).

Table 3 – Weight status (mis)classification

		Based on self-reported data			
		Underweight N (%)	**Normal-weight N (%)**	**Overweight N(%)**	**Total**
Based on measured data	**Underweight, N (%)**	74 (68%)*	33 (31%)	1 (1%)	108 (18%)
	Normal-weight, N (%)	34 (9%)	322 (87%)*	14 (4%)	370 (62%)
	Overweight, N (%)	4 (4%)	20 (17%)	92 (79%)*	116 (20%)
	Total	112 (19%)	375 (63%)	107 (18%)	594 (100%)

* agreement on weight status between weight status based on self-reported data and based on measured data.

DISCUSSION

Summary

Parents of underweight and overweight children aged 2-8 years reported a significantly higher and lower weight respectively, compared to measured weight. Normal-weight and overweight children aged 9-17 reported a significantly lower weight than measured. When looking at boys and girls separately, both normal-weight and overweight boys and girls aged 9-17 reported a significantly lower weight than measured. Parents of overweight girls aged 2-8 years reported a significantly lower weight than measured.

Strength and limitations

The current study is one of the first to investigate the differences in reported and measured weight status in three different weight groups, split by age, in primary care. We were therefore able to investigate both how parents' reported weight and height of young children differed from measured values, and how reported weight and height by older children differed from measured values.

By inviting every child visiting the GP during the inclusion period, we tried to minimize selection bias. However, when comparing our study population to the overall Dutch population, parents of included children in our cohort were more often born in the Netherlands (84% vs 79%) and more often highly educated (42% vs 32%) (9). Since overweight and obesity is more prevalent in ethnic minorities and families of lower SES, selection bias in the current study may have led to an underestimation of the percentage overweight and obese children, and to an overestimation of underweight children (10). This is reflected by prevalence differences in underweight children of the current study (18.2%) when compared to the prevalence (1.6%) reported by the World Health Organization (WHO) (11) and reported by the Dutch Central Bureau of Statistics (5.7%) (12). Therefore, we may have to be careful to generalize the results of the current study to a wider perspective. However, the differences in percentage underweight children between the current study and the WHO may be associated with the different cut-off points that were used to classify children as underweight, normal-weight or overweight (6, 7, 13). The WHO uses the WHO growth references, which rely on age-sex-specific BMI centiles or SD scores to define the weight status cut-offs, while the current study used an international standard growth chart which was developed by The International Obesity Task Force (IOTF), to enable global comparison (6, 7, 13). However, since we were primarily interested in differences between reported and measured values within the different weight groups, we believe this did not significantly impact our results.

The size of our study sample was smaller than intended, which may have introduced a power problem (5). However, since we were able to show significant differences in reported and measured weight and height, we believe a larger study sample would not significantly change our results.

Lastly, when the GP measured the child's weight status during consultation, the results were recorded into the medical file of the child, and not per se concealed from the parent/child. We believe enough time passed from this consultation to when the baseline questionnaire was filled out by parents or the child, so that the parent/child did not remember what the GP had measured during consultation. Furthermore, this procedure was identical for every included child. We therefore believe that this procedure did not have a significant impact on our results.

Comparison with existing literature

Our findings are in line with previous literature (2), showing that reported weight in overweight and obese young children is not accurate compared to measured values. Previous literature already showed that parents often misperceive the weight(status) of their overweight child (3). However, the current study showed that parents are also inaccurate in reporting weight of their underweight child. Not only parents, but also children aged 9-17 fail to accurately report their own weight (14). As a result, 32% of the underweight children and 21% of the overweight children in our study would be misclassified in the different weight categories.

Although no significant differences in SES between underweight, normal-weight and overweight children were found, a trend is seen where overweight children come from families with a lower SES than underweight and normal-weight children. This is in line with other literature showing that obesity is more prevalent in children from ethnic minorities with a lower SES and level of education (15). However, in the current study, reported weight within a weight class was not significantly different between levels of SES, thus SES does not seem to influence the ability to accurately report weight.

Implications for research and/or practice

According to international guidelines for primary care, the GP plays an important role in screening children on their weight status (16). In the Netherlands, school physicians also play a role in screening children, since they measure height and weight at age 5-6 and 10-11 years. However, these data are not transferred to GPs (17). In the UK, a similar program is active, namely the National Child Measurement Programme (18). However, besides these set measurement times, no measured data is available and GP's will rely on self-reported data. However, if a GP would rely on the reported weight measures of parents and children, part of these under- or overweight children would potentially be missed and therefore not receive proper treatment or referral. Thus, the GP cannot rely on reported weight and height measures from parents and children. In case of suspected under- or overweight in children, it should be advised to measure weight and height in general practice. However, it is known that GP's find it difficult to discuss weight issues during consultation (19). Furthermore, research showed that although most GP's are able to identify the underweight and obese children at the end of the spectrum, many are not able to correctly identify the weight status of children who are just underweight, or just obese (20). Therefore, it could be argued that, to overcome these two issues, all children visiting the GP should be measured (at least yearly) as part of routine measurements so that accurate treatment and follow-up can be discussed during consultation.

REFERENCES

1. James PT, Leach R, Kalamara E, Shayeghi M. The worldwide obesity epidemic. *Obes Res* 2001;**9 Suppl 4:** 228S-233S.
2. 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.
3. Rietmeijer-Mentink M, Paulis WD, van Middelkoop M, Bindels PJ, van der Wouden JC. Difference between parental perception and actual weight status of children: a systematic review. *Matern Child Nutr* 2013;**9:** 3-22.
4. Paulis WD, Palmer M, Chondros P, Kauer S, van Middelkoop M, Sanci LA. Health profiles of overweight and obese youth attending general practice. *Arch Dis Child* 2017;**102:** 434-439.
5. Paulis WD, van Middelkoop M, Bueving H, Luijsterburg PA, van der Wouden JC, Koes BW. Determinants of (sustained) overweight and complaints in children and adolescents in primary care: the DOERAK cohort study design. *BMC Fam Pract* 2012;**13:** 70.
6. 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.
7. 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.
8. Centraal Bureau Voor De Statistiek. International Standard Classification of Education: Inpassen van het Nederlandse onderwijs in ESCED 2011. *Voorburg* 2011;**Netherlands**.
9. Centraal Bureau voor de Statistiek. Bevolking; onderwijsniveau; geslacht, leeftijd en migratieachtergrond: CBS; 2017. Available from: http://statline.cbs.nl/StatWeb/publication/?VW=T&DM=SLnl&PA=82275NED&LA=nl.
10. Stamatakis E, Primatesta P, Chinn S, Rona R, Falascheti E. Overweight and obesity trends from 1974 to 2003 in English children: what is the role of socioeconomic factors? *Arch Dis Child* 2005;**90:** 999-1004.
11. The World Bank. Prevalence of underweight, weight for age (% of children under 5) 1980 [16-02-2018]. Available from: https://data.worldbank.org/indicator/SH.STA.MALN.ZS?locations=NL.
12. Centraal Bureau voor de Statistiek. Lengte en gewicht van personen, ondergewicht en overgewicht; vanaf 1981 2016 [16-02-2018]. Available from: http://statline.cbs.nl/StatWeb/publication/?DM=SLNL&PA=81565NED.
13. de Onis M, Onyango AW, Borghi E, Siyam A, Nishida C, Siekmann J. Development of a WHO growth reference for school-aged children and adolescents. *Bull World Health Organ* 2007;**85:** 660-667.
14. Sherry B, Jefferds ME, Grummer-Strawn LM. Accuracy of adolescent self-report of height and weight in assessing overweight status: a literature review. *Arch Pediatr Adolesc Med* 2007;**161:** 1154-1161.
15. Gishti O, Kruithof CJ, Felix JF, Raat H, Hofman A, Duijts L, *et al.* Ethnic disparities in general and abdominal adiposity at school age: a multiethnic population-based cohort study in the Netherlands. *Ann Nutr Metab* 2014;**64:** 208-217.
16. Richardson L, Paulis WD, van Middelkoop M, Koes BW. An overview of national clinical guidelines for the management of childhood obesity in primary care. *Prev Med* 2013;**57:** 448-455.
17. Gemeentelijke Gezondheidsdienst. Jeugd & Gezondheid 2018 [cited 2018 05-06-2018]. Available from: https://www.vggm.nl/ggd/jeugd_en_gezondheid/wat_doet_de_jgz_4-18_jaar_/basisonderwijs.
18. National Health Service. National Child Measurement Programme 2018 [cited 2018 05-06-2018]. Available from: https://digital.nhs.uk/services/national-child-measurement-programme/.
19. Dettori H, Elliott H, Horn J, Leong G. Barriers to the management of obesity in children- A cross sectional survey of GPs. *Aust Fam Physician* 2009;**38:** 460-464.
20. Gage H, Erdal E, Saigal P, Qiao Y, Williams P, Raats MM. Recognition and management of overweight and obese children: a questionnaire survey of general practitioners and parents in England. *J Paediatr Child Health* 2012;**48:** 146-152.

Part II

Consequences

Chapter 3

Differences in bone mineral density between normal-weight children and children with overweight and obesity: a systematic review and meta-analysis

Janneke van Leeuwen, Bart W. Koes, Winifred D. Paulis, Marienke van Middelkoop

Obes Rev. 2017. 18(5): 525-546

ABSTRACT

Objective

To examine the differences in bone mineral density between normal-weight children and children with overweight or obesity.

Methods

A systematic review and meta-analysis of observational studies (published up to June 22nd 2016) on the differences in bone mineral density between normal weight children and overweight and obese children was performed. Results were pooled when possible and mean differences were calculated between normal-weight and overweight and normal-weight and obese children for bone content and density measures at different body sites.

Results

Twenty-seven studies, with a total of 5958 children, were included. There was moderate and high quality of evidence that overweight (MD 213 grams; 95%CI 166, 261) and obese children (MD 329 grams; 95%CI 229, 430) have a significantly higher whole body bone mineral content than normal-weight children. Similar results were found for whole body bone mineral density. Sensitivity analysis showed the association was stronger in girls.

Conclusions

Overweight and obese children have a significantly higher bone mineral density compared to normal-weight children.

Since there was only one study included with a longitudinal design, the long term impact of childhood overweight and obesity on bone health at adulthood is not clear.

INTRODUCTION

Obesity in both children and adolescents has been increasing dramatically worldwide (1). In 1990 it was estimated that 32 million children under the age of 5 were overweight or obese, and this number has risen to 41 million children in 2014 (1). Of all continents, Europe has the highest prevalence (13%) of children having overweight (1). These numbers indicate that childhood obesity is a growing problem, and even more so with the knowledge that obese children are more likely to stay obese into adulthood (1).

It has been shown that childhood obesity can, among other diseases, lead to diabetes, pulmonary complaints and cardiovascular diseases like hypertension, with symptoms of these diseases already apparent during childhood, and carrying on to adulthood (2, 3). In addition it has been shown that childhood obesity increases the chance of developing musculoskeletal complaints, injuries and fractures as early as in childhood (4, 5).

The mechanism behind the increased injury and fracture risk in obese children is not clear and therefore different theories have been proposed. Childhood obesity is associated with a decline in motor skills, these children may therefore be more prone to falling with injuries or fractures as a result (6). Furthermore, attaining a high peak bone mass by bone mass accrual during childhood, and maintaining bone mass through life is associated with a lower fracture risk later in life (7, 8). It is however unknown whether children with obesity have a normal bone mass accrual during childhood.

Furthermore, several studies have investigated the role of overweight and obesity on bone mineral content (BMC) and bone mineral density (BMD) in adults(9, 10). These studies show a positive relationship between BMI and BMC and BMD. These relationships have been studied less extensively in children, and the mechanism and factors influencing bone density in children seems more complex.

Research that has been conducted on children suggests that more adipose tissue in obese children is related to greater total bone mineral density by causing a greater mechanical load on the bone, however this relation is still under investigation (11, 12, 13). On the other hand, the lower physical activity levels in obese children, may contribute to a lower BMD in obese children compared to children with a normal weight (8, 14). Because of this contradictory uncertainty in the literature and the many studies performed on the association between BMD and weight status, this review will provide a systematic overview and meta-analysis on the differences in BMD between normal-weight children and children with overweight and obesity, in order to be able to draw a more uniform conclusion on this suggested association.

METHODS

Search methods

We searched the following databases for relevant articles available for all years up to June 22nd 2016: Medline (OVID), Embase, Cochrane, Web of Science (WoS), Cinahl ebsco, Pubmed publisher and Google scholar. The search string contained the terms obesity, BMD and children. The search string (see Appendix 1) was adapted to the different databases to facilitate a comprehensive search.

A study had to fulfill the following criteria to be included in this review:

Study design

Cross-sectional and longitudinal studies that investigated the differences in BMD between normal-weight children and overweight and obese children were included.

Participants

Participants had to be children aged between 2 and 18.

Exposure

The exposure was childhood overweight or obesity, with children of normal weight as control group. The definition of the different weight groups, i.e. normal-weight, overweight and/or obese, based on BMI, fat percentage or body weight had to be clarified in the study and children had to be categorized in these groups by each individual study.

Outcome

The outcome measure had to be BMD in g/cm^2, BMAD (bone mineral apparent density) in g/cm^3, or bone mineral content (BMC) expressed in kg's or grams, measured by dual x-ray absorptiometry (DEXA) or volumetric BMD (vBMD) in mg/cm^3 or mg/mm^3 measured by peripheral quantitative computed tomography (pQCT). The outcome measures could be measured at any site of the body. All outcome measures had to be reported on a continuous scale.

Exclusion criteria

Studies including children with any underlying (chronic/ systemic) disease including growth hormone deficiency, diabetes type 2, cystic fibrosis, kidney disease, liver disease or transplantation, inflammatory bowel disease and eating disorders were excluded. Studies including children with genetic defects were also excluded. Articles written in a language other than English or Dutch were excluded.

Study selection

Four reviewers (JvL, BK, MvM, WP) independently screened the relevant articles identified by the search strategy on in-and exclusion criteria. After the first screening, based on title and abstract, the full texts of the remaining articles were reviewed. Any discrepancies between the reviewers were resolved by discussing the original article and reaching consensus.

Risk of bias assessment

Three reviewers (JvL, MvM, BK) performed a risk of bias assessment, using an adjusted version of the quality assessment score of Paulis et al. (5) and the Newcaste-Ottowa Scale (NOS) (15) (see Appendix 2). The quality assessment list contained 16 criteria to assess the risk of bias, of which 14 are applicable to cross-sectional studies and all 16 items apply to longitudinal studies (see Appendix 2). The studies were then rated on these 16 items as 'positive', 'negative', or 'unclear'. Disagreements between the authors were resolved by a discussion. The final risk of bias was calculated by adding up the items with positive scores and dividing them by the total number of items. If more than 50% of the items were scored positive, the risk of bias was arbitrarily rated as low.

Data management

Data were extracted by three independent researchers (JvL, MvM, BK) using a standardized data extracting form. Study characteristics extracted were: study design, setting, country in which the study was performed, number of participants, mean age of participants, gender, weight status assessment, weight status definition, BMC and BMD assessment, sites of BMC and BMD assessment and BMC and BMD definition.

The bone mineral density measures (means and standard deviations) at different body sites for each weight group were extracted.

If standard deviations were not reported we used the confidence intervals to calculate the standard deviation. If the confidence interval was also not reported, an estimation of the standard deviation was made based on study data of comparable studies in terms of measurements and sample size.

If studies only reported their outcome as graphs, the means and (when shown) standard deviations were estimated from these graphs.

Data analysis

Data were pooled of studies which were clinically homogeneous and reported on the same outcome measures. Mean differences with 95% confidence intervals (CI) between overweight and normal-weight, and obese and normal-weight children were calculated. If a study grouped overweight and obese children into one group, this group was used as an 'overweight' group in the analyses, but additional analyses were performed to investigate potential differences between overweight and obese children when possible. Sensitivity analysis were performed to investigate potential differences between overweight and normal weight, and obese and normal weight children by gender.

For pooling we used the random effects model. Review manager 5.0 software was used to calculate the total mean differences with accompanying 95%CI. Statistical heterogeneity was tested with the chi^2 and I^2 test. For the pooled studies, we used funnel plots to analyze potential publication bias. If the funnel plot was symmetrical no publication bias was considered. If outcome measures were presented on different scales, the outcome measure was transformed to the most frequently reported scale. If pooling was not possible, data were analyzed descriptively.

Strength of evidence

In order to evaluate the strength of evidence of the pooled results, the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach was used (16). The rating of evidence started at high quality, because observational studies were the most appropriate design for the current review. The quality of evidence was downgraded by one level if there was inconsistency (I^2>40%), uncertainty (n < 400), or probability of bias (>25% of patients come from a study with a high risk of bias, or the funnel plot indicated publication bias). It was upgraded by one level if strong evidence of associations was found (MD >2SD). The following levels of evidence were distinguished.

- High: further research is unlikely to change the level of evidence. There are no known or suspected reporting biases
- Moderate: further research is likely to have an important impact on confidence of the estimate of effect and may change the estimate
- Low: further research is likely to have an important impact on confidence of the estimate of effect and is likely to change the estimate
- Very low: the estimate of effect is very uncertain

RESULTS

Study selection

From our search we obtained 5028 articles (Figure 1). After screening on title and abstract, 282 articles remained for potential inclusion for which full text was assessed. Finally, 27 articles were included in this systematic review (12, 17-42).

Study characteristics

Of the 27 included studies, five had a longitudinal design and the other 22 studies had a cross-sectional or case-control design. Of four of the five longitudinal studies (31, 38,

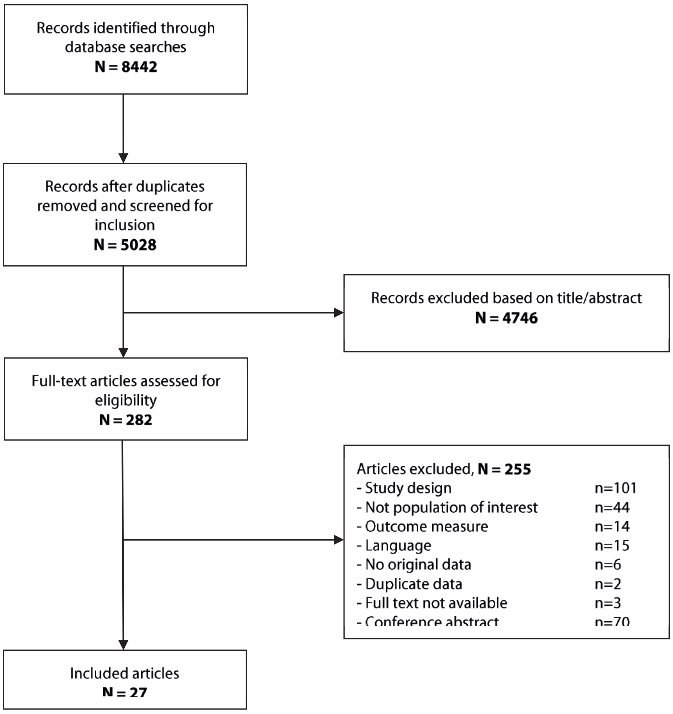


Figure 1 – Flowchart of selected papers.

41, 42) only baseline data were used since our outcome of interest was not reported at follow-up. These were therefore considered as cross-sectional.

The study characteristics of the included studies are shown in Table 1. The 27 included studies were conducted in 17 different countries across the world. Children were recruited in different settings, ranging from a random selection from an open population to schools and outpatient clinics. The most frequently reported outcomes were total body BMC (g), total body BMD (g/cm2), lumbar spine BMD (g/cm2) and femoral neck BMD (g/cm2). Only two studies did not report on any of these outcomes, but only on bone densities at different body sites (31, 39). The cross sectional studies included a total of 5126 children aged four to 18 years. The longitudinal study included 832 children.

Risk of bias assessment

Table 2 shows the final risk of bias assessment with 26 studies with a cross-sectional or case control design and one study with a longitudinal design. The reviewers agreed on 89.6% of the items of the 27 included studies (403 of 450), and reached consensus on all items after discussing them. Of the 27 included studies, 23 had a low risk of bias. Most studies (n=20) scored negative on the inclusion of at least 50 cases. Nearly all studies (n=26) reported a clear weight status and BMD definition.

Table 1 – study characteristics of included studies

Study	Country	Design	Setting	N	Age (years), range and/or mean (sd)	Gender %male	Weight status assessment	Weight status definition	BMD assessment	Sites of BMD assessment	BMD definition
De la Torre 1990	Not described	Case-control	Not described	11`	Control: 10.3 (1.7) Obese: 10.5 (1.7)	Not described	Not described	Not described	DXA	Whole body	BMD (g/cm^2)
Dimitri 2015	United Kingdom	Case-control	Tertiary pediatric endocrine unit and open population	36	Lean: 12.9 (2.0) Obese: 12.6 (1.9)	Not `described	BMI measured, cut-off based on Cole (43)	BMI <91st percentile is lean, BMI > 98th percentile is obese	High resolution peripheral quantitative computed tomography (HR-pQCT),	Non-dominant distal radius and non-dominant distal tibia	Total density (Dtot) (mg/cm^3), cortical density (CoD) (mg/cm^3), trabecular density (TrD) (mg/cm^3)
Ducher 2009	Australia	Cross-sectional	Schools	427	Range: 7-10 Normal-weight: 8.4 (0.4) Overweight: 8.3 (0.4)	48%	BMI measured, cut-off based on Cole (44)	Corresponds to adult percentile: BMI < 25 is non-overweight, BMI ≥ 25 overweight/obese	Peripheral quantitative computed tomography	Non-dominant distal forearm and contralateral distal lower leg	BMC (g/cm), Trabecular density (TrD) (mg/cm^3), Cortial density (CoD) (mg/cm^3)
El-Dorry 2015	Egypt	Case-control	Outpatient clinics	80	Range: 6-10	Not described	BMI measured, cut off according to Egyptian Growth Charts (45)	BMI 5th-85th percentile is non-obese, BMI >95th percentile is obese	DXA	Whole-body	BMC (g), BMD (g/cm^2)

Table 1 – study characteristics of included studies (continued)

Study	Country	Design	Setting	N	Age (years), range and/or mean (sd)	Gender %male	Weight status assessment	Weight status definition	BMD assessment	Sites of BMD assessment	BMD definition
Ellis 2003	USA	Cross-sectional	Pediatricians	865	Males: Normal-weight: 11.2 (4.1) Overweight: 11.0 (3.8) Obese: 11.6 (2.4) Females: Normal-weight: 11.4 (3.3) Obese: 12.2 (3.3) Obese 12.1 (3.4)	49%	% Fat by DXA	<25% fat is normal 25-20% fat is overweight >30% is obese	DXA	Whole-body	BMC (g)
Eriksson 2008	Sweden	Cross-sectional	Schools	96	Overall: 8.17 (0.34) Normal-weight: 8.17 (0.36) Overweight/obese: 8.20 (0.20)	56%	BMI measured, cut-off based on Cole (44)	Corresponds to adult percentile: BMI < 25 is non-overweight, BMI ≥ 25 overweight/obese	DXA	Whole-body, lumbar spine (ls), femoral neck (fn)	BMC (g), BMD (g/cm^2)
Fintini 2011	Italy	Cross-sectional	Outpatient clinic	151	14.5 (2.4)	46%	BMI measured, cut-off baed on BMI-SD scores (46)	BMD-SDS <2.0 is normal, BMD-SDS >2.0 is obese	DXA	Whole-body, Lumbar spine	BMD (g/cm^2),

Table 1 – study characteristics of included studies (continued)

Study	Country	Design	Setting	N	Age (years), range and/or mean (sd)	Gender %male	Weight status assessment	Weight status definition	BMD assessment	Sites of BMD assessment	BMD definition
Fischer 2000	Chili	Cross-sectional, case control	Outpatient clinic	32	Range: 5-13	50%	BMI measured, cut off based on National Center for Health Statistics (47)	More than 2 standard deviations of height/weight ratio is obese	DXA	Total body, Lumbar spine, femoral neck	BMD (g/cm^2), BMC (g)
Gracia-Marco 2011	Spain	Cross-sectional	Open population	330	Range: 12.5-17.5 Boys: 14.7 (1.3) Girls: 14.7 (1.1)	51%	BMI measured, cut off based on Cole (44, 48)	Corresponds to adult percentile: BMI < 25 is non-overweight, BMI ≥ 25 overweight/obese	DXA	Whole body, total hip, femoral neck and lumbar spine	BMC (g), BMD (g/cm^2)
Hanks 2015	USA	Cross-sectional	Participants at research at department of nutrition sciences	69	Range: 7-12 Overall: 9.5 (1.8) Non-obese: 9.2 (2.0) Obese: 9.8 (1.3)	38%	BMI-z score measured, using CDC growth charts (49)	BMI z-score < 1.64 is non-obese, BMI z-score ≥ 1.64 is obese	DXA	Whole body	BMC (kg), BMD (g/cm^3)

Table 1 – study characteristics of included studies (continued)

Study	Country	Design	Setting	N	Age (years), range and/or mean (sd)	Gender %male	Weight status assessment	Weight status definition	BMD assess-ment	Sites of BMD assessment	BMD definition
Haroun 2005	United Kingdom	Case-control	Hospitals, community clinic, ongoing studies in, obesity clinics	50	Range: 7-14 Boys: Control: 11.1 (1.6) Obese: 10.4 (2.1) Girls Control: 11.9 (2.0) Obese: 10.8 (2.2)	46%	BMI measured, converted to SDS using UK reference data (43)	BMI standard deviation scores (SDS)-2 to 1.61 is normal, BMI > 95th percentile, 1.61BMI SDS is obese.	DXA	Whole body	BMC (kg)
Hasano-glu 2000	Turkey	Cross-sectional	Not described	74	Range: 5-15 Control: 10.5 (2.8) Obese: 10.2 (3.2)	59%	BMI measured, cut off based on Hammer et al. (50)	BMI>95th percentile, and weight-length index >120 is obese	DXA	Lumbar spine	BMD (g/cm^2)
Ivuškāns 2014	Estonia	Cross-sectional	Schools	264	Range: 11-13 Normal-weight: 12.1 (0.8) Overweight: 12.0 (0.8)	100%	% body fat, cut-off based on McCarthy (51)	< 21.3-22.8 fat is normal ≥ 21.3-22.8 is overweight	DXA	Whole-body, lumbar spine (LS), femoral neck (FN)	BMD (g/cm^2), BMC (g)

Table 1 – study characteristics of included studies (continued)

Study	Country	Design	Setting	N	Age (years), range and/or mean (sd)	Gender %male	Weight status assessment	Weight status definition	BMD assessment	Sites of BMD assessment	BMD definition
Jeddi 2015	Iran	Cross-sectional	Schools	472	Range: 9-18	50%	BMI measured, cut off based on IOTF (44)	BMI <85th percentile is normal, BMI 85-95th percentile is overweight BMI ≥ 95th percentile is obese	DXA	Whole body BMD, lumbar spine (LS), femoral neck (FN)	BMD (g/cm^2), BMC (g)
Klein 1998	USA	Cross-sectional	Not described	48	Non-obese: 10.0 (1.9) Obese: 8.9 (1.8)	52%	BMI measured, cut off based on Frisch et al. (52)	BMI <85th percentile is non-obese, BMI > 95th percentile is obese	DXA	Whole body	BMD (g/m^2)
Kouda 2012	Japan	Longitudinal, but can only use baseline data (no-f-up BMD)	Schools	550	Unknown	52%	BMI, cut off based on Cole (44, 48)	Corresponds to adult: BMI <18.5 is underweight BMI < 25 is non-overweight, BMI ≥ 25 overweight/obese	DXA	Whole body	Bone mineral content index (BMCI) (kg/m^2)

Table 1 – study characteristics of included studies (continued)

Study	Country	Design	Setting	N	Age (years), range and/or mean (sd)	Gender %male	Weight status assessment	Weight status definition	BMD assessment	Sites of BMD assessment	BMD definition
Leonard 2015	USA	Cross-sectional	Hospital and open population	142	Range: 10-15 Non-obese: 14.5 (2.0) Obese: 12.2 (1.2)	36%	BMI measured, cut off on Ogden growth chart (53)	BMI >5th and < 85th percentile is non-obese, BMI > 97th percentile is obese	pQCT	Tibia and radius	CoD (mg/cm^3), TrD (mg/cm^3)
Lucas 2012	Portugal	Prospective cohort	Schools	346	Unknown	0%	BMI measured, cut off based on CDC (54)	BMI < 85th percentile at both timepoints is normal-weight, BMI ≥ 85th percentile at least at one timepoint is overweight	DXA	Nondominant distal forearm	BMD (g/cm^2)
Manzoni 1996	Italy	Cross-sectional	Not reported	115	Range: 5-18 Normal-weight: 11.4 (3.4) Obese: 11.1 (2.9)	50%	Relative body weight (RBW) (55)	RBW 80-120% is normal-weight, RBW > 120% is obese	DXA	Whole body, arms, trunk, legs	BMC (g)
Rocher 2008	France	Cross-sectional	Schools	43	Range: 9-12 Controls: 10.9 (1.1) Obese: 10.7 (1.2)	53%	BMI measured, cut off based on Cole (44)	Corresponds to adult: BMI < 25 is control, BMI ≥ 25 overweight/obese	DXA	Whole body, Lumbar spine	BMC (g), BMD (g/cm^2), BMAD (g/cm^3)

Table 1 – study characteristics of included studies (continued)

Study	Country	Design	Setting	N	Age (years), range and/or mean (sd)	Gender %male	Weight status assessment	Weight status definition	BMD assess-ment	Sites of BMD assessment	BMD definition
Rocher 2013	France	Cross-sectional	Schools	77	Range: 7-11 Normal-weight: 10.4 (1.5) Obese: 10.3 (1.4)	42%	BMI measured, cut off based on Cole (44)	Not reported	DXA	Whole body, lumbar spine (ls), nondominant forearm (tf), nondominant hip (th)	BMC (g), BMD (g/cm^2)
Shin 2011	Korea	Case-control	High schools	60	Unknown	0%	Kg	<51 kg is light weight 51-56.9kg is middle weight >57 is heavy weight	DXA	Lumbar spine, femoral neck	BMD (g/cm^2)
Temple-ton 2010	USA	Longi-tudinal, use only baseline data	Previous studies	96	Normal-weight: 11.55 (2.18) Overweight: 12.32 (2.34) Obese: 11.3 (2.5)	64%	BMI measured	BMI <85th percentile is normal-weight, BMI ≥ and < 95th percentile is overweight, BMI ≥95th percentile is obese	DXA	Whole body, arm, leg, trunk	BMC (kg)
Tubíc 2012	Sweden	Cross-sectional	Schools	41	Rage: 4-5 Normal-weight: 4.45 (0.36) Obese: 4.57 (0.32)	68%	BMI measured, cut off based on Karlberg et al. (56)	Not described	DXA	Heel	BMC (g), BMD (g/cm^2), BMAD (g/cm^3)

Table 1 – study characteristics of included studies (continued)

Study	Country	Design	Setting	N	Age (years), range and/or mean (sd)	Gender %male	Weight status assessment	Weight status definition	BMD assessment	Sites of BMD assessment	BMD definition
Uusi-Rasi 2012	Finland	Prospective cohort	Radomly selected from national population register	832	12 at baseline, mean 36.1(2.7) at follow up	45%	BMI measured at age 12.5, cut-off based on Cole (44)	Males: BMI >21.56 is overweight Females: BMI > 22.14 is overweight	pQCT	Distal radius, distial tibia, tibia shaft and radial shaft.	TrD (mg/cm^3), CoD (mg/cm^3)
Vaitkeviciute 2014	Estonia	Longitudinal, but use only baseline data	Schools	206	Underweight: 11.7 (0.47) Normal-weight: 12.1 (0.69) Overweight: 11.9 (0.74) Obese: 12.1 (0.95)	100%	BMI measured, cut-off based on Cole et al. (48)	BMI < 15.35 is underweight, BMI ≥ 15.35-21.22 is normal-weight, BMI ≥ 21.22-26.02 is overweight, BMI > 26.02 is obese	DXA	Whole body, lumbar spine (ls), femoral neck (fn)	BMD (g/cm^2)
Wetzsteon 2008	Canada	Longitudinal, but only use baseline data	Schools	445	Normal-weight: 10.2 (0.6) Overweight: 10.1 (0.6)	51%	BMI measured, cut-off based on CDC (54)	BMI ≤ 75th percentile is healthy weight, BMI ≥ 85th percentile is overweight	pQCT	Left tibia at 8% (total density), 50% and 66% site	Total density (mg/mm^3), CoD (mg/mm^3)

Table 2 – Quality assessment scores of included studies. Scoring options were positive (1), negative (0), unclear (2), or not applicable (na).

Study	Study groups are clearly defined	Participation ≥ 70%	Number of cases ≥ 50	Weight status definition	Assessment of weight status	Weight status assessment by independent person	BMD definition	Assessment of BMD	Blind for weight status	Longitudinal design	Inclusion and exclusion criteria	Follow-up period ≥1 year	Information completers vs withdrawals	Data presentation	Consideration of confounders	Control for confounding	Total percentage
								Cross-sectional studies									
De la Torre 1990	0	2	0	0	0	2	1	0	2	0	0	na	na	1	0	0	14
Dimitri 2015	1	2	0	1	1	1	1	1	2	0	1	na	na	1	1	1	71
Ducher 2009	1	1	1	1	1	1	1	1	2	0	0	na	na	1	1	1	79
El-Dorry 2015	0	2	0	1	1	1	1	1	2	0	1	na	na	0	0	0	43
Ellis 2003	1	2	0	1	1	1	1	1	2	0	0	na	na	1	1	1	64
Eriksson 2008	1	1	0	1	0	1	1	1	2	0	1	na	na	1	1	0	64
Fintini 2011	1	2	0	1	1	1	1	1	2	0	1	na	na	1	1	1	71
Fischer 2000	1	1	0	1	0	2	1	1	2	0	0	na	na	1	1	1	58
Gracia-Marco 2011	0	1	0	1	0	1	1	1	2	0	0	na	na	0	1	1	50
Hanks 2015	1	2	0	1	1	1	1	1	2	0	1	na	na	1	1	1	71
Haroun 2005	1	1	0	1	1	1	1	1	2	0	0	na	na	1	1	0	64
Hasanoglu 2000	1	1	0	1	0	2	1	1	2	0	0	na	na	1	0	0	43
Ivuskans 2014	1	2	1	1	1	1	0	1	2	0	1	na	na	1	0	0	57
Jeddi 2015	1	2	0	1	1	1	1	1	2	0	1	na	na	1	1	0	64
Klein 1998	1	2	0	1	2	2	1	1	2	0	0	na	na	1	1	1	50
Leonard 2015	1	2	1	1	1	1	1	1	2	0	1	na	na	1	1	1	79
Manzoni 1996	1	2	1	1	1	1	1	1	2	0	2	na	na	1	0	0	57
Rocher 2008	1	2	0	1	1	1	1	1	2	0	1	na	na	1	1	1	71
Rocher 2013	1	2	1	1	1	1	1	1	2	0	1	na	na	1	1	1	79
Shin 2011	1	2	0	1	0	2	1	1	2	0	1	na	na	1	0	0	43
Templeton 2011	1	2	0	1	1	1	1	1	2	1	2	na	na	1	1	1	71
Tubíc 2012	1	2	0	1	1	1	1	1	2	0	1	na	na	1	1	1	71
Kouda 2012	0	1	0	1	1	0	1	1	2	1	1	na	na	1	1	1	71
Lucas 2012	1	1	1	1	1	1	1	1	2	1	1	na	na	1	0	0	79
Vaitkeviciute 2014	1	2	0	1	1	1	1	1	1	1	1	na	na	1	1	1	86
Wetzsteon 2008	1	2	1	1	1	1	1	1	2	1	1	na	na	1	1	1	86
								Longitudinal studies									
Uusi-Rasi 2012	1	0	0	1	2	2	1	1	2	1	0	1	0	1	1	1	56

Mean differences

Prospective study

Uusi-Rasi et al. (40) reported prospective data on the differences in BMD between overweight and non-overweight children. They concluded that childhood overweight may lead to higher trabecular density at the tibia in adult women only with mean difference (MD) 17 mg/cm^3 (95%CI 3.73, 29.27), and adult men have a somewhat lower cortical density at tibia (MD-13 mg/cm^3 (95%CI-13.48,-0.52)).

Cross-sectional studies

Total body bone mineral content(g)

A total of 13 studies reported total body BMC (g) per weight group. Of these, six (20, 21, 24, 28, 29, 38) reported the BMC for normal-weight and overweight children and ten (19, 20, 23, 25, 26, 29, 34, 35, 36, 38) for normal-weight and obese children. Figure 2a shows the pooled results of the differences in BMC between normal-weight and overweight children (MD 214 grams (95%CI 166, 261; I^2=17%)). Low heterogeneity, low uncertainty (n>400) and low probability of bias lead to high quality of evidence showing that overweight children have a significantly higher whole body BMC than normal-weight children.

Pooled data of nine studies comparing whole body BMC between obese and normal-weight children showed a significant MD of 329 grams (95%CI 229, 430) (Figure 2b). The test for heterogeneity showed an I^2 of 63% (p=0.003), therefore the quality of evidence for this significant difference in BMC was downgraded by only one level leading to moderate quality.

Templeton et al. (38) reported BMC for both overweight and obese children, but their results could not be used in both meta-analyses due to different outcome scales, though comparable results were found.

Analysis between overweight and obese children including the results of two studies (20, 29), showed a MD of total body BMC of 112 grams ((95%CI-3, 227), I^2=0% (P=0.88)) leading to high quality of evidence for no significant difference in total body BMC between obese and overweight children (see appendix 3a).

Whole body bone mineral density (g/cm^2)

Six studies (21, 24, 28, 29, 33, 41) reported the BMD for normal-weight and overweight children and pooled results showed a significant MD of 0.04 g/cm^2 (95%CI 0.02, 0.05), I^2=70 (Figure 3a). Pooled data of nine studies (17, 19, 22, 23, 29, 30, 35, 36, 41) showed a significant difference in BMD between normal-weight and obese children (MD 0.05 g/cm^2 (95%CI 0.02, 0.09)) (Figure 3b). Statistical significant heterogeneity (I^2=82) was found and therefore moderate quality of evidence was found for a significant mean difference in BMD between normal weight children and overweight and obese children.

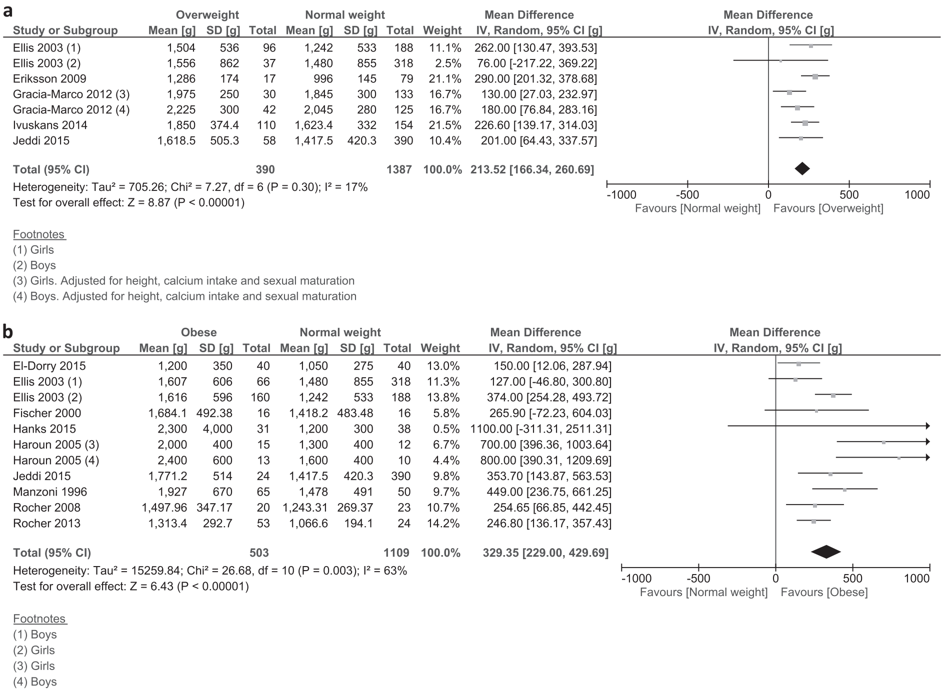


Figure 2 – (a) Pooled results of the studies that reported whole body BMC(g) for normal weight and overweight children. (b) Pooled results of the studies that reported whole body BMC(g) for normal weight and obese children. BMC, bone mineral content.

Analysis between overweight and obese children including the results of two studies (29, 41) showed a MD of total body BMD of 0.05 g/cm^2 (95%CI 0.03, 0.08), I^2=0% (P=0.88). However, since there was uncertainty (n<400), the quality of evidence was downgraded by one level to moderate quality of evidence for a significantly higher BMD in obese children compared to overweight children (see appendix 3b).

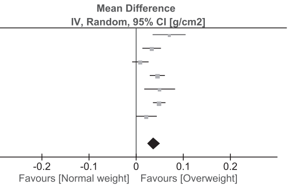
Lumbar spine BMD (g/cm^2)

Six studies (21, 24, 28, 29, 37, 41) reported on the differences in lumbar spine BMD between normal-weight and overweight children and pooled results showed a significant MD of 0.04 g/cm^2 (95%CI 0.01, 0.06), I^2= 75% (Figure 4a). Additionally, pooled data of eight studies (22, 23, 27, 29, 35, 36, 37, 41) comparing lumbar spine BMD between normal-weight and obese children showed a significant MD of 0.08 g/cm^2 (95%CI 0.05, 0.11) (Figure 4b). Statistically significant heterogeneity (I^2 = 73%) was found and therefore moderate quality of evidence was found for a significant mean difference in lumbar spine BMD between normal-weight children and overweight and obese children.

a

Study or Subgroup	Overweight Mean [g/cm2]	Overweight SD [g/cm2]	Overweight Total	Normal Mean [g/cm2]	Normal SD [g/cm2]	Normal Total	Weight	Mean Difference IV, Random, 95% CI [g/cm2]
Eriksson 2009	0.92	0.07	17	0.85	0.05	79	9.2%	0.07 [0.03, 0.11]
Gracia-Marco 2012 (1)	1.065	0.048	30	1.032	0.057	133	15.2%	0.03 [0.01, 0.05]
Gracia-Marco 2012 (2)	1.065	0.049	42	1.056	0.053	125	16.3%	0.01 [-0.01, 0.03]
Ivuskans 2014	1.007	0.066	110	0.962	0.065	154	17.0%	0.04 [0.03, 0.06]
Jeddi 2015	0.91	0.12	58	0.86	0.11	390	9.9%	0.05 [0.02, 0.08]
Lucas 2012	0.398	0.058	95	0.349	0.052	251	18.2%	0.05 [0.04, 0.06]
Vaitkeviciute 2014	1.001	0.047	22	0.979	0.057	133	14.2%	0.02 [0.00, 0.04]
Total (95% CI)			**374**			**1265**	**100.0%**	**0.04 [0.02, 0.05]**

Heterogeneity: Tau² = 0.00; Chi² = 19.88, df = 6 (P = 0.003); I² = 70%
Test for overall effect: Z = 5.27 (P < 0.00001)

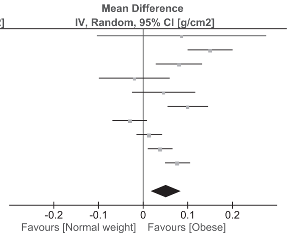


Footnotes
(1) Girls
(2) Boys

b

Study or Subgroup	Obese Mean [g/cm2]	Obese SD [g/cm2]	Obese Total	Normal weight Mean [g/cm2]	Normal weight SD [g/cm2]	Normal weight Total	Weight	Mean Difference IV, Random, 95% CI [g/cm2]
De la Torre 1990	0.96	0.09	6	0.874	0.2	5	2.6%	0.09 [-0.10, 0.28]
El-Dorry 2015	0.75	0.12	40	0.6	0.11	40	10.5%	0.15 [0.10, 0.20]
Fintini 2011 (1)	1.08	0.12	40	1	0.12	42	10.4%	0.08 [0.03, 0.13]
Fintini 2011 (2)	1.08	0.12	41	1.1	0.19	28	7.8%	-0.02 [-0.10, 0.06]
Fischer 2000	0.818	0.1	16	0.772	0.105	16	8.5%	0.05 [-0.03, 0.12]
Jeddi 2015	0.96	0.11	24	0.86	0.11	390	11.0%	0.10 [0.05, 0.15]
Klein 1998	0.79	0.06	30	0.82	0.07	18	11.6%	-0.03 [-0.07, 0.01]
Rocher 2008	0.927	0.01	20	0.913	0.07	23	12.5%	0.01 [-0.01, 0.04]
Rocher 2013	0.883	0.069	53	0.845	0.052	24	12.6%	0.04 [0.01, 0.07]
Vaitkeviciute 2014	1.056	0.067	24	0.979	0.057	133	12.5%	0.08 [0.05, 0.11]
Total (95% CI)			**294**			**719**	**100.0%**	**0.05 [0.02, 0.09]**

Heterogeneity: Tau² = 0.00; Chi² = 50.47, df = 9 (P < 0.00001); I² = 82%
Test for overall effect: Z = 3.05 (P = 0.002)



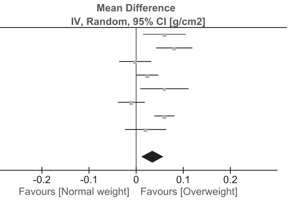
Footnotes
(1) Girls
(2) Boys

Figure 3 – (a) Pooled results of the studies that reported whole body BMD (g/cm2) for normal weight and overweight children. (b) Pooled results of the studies that reported whole body BMD (g/cm2) for normal weight and obese children. BMD, bone mineral density.

a

Study or Subgroup	Overweight Mean [g/cm2]	Overweight SD [g/cm2]	Overweight Total	Normal weight Mean [g/cm2]	Normal weight SD [g/cm2]	Normal weight Total	Weight	Mean Difference IV, Random, 95% CI [g/cm2]
Eriksson 2009	0.741	0.09	17	0.681	0.07	79	10.6%	0.06 [0.01, 0.11]
Gracia-Marco 2012 (1)	1	0.097	30	0.919	0.098	133	11.9%	0.08 [0.04, 0.12]
Gracia-Marco 2012 (2)	0.867	0.098	42	0.869	0.095	125	12.8%	-0.00 [-0.04, 0.03]
Ivuskans 2014	0.839	0.09	110	0.815	0.103	154	15.0%	0.02 [0.00, 0.05]
Jeddi 2015	0.89	0.19	58	0.83	0.16	390	9.5%	0.06 [0.01, 0.11]
Shin 2011 (3)	1.12	0.03	10	1.13	0.035	10	13.9%	-0.01 [-0.04, 0.02]
Shin 2011 (4)	0.93	0.03	10	0.87	0.017	10	15.3%	0.06 [0.04, 0.08]
Vaitkeviciute 2014	0.849	0.097	22	0.829	0.098	133	10.9%	0.02 [-0.02, 0.06]
Total (95% CI)			**299**			**1034**	**100.0%**	**0.04 [0.01, 0.06]**

Heterogeneity: Tau² = 0.00; Chi² = 28.16, df = 7 (P = 0.0002); I² = 75%
Test for overall effect: Z = 2.93 (P = 0.003)

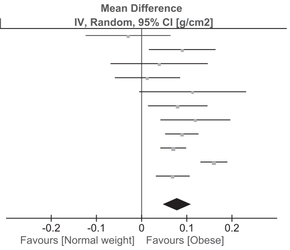


Footnotes
(1) Girls. Adjusted for height, calcium intake and sexual maturation
(2) Boys. Adjusted for height, calcium intake and sexual maturation
(3) Taekwando
(4) Control

b

Study or Subgroup	Obese Mean [g/cm2]	Obese SD [g/cm2]	Obese Total	Normal weight Mean [g/cm2]	Normal weight SD [g/cm2]	Normal weight Total	Weight	Mean Difference IV, Random, 95% CI [g/cm2]
Fintini 2011 (1)	0.87	0.13	41	0.9	0.23	28	6.3%	-0.03 [-0.12, 0.06]
Fintini 2011 (2)	0.97	0.18	40	0.88	0.16	42	8.1%	0.09 [0.02, 0.16]
Fischer 2000	0.72487	0.17175	16	0.686	0.13708	16	5.4%	0.04 [-0.07, 0.15]
Hasanoglu 2000 (3)	0.575	0.14	19	0.562	0.079	19	8.2%	0.01 [-0.06, 0.09]
Hasanoglu 2000 (4)	0.746	0.24	18	0.633	0.09	18	4.7%	0.11 [-0.01, 0.23]
Jeddi 2015	0.91	0.16	24	0.83	0.16	390	8.9%	0.08 [0.01, 0.15]
Rocher 2008	0.774	0.16	20	0.655	0.08	23	7.7%	0.12 [0.04, 0.20]
Rocher 2013	0.683	0.093	53	0.594	0.068	24	12.2%	0.09 [0.05, 0.13]
Shin 2011 (5)	1.2	0.03	10	1.13	0.035	10	13.2%	0.07 [0.04, 0.10]
Shin 2011 (6)	1.03	0.045	10	0.87	0.017	10	13.0%	0.16 [0.13, 0.19]
Vaitkeviciute 2014	0.898	0.084	24	0.829	0.098	133	12.2%	0.07 [0.03, 0.11]
Total (95% CI)			**275**			**713**	**100.0%**	**0.08 [0.05, 0.11]**

Heterogeneity: Tau² = 0.00; Chi² = 36.44, df = 10 (P < 0.0001); I² = 73%
Test for overall effect: Z = 5.00 (P < 0.00001)



Footnotes
(1) Boys
(2) Girls
(3) Prepubertal
(4) Pubertal
(5) Taekwando
(6) Control

Figure 4 – (a) Pooled results of the studies that reported lumbar spine BMD (g/cm2) for normal weight and overweight children. (b) Pooled results of the studies that reported lumbar spine BMD (g/cm2) for normal weight and obese children. BMD, bone mineral density.

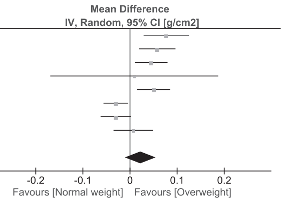
Femoral neck BMD (g/cm^2)

Pooled results of six studies (21, 24, 28, 29, 37, 41) showed an MD of 0.02 g/cm^2 (95%CI -0.01, 0.06), indicating that there is no significant difference in femoral neck BMD between overweight and normal-weight children. The MD of femoral neck BMD between obese and normal-weight children was 0.07 g/cm^2 (95%CI 0.04, 0.09), which was obtained from 5 different studies (23, 29, 36, 37, 41) (Figure 5a and 5b). The heterogeneity for these associations was 81% (P<0.001) and 55% (P=0.05) respectively. This led to a moderate quality of evidence for the non-significant mean difference in femoral neck BMD between normal-weight and overweight children and for the significant mean difference in femoral neck BMD between normal-weight and obese children.

a

Study or Subgroup	Overweight Mean [g/cm2]	Overweight SD [g/cm2]	Overweight Total	Normal weight Mean [g/cm2]	Normal weight SD [g/cm2]	Normal weight Total	Weight	Mean Difference IV, Random, 95% CI [g/cm2]
Eriksson 2009	0.837	0.09	17	0.76	0.1	79	12.3%	0.08 [0.03, 0.13]
Gracia-Marco 2012 (1)	0.889	0.097	30	0.831	0.099	133	13.7%	0.06 [0.02, 0.10]
Gracia-Marco 2012 (2)	0.94	0.1	42	0.895	0.097	125	14.2%	0.04 [0.01, 0.08]
Ivuskans 2014	0.904	0.95	110	0.895	0.101	154	2.8%	0.01 [-0.17, 0.19]
Jeddi 2015	0.75	0.13	58	0.7	0.12	390	14.1%	0.05 [0.01, 0.09]
Shin 2011 (3)	0.8	0.03	10	0.83	0.03	10	15.3%	-0.03 [-0.06, -0.00]
Shin 2011 (4)	1.06	0.025	10	1.09	0.046	10	14.5%	-0.03 [-0.06, 0.00]
Vaitkeviciute 2014	0.913	0.092	22	0.906	0.099	133	13.2%	0.01 [-0.03, 0.05]
Total (95% CI)			**299**			**1034**	**100.0%**	**0.02 [-0.01, 0.06]**

Heterogeneity: Tau² = 0.00; Chi² = 36.52, df = 7 (P < 0.00001); I² = 81%
Test for overall effect: Z = 1.40 (P = 0.16)

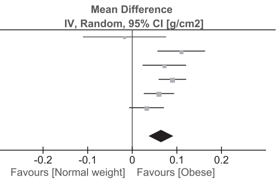


Footnotes
(1) Girls. Adjusted for height, calcium intake and sexual maturation
(2) Boys. Adjusted for height, calcium intake and sexual maturation
(3) Control
(4) Taekwando

b

Study or Subgroup	Obese Mean [g/cm2]	Obese SD [g/cm2]	Obese Total	Normal weight Mean [g/cm2]	Normal weight SD [g/cm2]	Normal weight Total	Weight	Mean Difference IV, Random, 95% CI [g/cm2]
Fischer 2000	0.7844	0.11705	16	0.80167	0.15034	16	6.6%	-0.02 [-0.11, 0.08]
Jeddi 2015	0.81	0.13	24	0.7	0.12	390	14.3%	0.11 [0.06, 0.16]
Rocher 2013	0.742	0.108	53	0.67	0.098	24	15.7%	0.07 [0.02, 0.12]
Shin 2011 (1)	0.92	0.04	10	0.83	0.03	10	22.7%	0.09 [0.06, 0.12]
Shin 2011 (2)	1.15	0.03	10	1.09	0.046	10	21.4%	0.06 [0.03, 0.09]
Vaitkeviciute 2014	0.938	0.088	24	0.906	0.099	133	19.3%	0.03 [-0.01, 0.07]
Total (95% CI)			**137**			**583**	**100.0%**	**0.07 [0.04, 0.09]**

Heterogeneity: Tau² = 0.00; Chi² = 11.03, df = 5 (P = 0.05); I² = 55%
Test for overall effect: Z = 4.75 (P < 0.00001)



Footnotes
(1) Control
(2) Taekwando

Figure 5 – (a) Pooled results of the studies that reported femoral neck BMD (g/cm2) for normal weight and overweight children. (b) Pooled results of the studies that reported femoral neck BMD (g/cm2) for normal weight and obese children.

Other outcome measures

Several outcome measures were reported by only one or two individual studies. Outcome measures that were reported by two studies were pooled. A summarized overview of these results are presented in Table 3a (overweight vs normal-weight) and Table 3b (obese vs normal-weight). Overweight children had significantly higher values at all different body sites, except at the distal radius and tibia (CoD) and the lumbar spine and femoral neck (BMC). Obese children showed significantly higher values at all body sites, except at the distal radius and tibia (CoD and TrD), at the forearm (BMD), and for the total bone mineral apparent density.

Sensitivity analyses

Sensitivity analysis on gender for total body BMC, including 3 studies (20, 24, 29), showed that the MD of total body BMC between overweight and normal weight boys was 184 grams ((95%CI 95, 273), I^2=0%, p=0.59). For girls this MD was 172 grams ((95%CI 89, 256), I^2=24%, p=0.27). Both significant MD's had high quality of evidence (see Appendix 4a). The MD of total body BMC between obese and normal weight boys was 353 grams ((95%CI -10, 717), I^2=77%, p=0.01) and for girls 473 grams ((95%CI 300, 645), I^2=50%, p=0.14), based on the same three studies (20, 24, 29). The quality of evidence for these MD's was moderate (see Appendix 4b).

For several other outcome measures, only a maximum of 2 studies reported outcomes for boys and girls separately. A summarized overview of these pooled results are shown in appendix 5.

DISCUSSION

The purpose of this systematic review was to obtain insight in the differences in BMD between normal-weight children and overweight and obese children. The current study shows that overweight and obese children have a significantly higher whole body BMC and BMD than normal-weight children. Measurements of bone density of specific body sites showed an overall trend towards, often significantly, higher bone density values in overweight and obese children. The quality of the evidence found was of moderate or high quality.

For all but two outcome measures there was significant heterogeneity between the studies with an I^2 of 63% to 81%. The heterogeneity was mainly caused by three studies (24, 26, 37). These studies reported outcome measures separately for boys and girls, or for taekwondo and control group, which might partly explain the heterogeneity. When removing these studies from the analyses the heterogeneity dropped substantially and the outcomes remained almost similar. Only for the outcome femoral neck BMD in overweight and normal-weight children, the MD became positive and significant when removing Shin et al. (37) from the analysis (MD 0.05 g/cm^2 (95%CI 0.03, 0.06)). Other possible explanations for heterogeneity could be different cut-off systems used to define the weight groups or the wide age range in the study populations. Overall, the heterogeneity did not seem to impact our results substantially.

Additional analysis between overweight and obese children showed no significant difference for total body BMC between these groups, but moderate quality of evidence was found for a significant difference in total body BMD between overweight and obese children. This indicates that being obese compared to overweight does not have as much impact as being obese or overweight compared to being of normal weight.

Table 3 – (a) Outcome measures overweight vs. non-overweight

Body site with outcome measure	Studies included	N	Mean difference (95%CI)
Radius Metaphysis BMC (g/cm)	1 (12)	427	0.06 (0.04, 0.08)**
Radius Diaphysis BMC (g/cm)	1 (12)	427	0.06 (0.04, 0.08)**
Tibia Metaphysis BMC (g/cm)	1 (12)	427	0.27 (0.19, 0.35)**
Tibia Diaphysis BMC (g/cm)	1 (12)	427	0.28 (0.22, 0.34)**
Distal radius cortical density (g/cm^3)	1 (12)	427	5.10 (-5.07, 15.27)
Distal radius trabecular density (g/cm^3)	1 (12)	427	15.40 (8.54, 22.26)**
Distal tibia cortical density (g/cm^3)	2 (12, 42)	872	-0.44 (-5.01, 4.14)
Distal tibia trabecular density (g/cm^3)	1 (12)	427	15.50 (7.77, 23.23)**
Lumbar Spine BMC (g)	1 (24)	330	0.22 (-2.5, 2.94)
Bone mineral content index (kg/m^2)	1 (31)	482	0.01 (0.01, 0.01)**
Heel BMC (g)	1 (39)	41	0.04 (0.02, 0.06)**
Heel BMD (g/cm^2)	1 (39)	41	0.05 (0.02, 0.08)**
Heel BMAD (g/cm^3)	1 (39)	41	13.30 (3.15, 23.45)*
Total hip BMC (g)	1 (24)	330	1.51 (0.04,2.99*
Total hip BMD (g/cm^2)	1 (24)	330	0.04 (0.02, 0.07)*
Femoral neck BMC (g)	1 (24)	330	0.25 (0.06, 0.44)*

*$p < 0.05$. **$p < 0.001$. BMAD, bone mineral apparent density; BMC, bone mineral content; BMD, bone mineral density; CI, confidence interval.

Table 3 – (b) Outcome measures obese vs. normal weight

Body site with outcome measure	Studies included	N	Mean difference (95%CI)
Distal radius cortical density (g/cm^3)	2 (18, 32)	178	-1.67 (-59.24, 55.90)
Distal radius trabecular density (g/cm^3)	2 (18, 32)	178	-0.61 (-10.33, 9.12)
Distal tibia cortical density (g/cm^3)	2 (18, 32)	181	-16.66 (-51.26, 17.93)
Distal tibia trabecular density (g/cm^3)	2 (18, 32)	178	-0.73 (-10.38, 8.93)
Total Bone Mineral Apparent Density (g/cm^3)	2 (25, 35)	112	0.04 (-0.07, 0.15)
Lumbar Spine BMC (g)	2 (35, 36)	120	3.63 (1.77, 5.49)**
Lumbar spine BMAD (g/cm^3)	1 (35)	43	0.02 (0.01, 0.03)**
Arm BMC (g)	1 (34)	115	34.00 (7.31, 60.69)*
Trunk BMC (g)	1 (34)	115	127.00 (55.35, 198.65)**
Leg BMC (g)	1 (34)	115	248.60 (143.90, 353.30)**
Total hip BMC (g)	1 (36)	77	2.66 (0.32, 5.00)*
Total hip BMD (g/cm^2)	1 (36)	77	0.07 (0.02, 0.11)*
Femoral neck BMC (g)	1 (36)	77	0.45 (0.12, 0.78)*
Forearm BMC (g)	1 (36)	77	0.64 (0.24, 1.04)*
Forearm BMD (g/cm2)	1 (36)	77	0.02 (-0.00, 0.04)

*$p < 0.05$. **$p < 0.001$. BMAD, bone mineral apparent density; BMC, bone mineral content; BMD, bone mineral density; CI, confidence interval.

We decided to include studies with either longitudinal or cross-sectional designs. Surprisingly our search resulted in only one study investigating the long term consequences of obesity on bone mineral density. This study found a higher trabecular density at the tibia in adult women and a somewhat lower cortical density at tibia in adult men who were obese in childhood.

The studies with a cross-sectional design mostly found a significantly higher bone density in overweight and obese children. Given the results of the cross-sectional studies and the lack of evidence on the long term consequences of childhood obesity on BMD, more prospective research should be done in this field in order to gain more knowledge on the long-term consequences of childhood obesity on the quality and strength of the bones.

Some of the cross-sectional studies analyzed girls and boys separately. Therefore, sensitivity analyses for gender were performed. Although only few studies could be included in this analyses, the analyses still showed for most outcome measures more often a significant difference between normal weight and overweight or obese in girls than boys. These findings, in combination with the outcomes of the single longitudinal study, may indicate that overall excess weight in girls leads to a higher bone density than it does in boys. One could suggest that this might be due to the difference in hormonal development in girls and boys.

The results of the current study imply that overall, overweight and obese children develop a higher peak bone mass during childhood than normal weight children. It has been suggested that increased mechanical loading, seen in children with excess weight, increases bone mineral density (12, 13). Furthermore, physical activity has been shown to increase bone mineral density as well (57, 58, 59). However, children with excess weight seem to be less physically active (60, 61). It is therefore questionable whether the effect of increased mechanical loading in overweight and obese children on BMD is as large as the effect of physical activity in normal weight children on BMD, and if the increased mechanical loading in obese children will therefore compensate for the lack of physical activity for the effect on BMD.

To compare the impact of overweight and obesity on BMD with the impact of physical activity on BMD, we compared the results of the current study with studies investigating the BMD in athletes and non-athletes (57, 58, 59). The current review showed a total body BMD MD range of 0.04-0.05 g/cm^2 versus a total body BMD MD of 0.012-0.13 g/cm^2 in studies investigating non-athletes versus athletes (57, 58, 59). The MD at the lumbar spine ranged from 0.04-0.08 g/cm^2 in the current review and from 0.06-0.076 g/cm^2 in the studies on non-athletes and athletes (57, 59). These results indicate that an increased mechanical loading, caused by for instance being overweight or obese, seems to have similar impact in the bone density, especially in the lumbar spine, as does being physically active.

In addition to the different theories mentioned above trying to explain a higher bone density in overweight and obese children, it has also been suggested that obesity may lead to an increase in circulating leptin. The role of leptin in the development of BMD is however still speculative. Leptin is known to have a direct effect on bone density, since it is a growth factor on chondrocytes of skeletal growth centers (18, 62). This could potentially contribute to increased skeletal mass in obese children (63), and to a higher peak bone mass at a younger age compared to non-overweight children (30). However, leptin also has an indirect effect on bone formation by influencing other hormones affecting the bone density (growth hormone, androgens, cortisol) (64). It has also been suggested that leptin alters the microstructure of the bones and that a higher proportion of fat mass is negatively associated with bone strength which both could lead to an increase in the propensity to fracture (12, 18). Moreover, leptin resistance, a state often met in children with obesity, seems to be related to a poorer bone health outcome (64). This may explain why obese children encounter more fractures (4, 5), and in particular fractures of the forearm (65).

Besides leptin, estrogen is also found to play an important role in bone formation and estrogen deficiency leads to increased osteoclast formation (66). One of the main sites of metabolism of estrogen is fat tissue. Since bodies of the overweight and obese contain increased fat tissue, they consequently have increased levels of estrogen (67), which could lead to the growth and positive regulation on bone formation (66).

Strengths and limitations

This is the first systematic review examining the differences in BMD between normal weight children and overweight and obese children. The literature was searched systematically and extensively, and data extraction and risk of bias assessment were done by three independent reviewers. Additionally, meta-analyses were performed to summarize the mean differences of interest.

A large percentage of the included studies reported bodyweight and height as possible confounders. In this review data were not adjusted for confounders, since most included studies only presented unadjusted data. Of the studies that did adjust for potential confounders, only in one study the association between obesity and the outcome measure changed. Confounders that would be of much interest here are for instance muscle mass and physical activity since these, among other factors, are known to play a role in the development of bone mineral density (10, 68, 69), and could therefore have influenced the outcomes in the studies.

Statistical heterogeneity was found in most pooled analyses and is likely to be explained by methodologic differences between studies. In order to deal with the heterogeneity we made use of a random effects model. We interpreted the outcome measures with care by downgrading the level of evidence by one level when heterogeneity was present (I^2 >40%) .

Since most studies included in this review were small studies with less than 50 cases of overweight or obese participants per study, one must be aware of publication bias. The funnel plots for the pooled outcome measures showed some signs of publication bias, since there are only a few larger studies showing a significant effect. The smaller studies however are symmetrically spread around the point estimate, which points to a small risk of publication bias.

It is possible that the classified ‘normal weight’ children will also include a subgroup of children with underweight. These underweight children could not be separately analyzed but may have had impact on our results by lowering the mean BMI of the normal weight group.

Implications

The relation between overweight and obese children and their BMD has widely been studied. It is now shown that overweight and obese children do have a higher BMC and BMD compared to normal-weight children. However, little is known on the development of bone mass into adulthood, since we only found one study investigating this longitudinal relation. Future research should therefore focus on the potential long-term effects and the development of BMC and BMD in time in both overweight and obese children.

Even though obese children develop a higher bone density during childhood, it is apparent that more injuries and fractures are seen in these children than in normal-weight children (4, 5). These fractures may be caused by increased falling because of clumsiness (6). It could be suggested that the higher bone density in obese children may be a normal adaptation to the increased weight, which is supported by two studies where after adjustment for body weight, no difference between bone density between normal weight and obese children was found (35, 36). However, it has been studied that the quality of the bone in the obese is not as high as in normal weight children and therefore the bones may be insufficient to compensate for the excess body fat and elevated body weight applied to the skeleton (35, 42).

Conclusion

Overweight and obese children have a significantly higher bone mineral density compared to normal-weight children. No conclusions can be drawn on the development of bone density from childhood into adulthood.

REFERENCES

1. World Health Organization. Report of the Commission on Ending Childhood Obesity. 2016.
2. Daniels SR. Complications of obesity in children and adolescents. *Int J Obes (Lond)* 2009;**33 Suppl 1:** S60-65.
3. 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.
4. 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.
5. 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.
6. Cheng J, East P, Blanco E, Kang Sim E, Castillo M, Lozoff B*, et al.* Obesity leads to declines in motor skills across childhood. *Child Care Health Dev* 2016;**42:** 343-350.
7. Heaney RP, Abrams S, Dawson-Hughes B, Looker A, Marcus R, Matkovic V*, et al.* Peak bone mass. *Osteoporos Int* 2000;**11:** 985-1009.
8. McKay H, Smith E. Winning the battle against childhood physical inactivity: the key to bone strength? *J Bone Miner Res* 2008;**23:** 980-985.
9. Nava-Gonzalez EJ, Cerda-Flores RM, Garcia-Hernandez PA, Jasso-de la Pena GA, Bastarrachea RA, Gallegos-Cabriales EC. [Bone mineral density and its association with body composition and metabolic biomarkers of insulin-glucose axis, bone and adipose tissue in women]Densidad mineral osea y su asociacion con la composicion corporal y biomarcadores metabolicos del eje insulino-glucosa, hueso y tejido adiposo en mujeres. *Gac Med Mex* 2015;**151:** 731-740.
10. Doyle F, Brown J, Lachance C. RELATION BETWEEN BONE MASS AND MUSCLE WEIGHT. *The Lancet* 1970;**295:** 391-393.
11. Kemp JP, Sayers A, Smith GD, Tobias JH, Evans DM. Using Mendelian randomization to investigate a possible causal relationship between adiposity and increased bone mineral density at different skeletal sites in children. 2016.
12. Ducher G, Bass SL, Naughton GA, Eser P, Telford RD, Daly RM. Overweight children have a greater proportion of fat mass relative to muscle mass in the upper limbs than in the lower limbs: Implications for bone strength at the distal forearm. *Am J Clin Nutr* 2009;**90:** 1104-1111.
13. Leonard MB, Shults J, Wilson BA, Tershakovec AM, Zemel BS. Obesity during childhood and adolescence augments bone mass and bone dimensions. *Am J Clin Nutr* 2004;**80:** 514-523.
14. Frost HM. Obesity, and bone strength and “mass”: a tutorial based on insights from a new paradigm. *Bone* 1997;**21:** 211-214.
15. Wells GA, Shea B, O’Connell D, et al. The Newcaste-Ottowa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analysis: Ottowa Hospital Research Insititute; 2011 [May 25th, 2016]. Available from:http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp.
16. Atkins D, Best D, Briss PA, Eccles M, Falck-Ytter Y, Flottorp S*, et al*. Grading quality of evidence and strength of recommendations. *Bmj* 2004;**328:** 1490.
17. De la Torre W, Pasquel M, Guevara J, Garcia A, De Leiva A. Bone mineral analysis in obese children (I). *ACTA PAEDIATR SCAND* 1990;**79:** 362-363.
18. Dimitri P, Jacques RM, Paggiosi M, King D, Walsh J, Taylor ZA*, et al.* Leptin may play a role in bone microstructural alterations in obese children. *J Clin Endocrinol Metab* 2015;**100:** 594-602.
19. El-Dorry G, Ashry H, Ibrahim T, Elias T, Alzaree F. Bone density, osteocalcin and deoxypyridinoline for early detection of osteoporosis in obese children. *Maced J Med Sci* 2015;**3:** 413-419.

20. Ellis KJ, Shypailo RJ, Wong WW, Abrams SA. Bone mineral mass in overweight and obese childre: Diminished or enhanced? *Acta Diabetol* 2003;**40:** S274-S277.
21. Eriksson S, Mellström D, Strandvik B. Volumetric bone mineral density is an important tool when interpreting bone mineralization in healthy children. *Acta Paediatr Int J Paediatr* 2009;**98:** 374-379.
22. Fintini D, Brufani C, Grossi A, Ubertini G, Fiori R, Pecorelli L*, et al.* Gender differences in bone mineral density in obese children during pubertal development. *J Endocrinol Invest* 2011;**34:** e86-91.
23. Fischer S, Milinarsky A, Giadrosich V, Dib G, Arriagada M, Arinoviche R. X-ray absorptiometry of bone obese and eutrophic children from Valparaiso, Chile. *J Rheumatol* 2000;**27:** 1294-1296.
24. Gracia-Marco L, Ortega FB, Jimenez-Pavon D, Rodriguez G, Castillo MJ, Vicente-Rodriguez G*, et al.* Adiposity and bone health in Spanish adolescents. The HELENA study. *Osteoporos Int* 2012;**23:** 937-947.
25. Hanks LJ, Casazza K, Ashraf AP, Wallace S, Gutiérrez OM. Fibroblast growth factor-21, body composition, and insulin resistance in pre-pubertal and early pubertal males and females. *Clin Endocrinol* 2015;**82:** 550-556.
26. Haroun D, Wells JCK, Williams JE, Fuller NJ, Fewtrell MS, Lawson MS. Composition of the fat-free mass in obese and nonobese children: Matched case-control analyses. *Int J Obes* 2005;**29:** 29-36.
27. Hasanoğlu A, Bideci A, Cinaz P, Tümer L, Ünal S. Bone mineral density in childhood obesity. *J Pediatr Endocrinol Metab* 2000;**13:** 307-311.
28. Ivuškans A, Jürimäe T, Lätt E, Jürimäe J, Purge P, Saar M*, et al.* Role of physical activity in bone health in peripubertal boys. *Pediatr Int* 2014;**56:** 763-767.
29. Jeddi M, Dabbaghmanesh MH, Omrani GR, Ayatollahi SMT, Bagheri Z, Bakhshayeshkaram M. Relative importance of lean and fat mass on bone mineral density in Iranian children and adolescents. *Int J Endocrinol Metab* 2015;**13**.
30. Klein KO, Larmore KA, De Lancey E, Brown JM, Considine RV, Hassink SG. Effect of obesity on estradiol level, and its relationship to leptin, bone maturation, and bone mineral density in children. *J Clin Endocrinol Metab* 1998;**83:** 3469-3475.
31. Kouda K, Nakamura H, Fujita Y, Iki M. Relationship between body mass index at age 3 years and body composition at age 11 years among Japanese children: The Shizuoka population-based study. *J Epidemiol* 2012;**22:** 411-416.
32. Leonard MB, Zemel BS, Wrotniak BH, Klieger SB, Shults J, Stallings VA*, et al.* Tibia and radius bone geometry and volumetric density in obese compared to non-obese adolescents. *Bone* 2015;**73:** 69-76.
33. Lucas R, Ramos E, Oliveira A, Monjardino T, Barros H. Low-grade systemic inflammation and suboptimal bone mineral density throughout adolescence: A prospective study in girls. *Clin Endocrinol* 2012;**77:** 665-671.
34. Manzoni P, Brambilla P, Pietrobelli A, Beccaria L, Bianchessi A, Mora S*, et al.* Influence of body composition on bone mineral content in children and adolescents. *AM J CLIN NUTR* 1996;**64:** 603-607.
35. Rocher E, Chappard C, Jaffre C, Benhamou CL, Courteix D. Bone mineral density in prepubertal obese and control children: Relation to body weight, lean mass, and fat mass. *J Bone Miner Metab* 2008;**26:** 73-78.
36. Rocher E, El Hage R, Chappard C, Portier H, Rochefort GY, Benhamou CL. Bone mineral density, hip bone geometry, and calcaneus trabecular bone texture in obese and normal-weight children. *J Clin Densitometry* 2013;**16:** 244-249.
37. Shin YH, Jung HL, Kang HY. Effects of Taekwondo Training on Bone Mineral Density of High School Girls in Korea. *Biology of Sport* 2011;**28:** 195-198.
38. Templeton DL, Kelly AS, Steinberger J, Dengel DR. Lower relative bone mineral content in obese adolescents: role of non-weight bearing exercise. *Pediatr Exerc Sci* 2010;**22:** 557-568.

39. Tubić B, Magnusson P, Swolin-Eide D, Mårild S. Relation between bone mineral density, biological markers and anthropometric measures in 4-year-old children: A pilot study within the IDEFICS study. *Int J Obes* 2011;**35:** S119-S124.
40. Uusi-Rasi K, Laaksonen M, Mikkilä V, Tolonen S, Raitakari OT, Viikari J*, et al.* Overweight in childhood and bone density and size in adulthood. *Osteoporosis Int* 2012;**23:** 1453-1461.
41. Vaitkeviciute D, Lätt E, Mäestu J, Jürimäe T, Saar M, Purge P*, et al.* Physical activity and bone mineral accrual in boys with different body mass parameters during puberty: A longitudinal study. *PLoS ONE* 2014;**9**.
42. Wetzsteon RJ, Petit MA, Macdonald HM, Hughes JM, Beck TJ, McKay HA. Bone structure and volumetric BMD in overweight children: A longitudinal study. *J Bone Miner Res* 2008;**23:** 1946-1953.
43. Cole TJ, Freeman JV, Preece MA. Body mass index reference curves for the UK, 1990. *Arch Dis Child* 1995;**73:** 25-29.
44. 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.
45. Ghalli I SN, Hussein F, Erfan M, El-Ruby M, Mazen I. Egyptian growth curves 2002 for infants, children and adolescents. *IntSartorio* 2008.
46. Luciano A, Bressan F, Zoppi G. Body mass index reference curves for children aged 3-19 years from Verona, Italy. *Eur J Clin Nutr* 1997;**51:** 6-10.
47. Hamill PV, Drizd TA, Johnson CL, Reed RB, Roche AF, Moore WM. Physical growth: National Center for Health Statistics percentiles. *Am J Clin Nutr* 1979;**32:** 607-629.
48. 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.
49. Wang Y, Chen H-J. Use of Percentiles and Z-Scores in Anthropometry. In: Preedy RV (ed). *Handbook of Anthropometry: Physical Measures of Human Form in Health and Disease*. Springer New York: New York, NY, 2012, pp 29-48.
50. Hammer LD, Kraemer HC, Wilson DM, Ritter PL, Dornbusch SM. Standardized percentile curves of body-mass index for children and adolescents. *Am J Dis Child* 1991;**145:** 259-263.
51. McCarthy HD, Cole TJ, Fry T, Jebb SA, Prentice AM. Body fat reference curves for children. *Int J Obes (Lond)* 2006;**30:** 598-602.
52. Frisch RE, Revelle R. Height and weight at menarche and a hypothesis of menarche. *Arch Dis Child* 1971;**46:** 695-701.
53. Ogden CL, Kuczmarski RJ, Flegal KM, Mei Z, Guo S, Wei R*, et al.* Centers for Disease Control and Prevention 2000 growth charts for the United States: improvements to the 1977 National Center for Health Statistics version. *Pediatrics* 2002;**109:** 45-60.
54. Kuczmarski RJ, Ogden CL, Guo SS, Grummer-Strawn LM, Flegal KM, Mei Z*, et al.* 2000 CDC Growth Charts for the United States: methods and development. *Vital Health Stat 11* 2002**:** 1-190.
55. Tanner JM, Whitehouse RH. Clinical longitudinal standards for height, weight, height velocity, weight velocity, and stages of puberty. *Arch Dis Child* 1976;**51:** 170-179.
56. Karlberg J, Luo ZC, Albertsson-Wikland K. Body mass index reference values (mean and SD) for Swedish children. *Acta Paediatr* 2001;**90:** 1427-1434.
57. Torstveit MK, Sundgot-Borgen J. Low bone mineral density is two to three times more prevalent in non-athletic premenopausal women than in elite athletes: a comprehensive controlled study. *Br J Sports Med* 2005;**39:** 282-287; discussion 282-287.
58. Andreoli A, Monteleone M, Van Loan M, Promenzio L, Tarantino U, De Lorenzo A. Effects of different sports on bone density and muscle mass in highly trained athletes. *Med Sci Sports Exerc* 2001;**33:** 507-511.

59. Courteix D, Lespessailles E, Peres SL, Obert P, Germain P, Benhamou CL. Effect of physical training on bone mineral density in prepubertal girls: a comparative study between impact-loading and non-impact-loading sports. *Osteoporos Int* 1998;**8:** 152-158.
60. Raistenskis J, Sidlauskiene A, Strukcinskiene B, Ugur Baysal S, Buckus R. Physical activity and physical fitness in obese, overweight, and normal-weight children. *Turk J Med Sci* 2016;**46:** 443-450.
61. Haerens L, Deforche B, Maes L, Cardon G, De Bourdeaudhuij I. Physical activity and endurance in normal weight versus overweight boys and girls. *J Sports Med Phys Fitness* 2007;**47:** 344-350.
62. Shimizu H, Shimomura Y, Hayashi R, Ohtani K, Sato N, Futawatari T*, et al.* Serum leptin concentration is associated with total body fat mass, but not abdominal fat distribution. *Int J Obes Relat Metab Disord* 1997;**21:** 536-541.
63. Maor G, Rochwerger M, Segev Y, Phillip M. Leptin acts as a growth factor on the chondrocytes of skeletal growth centers. *J Bone Miner Res* 2002;**17:** 1034-1043.
64. Upadhyay J, Farr OM, Mantzoros CS. The role of leptin in regulating bone metabolism. *Metabolism* 2015;**64:** 105-113.
65. Manning Ryan L, Teach SJ, Searcy K, Singer SA, Wood R, Wright JL*, et al.* The Association Between Weight Status and Pediatric Forearm Fractures Resulting From Ground-Level Falls. *Pediatr Emerg Care* 2015;**31:** 835-838.
66. Vaananen HK, Harkonen PL. Estrogen and bone metabolism. *Maturitas* 1996;**23 Suppl:** S65-69.
67. Kershaw EE, Flier JS. Adipose tissue as an endocrine organ. *J Clin Endocrinol Metab* 2004;**89:** 2548-2556.
68. Aloia JF, Vaswani A, Ma R, Flaster E. To what extent is bone mass determined by fat-free or fat mass? *Am J Clin Nutr* 1995;**61:** 1110-1114.
69. Courteix D, Lespessailles E, Loiseau-Peres S, Obert P, Ferry B, Benhamou CL. Lean tissue mass is a better predictor of bone mineral content and density than body weight in prepubertal girls. *Rev Rhum Engl Ed* 1998;**65:** 328-336.

Appendix 1- Search string for embase, medline, cinahl, cochrane, web-of-science, pubmed and google scholar

Embase.com

('obesity'/exp OR 'adipose tissue'/de OR 'abdominal fat'/de OR (('body weight'/de OR 'weight gain'/de OR 'body mass'/de OR 'body composition'/de OR 'body fat'/de OR 'body fat distribution'/exp) AND ('predictive value'/de OR prognosis/de OR 'regression analysis'/exp OR 'cohort analysis'/exp OR 'longitudinal study'/exp OR 'retrospective study'/exp OR 'prospective study'/exp OR 'follow up'/de)) OR (obes* OR overweight* OR adipos* OR ((body OR abdom*) NEXT/1 fat) OR ((BMI OR 'body mass' OR 'body composition' OR 'body weight' OR 'body fat') NEAR/6 (high* OR excess* OR content* OR predict* OR account* OR regression* OR correlat* OR retrospective* OR prospective* OR cohort* OR variable* OR assess* OR associat* OR change* OR effect* OR influen*))):ab,ti) AND ('bone density'/exp OR 'bone densitometry'/exp OR 'bone mineral'/exp OR 'bone mineralization'/exp OR 'bone strength'/de OR ((bone NEAR/3 (densit* OR mineral* OR demineral* OR strength* OR weak* OR microstructure*)) OR bmd):ab,ti) AND (child/exp OR adolescent/exp OR adolescence/exp OR 'child behavior'/de OR 'child parent relation'/de OR pediatrics/exp OR childhood/exp OR 'child nutrition'/de OR 'infant nutrition'/exp OR 'child welfare'/de OR 'child abuse'/de OR 'child advocacy'/de OR 'child development'/de OR 'child growth'/de OR 'child health'/de OR 'child health care'/exp OR 'child care'/exp OR 'childhood disease'/exp OR 'child death'/de OR 'child psychiatry'/de OR 'child psychology'/de OR 'pediatric ward'/de OR 'pediatric hospital'/de OR (adolescen* OR infan* OR newborn* OR (new NEXT/1 born*) OR baby OR babies OR neonat* OR child* OR kid OR kids OR toddler* OR teen* OR boy* OR girl* OR minors OR underag* OR (under NEXT/1 (age* OR aging)) OR juvenil* OR youth* OR kindergar* OR puber* OR pubescen* OR prepubescen* OR prepubert* OR pediatric* OR paediatric* OR school* OR preschool* OR highschool*):ab,ti)

Medline ovid

(exp "Overweight"/ OR exp "adipose tissue"/ OR exp "abdominal fat"/ OR ((exp "body weight"/ OR "Body Mass Index"/ OR exp "body composition"/) AND ("prognosis"/ OR exp "regression analysis"/ OR exp "cohort studies"/)) OR (obes* OR overweight* OR adipos* OR ((body OR abdom*) ADJ fat) OR ((BMI OR "body mass" OR "body composition" OR "body weight" OR "body fat") ADJ6 (high* OR excess* OR content* OR predict* OR account* OR regression* OR correlat* OR retrospective* OR prospective* OR cohort* OR variable* OR assess* OR associat* OR change* OR effect* OR influen*))).ab,ti.) AND ("Bone Density"/ OR "Calcification, Physiologic"/ OR ((bone ADJ3 (densit* OR mineral* OR demineral* OR strength* OR weak* OR microstructure*)) OR bmd).ab,ti.) AND (exp child/ OR exp infant/ OR adolescent/ OR exp pediatrics/ OR exp Child Health Services/ OR Hospitals, Pediatric/ OR (adolescen* OR infan* OR newborn* OR (new ADJ born*) OR baby OR babies OR neonat* OR child* OR kid OR kids OR toddler* OR teen* OR boy* OR girl* OR minors OR underag* OR (under ADJ (age* OR aging)) OR juvenil* OR youth* OR kindergar* OR puber* OR pubescen* OR prepubescen* OR prepubert* OR pediatric* OR paediatric* OR school* OR preschool* OR highschool*).ab,ti.)

Cinahl ebsco

(MH “Obesity+” OR MH “adipose tissue+” OR MH “abdominal fat+” OR MH “Adipose Tissue Distribution+” OR ((MH “body weight+” OR MH “Body Mass Index+” OR MH “body composition+”) AND (MH “prognosis” OR MH “regression+” OR MH “Prospective Studies+”)) OR (obes* OR overweight* OR adipos* OR ((body OR abdom*) N1 fat) OR ((BMI OR “body mass” OR “body composition” OR “body weight” OR “body fat”) N5 (high* OR excess* OR content* OR predict* OR account* OR regression* OR correlat* OR retrospective* OR prospective* OR cohort* OR variable* OR assess* OR associat* OR change* OR effect* OR influen*)))) AND (MH “Bone Density” OR ((bone N2 (densit* OR mineral* OR demineral* OR strength* OR weak* OR microstructure*)) OR bmd)) AND (MH child+ OR MH adolescence+ OR MH pediatrics+ OR (adolescen* OR infan* OR newborn* OR (new N1 born*) OR baby OR babies OR neonat* OR child* OR kid OR kids OR toddler* OR teen* OR boy* OR girl* OR minors OR underag* OR (under N1 (age* OR aging)) OR juvenil* OR youth* OR kindergar* OR puber* OR pubescen* OR prepubescen* OR prepubert* OR pediatric* OR paediatric* OR school* OR preschool* OR highschool*))

Cochrane

((obes* OR overweight* OR adipos* OR ((body OR abdom*) NEXT/1 fat) OR ((BMI OR ‘body mass’ OR ‘body composition’ OR ‘body weight’ OR ‘body fat’) NEAR/6 (high* OR excess* OR content* OR predict* OR account* OR regression* OR correlat* OR retrospective* OR prospective* OR cohort* OR variable* OR assess* OR associat* OR change* OR effect* OR influen*))):ab,ti) AND (((bone NEAR/3 (densit* OR mineral* OR demineral* OR strength* OR weak* OR microstructure*)) OR bmd):ab,ti) AND ((adolescen* OR infan* OR newborn* OR (new NEXT/1 born*) OR baby OR babies OR neonat* OR child* OR kid OR kids OR toddler* OR teen* OR boy* OR girl* OR minors OR underag* OR (under NEXT/1 (age* OR aging)) OR juvenil* OR youth* OR kindergar* OR puber* OR pubescen* OR prepubescen* OR prepubert* OR pediatric* OR paediatric* OR school* OR preschool* OR highschool*):ab,ti)

Web-of-science

TS=(((obes* OR overweight* OR adipos* OR ((body OR abdom*) NEAR/1 fat) OR ((BMI OR “body mass” OR “body composition” OR “body weight” OR “body fat”) NEAR/5 (high* OR excess* OR content* OR predict* OR account* OR regression* OR correlat* OR retrospective* OR prospective* OR cohort* OR variable* OR assess* OR associat*

OR change* OR effect* OR influen*)))) AND (((bone NEAR/2 (densit* OR mineral* OR demineral* OR strength* OR weak* OR microstructure*)) OR bmd)) AND ((adolescen* OR infan* OR newborn* OR (new NEAR/1 born*) OR baby OR babies OR neonat* OR child* OR kid OR kids OR toddler* OR teen* OR boy* OR girl* OR minors OR underag* OR (under NEAR/1 (age* OR aging)) OR juvenil* OR youth* OR kindergar* OR puber* OR pubescen* OR prepubescen* OR prepubert* OR pediatric* OR paediatric* OR school* OR preschool* OR highschool*)))

Pubmed publisher

(“Overweight”[mh] OR “adipose tissue”[mh] OR “abdominal fat”[mh] OR ((“body weight”[mh] OR “Body Mass Index”[mh] OR “body composition”[mh]) AND (“prognosis”[mh] OR “regression analysis”[mh] OR “cohort studies”[mh])) OR (obes*[tiab] OR overweight*[tiab] OR adipos*[tiab] OR body fat*[tiab] OR abdominal fat*[tiab] OR ((BMI OR “body mass” OR “body composition” OR “body weight” OR “body fat”) AND (high*[tiab] OR excess*[tiab] OR content*[tiab] OR predict*[tiab] OR account*[tiab] OR regression*[tiab] OR correlat*[tiab] OR retrospective*[tiab] OR prospective*[tiab] OR cohort*[tiab] OR variable*[tiab] OR assess*[tiab] OR associat*[tiab] OR change*[tiab] OR effect*[tiab] OR influen*[tiab])))) AND (“Bone Density”[mh] OR “Calcification, Physiologic”[mh] OR ((bone AND (densit*[tiab] OR mineral*[tiab] OR demineral*[tiab] OR strength*[tiab] OR weak*[tiab] OR microstructure*[tiab])) OR bmd)) AND (child[mh] OR infant[mh] OR adolescent[mh] OR pediatrics[mh] OR Child Health Services[mh] OR Hospitals, Pediatric[mh] OR (adolescen*[tiab] OR infan*[tiab] OR newborn*[tiab] OR (new born*[tiab]) OR baby OR babies OR neonat*[tiab] OR child*[tiab] OR kid OR kids OR toddler*[tiab] OR teen*[tiab] OR boy*[tiab] OR girl*[tiab] OR minors OR underag*[tiab] OR under ag*[tiab] OR juvenil*[tiab] OR youth*[tiab] OR kindergar*[tiab] OR puber*[tiab] OR pubescen*[tiab] OR prepubescen*[tiab] OR prepubert*[tiab] OR pediatric*[tiab] OR paediatric*[tiab] OR school*[tiab] OR preschool*[tiab] OR highschool*[tiab])) AND publisher[sb]

Google scholar

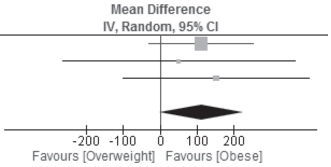
obesity|overweight|bmi prediction|predictive|regression|correlation|retrospective|prospective|longitudinal|cohort “bone density|mineral|mineralization|demineralization” adolescents|adolescence|infants|infancy|children|childhood

Appendix 2 - risk-of-bias assessment

Criteria for quality score	
Study population	
1. **Study groups (according to weight status) are clearly defined**	Positive if at least 2 of the following 3 items in all groups were reported: age, gender, BMI
2. **Participants ≥ 70%**	Positive if the participation of both the overweight and normal weight groups was ≥ 70%
3. **Number of cases ≥ 50**	Positives if the total number of cases was ≥ 50
Assessment of weight status	
4. **Weight status definition**	Positive if cut-off values for weight status definition were mentioned
5. **Assessment of weight status**	Positive if the method of assessment of weight status was described
6. **Blind for weight status assessment**	Positive if the weight status was assessed by an independent person and not based on self-report
Assessment of BMD	
7. **BMD definition**	Positive if the outcome was clearly defined
8. **BMD assessment**	Positive if the method of assessment of BMD was described
9. **Blind for weight status**	Positive if the BMD was assessed while blinded for the weight status
Study Design	
10. **Longitudinal design**	Positive if the study design was longitudinal
11. **Inclusion and exclusion criteria**	Positive if inclusion and exclusion criteria were described
12. **Follow-up period ≥ 1 year**	Positive if the follow-up period was ≥ 1 year
13. **Information on study completers versus withdrawals**	Positive if demographic information was given for completers and withdrawals
Analysis and data presentation	
14. **Data presentation**	Positive if risk estimates were presented or if raw data were given that allow the calculation of risk estimates, such as: odds or prevalence ratios or relative risks
15. **Consideration of confounders**	Positive if the confounders that were considered were described
16. **Control for confounding**	Positive if the method used to control for confounding was described

Study or Subgroup	Obese Mean	Obese SD	Obese Total	Overweight Mean	Overweight SD	Overweight Total	Weight	Mean Difference IV, Random, 95% CI
Ellis 2003	1,616	596	160	1,504	536	96	65.9%	112.00 [-29.51, 253.51]
Ellis 2003	1,607	606	66	1,556	862	37	13.4%	51.00 [-262.88, 364.88]
Jeddi 2015	1,771.2	541	24	1,618.5	505.3	58	20.7%	152.70 [-99.80, 405.20]
Total (95% CI)			**250**			**191**	**100.0%**	**112.25 [-2.63, 227.13]**

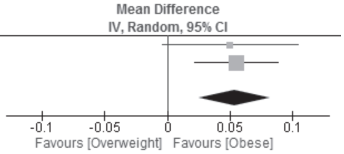
Heterogeneity: Tau² = 0.00; Chi² = 0.24, df = 2 (P = 0.88); I² = 0%
Test for overall effect: Z = 1.92 (P = 0.06)



Appendix 3a - Total body BMC of overweight and obese children

Study or Subgroup	Obese Mean	Obese SD	Obese Total	Overweight Mean	Overweight SD	Overweight Total	Weight	Mean Difference IV, Random, 95% CI
Jeddi 2015	0.96	0.11	24	0.91	0.12	58	27.6%	0.05 [-0.00, 0.10]
Vaitkeviciute 2014	1.056	0.067	24	1.001	0.047	22	72.4%	0.06 [0.02, 0.09]
Total (95% CI)			**48**			**80**	**100.0%**	**0.05 [0.03, 0.08]**

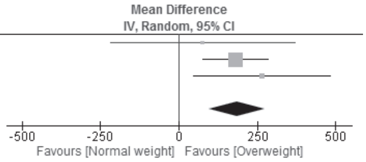
Heterogeneity: Tau² = 0.00; Chi² = 0.02, df = 1 (P = 0.88); I² = 0%
Test for overall effect: Z = 3.72 (P = 0.0002)



Appendix 3b - Total body BMD of overweight and obese children

Study or Subgroup	Overweight Mean	Overweight SD	Overweight Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Random, 95% CI
Ellis 2003	1,556	862	37	1,480	855	318	9.2%	76.00 [-217.22, 369.22]
Gracia-Marco 2012	2,225	300	42	2,045	280	125	74.3%	180.00 [76.84, 283.16]
Jeddi 2015	1,755	575	29	1,490.4	467.2	195	16.4%	264.60 [45.29, 483.91]
Total (95% CI)			**108**			**638**	**100.0%**	**184.35 [95.40, 273.29]**

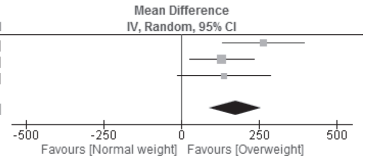
Heterogeneity: Tau² = 0.00; Chi² = 1.05, df = 2 (P = 0.59); I² = 0%
Test for overall effect: Z = 4.06 (P < 0.0001)



Boys

Study or Subgroup	Overweight Mean	Overweight SD	Overweight Total	Normal weight Mean	Normal weight SD	Normal weight Total	Weight	Mean Difference IV, Random, 95% CI
Ellis 2003	1,504	536	96	1,242	533	188	30.9%	262.00 [130.47, 393.53]
Gracia-Marco 2012	1,975	250	30	1,845	300	133	44.0%	130.00 [27.03, 232.97]
Jeddi 2015	1,482	388.1	29	1,344.6	353.9	195	25.1%	137.40 [-12.33, 287.13]
Total (95% CI)			**155**			**516**	**100.0%**	**172.61 [89.35, 255.86]**

Heterogeneity: Tau² = 1341.19; Chi² = 2.64, df = 2 (P = 0.27); I² = 24%
Test for overall effect: Z = 4.06 (P < 0.0001)

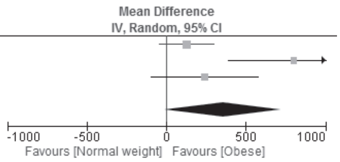


Girls

Appendix 4a - Outcomes of sensitivity analyses for gender for total body BMC normal weight vs overweight

Study or Subgroup	Obese Mean	Obese SD	Obese Total	Normal weight Mean	Normal weight SD	Normal weight Total	Weight	Mean Difference IV, Random, 95% CI
Ellis 2003	1,607	606	66	1,480	855	318	39.9%	127.00 [-46.80, 300.80]
Haroun 2005	2,400	600	13	1,600	400	10	28.2%	800.00 [390.31, 1209.69]
Jeddi 2015	1,732.2	608.1	13	1,490.4	467.2	195	31.9%	241.80 [-95.20, 578.80]
Total (95% CI)			**92**			**523**	**100.0%**	**353.31 [-9.94, 716.55]**

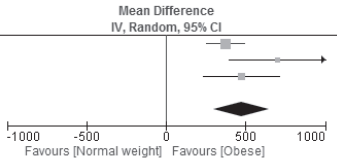
Heterogeneity: Tau² = 78161.65; Chi² = 8.79, df = 2 (P = 0.01); I² = 77%
Test for overall effect: Z = 1.91 (P = 0.06)



Boys

Study or Subgroup	Obese Mean	Obese SD	Obese Total	Normal weight Mean	Normal weight SD	Normal weight Total	Weight	Mean Difference IV, Random, 95% CI
Ellis 2003	1,616	596	160	1,242	533	188	49.7%	374.00 [254.28, 493.72]
Haroun 2005	2,000	400	15	1,300	400	12	21.6%	700.00 [396.36, 1003.64]
Jeddi 2015	1,817.4	399.7	11	1,344.6	353.9	195	28.7%	472.80 [231.43, 714.17]
Total (95% CI)			**186**			**395**	**100.0%**	**472.81 [300.22, 645.40]**

Heterogeneity: Tau² = 11870.44; Chi² = 4.00, df = 2 (P = 0.14); I² = 50%
Test for overall effect: Z = 5.37 (P < 0.00001)



Girls

Appendix 4b - Outcomes of sensitivity analyses for gender for total body BMC normal weight vs obese

Appendix 5 - Outcomes of sensitivity analyses for gender for different outcome measures

Body site with outcome measure	Studies included	N	Mean difference (95%CI)
Total body BMD normal weight vs overweight			
Males	2(27, 32)	391	0.02 (-0.01, 0.06)
Females	2(27, 32)	387	0.03 (0.01, 0.05)**
Total body BMD normal weight vs obese			
Males	2(25, 32)	277	0.02 (-0.05, 0.09)
Females	2(25, 32)	288	0.10 (0.05, 0.14)**
Lumbar spine BMD normal weight vs overweight			
Males	2(27, 32)	391	0.03 (-0.05, 0.11)
Females	2(27, 32)	387	0.07 (0.04, 0.11)**
Lumbar spine BMD normal weight vs obese			
Males	2(25, 32)	277	0.01 (-0.07, 0.09)
Females	2(25, 32)	288	0.11 (0.06, 0.16)**
Femoral neck BMD normal weight vs overweight			
Males	2(27, 32)	391	0.04 (0.01, 0.07)*
Females	2(27, 32)	387	0.06 (0.03, 0.09)**

*p<0.05, **p<0.001

Chapter 4

Overweight and obese children do not consult their GP more often than normal-weight children for musculoskeletal complaints during a 2 year follow up

Janneke van Leeuwen, Marienke van Middelkoop, Winifred D. Paulis, Herman J. Bueving, Patrick J.E. Bindels, Bart W. Koes

Arch Dis Child. 2018. 103(2) :149-154

ABSTRACT

Background

Childhood obesity is associated with self-reported musculoskeletal complaints, injuries, and fractures. In the current study we investigated the association between weight status of children and the frequency and type of musculoskeletal consultations at the GP during a two year follow-up.

Methods

Data from a prospective longitudinal cohort study including children aged 2-18 years presenting in general practices in the Netherlands were used. Height and weight were measured at baseline, at 6 months, 1 year and 2 year follow-up. Electronic medical files were used to collect information on the frequency and type of consultations at the GP during the two-year follow-up period. Associations between weight status and frequency and type of GP consultations were calculated.

Results

Of the 617 included children, 111 (18%) were overweight or obese and 506 (82%) were non-overweight. Overweight children were significantly older (mean age 9.8 years sd (3.6) versus 7.8 (4.0), p=0.004). Overweight children consulted the GP in general significantly more frequent during the 2-year follow up than non-overweight children (mean 7.3 (5.7) vs 6.7 (5.4), OR 1.09, 95%CI 1.01-1.18). No significant difference was seen in the number of overweight and non-overweight children consulting their GP for musculoskeletal complaints (OR 1.20 (0.86 – 1.68)). Additionally, no significant difference between overweight and non-overweight children was seen for the number of consultations for further specified musculoskeletal disorders.

Conclusion

No association was seen between childhood weight status and the frequency and type of musculoskeletal consultations at the GP during a two year follow-up.

INTRODUCTION

Childhood obesity is a worldwide health issue, especially in western countries (1). Previous studies, mostly carried out on population basis and in secondary healthcare settings, have shown that childhood overweight and obesity are associated with (in questionnaires reported) musculoskeletal complaints, injuries, and fractures as early as childhood (2, 3). The prevalence of musculoskeletal pain is 26% higher in overweight children compared to normal weight children, and the prevalence of injuries and fractures is 8% higher (2). In contrast with these findings, it has also been found that overweight children do not have an increased injury risk compared with normal weight sports participants (4). The mechanisms behind the suggested higher frequency of musculoskeletal complaints and increased risk of injuries and fractures in overweight and obese children is frequently discussed (5). One mechanism is based on altered loading of the joints, causing knee and/or hip pain and related pathologies (6, 7, 8). Altered loading of the joints and excessive weight put on the joints seen in obesity also increases the risk on later life osteoarthritis (OA) (8, 9). Other factors are also thought to play a role in the development of musculoskeletal pain. One of these include disturbed hormone and lipid levels found in overweight and obese adult, and children (10, 11, 12, 13). These are known to play a role in the pathogenesis of osteoarthritis in older adults, but it is unknown whether this mechanism already starts during childhood.

In daily practice, obese children are more likely to present to a pediatric emergency department with injuries and pain of the lower extremities compared to normal-weight children (3, 14). However, in the Netherlands, the general practitioner is the first point of care for non-emergency complaints, as in many other countries. Since previous literature suggests that overweight and obese children report more musculoskeletal problems than normal weight children, the current study will investigate whether these differences influence the frequency of consultations for musculoskeletal complaints at the general practitioner during a follow-up of two years.

METHODS:

Study Design

This study is a prospective longitudinal cohort study using data from the DOERAK cohort. The DOERAK (“Determinants of (sustained) Overweight and complaints; Epidemiological Research among Adolescents and Kids in general practice”) cohort was set up to gain knowledge on the differences between overweight and normal-weight children in general practice. The study protocol has previously been published (15). The study has been approved by the Institutional Review Board of the Erasmus University Medical Center, Erasmus MC.

Participant selection

Between December 2010 and April 2013, children were recruited from 73 general practices. All children visiting their GP or GP-trainee (from here on both defined as GP) in this timeframe were asked to participate in the study. In order to be eligible, children had to be between 2-18 years of age and they/their parents had to have a basic understanding of the Dutch language to be able to give informed consent and fill out Dutch questionnaires. Children having a mental or physical disability, children with co-morbidities affecting weight and children consulting their GP with emergency problems were not eligible to participate.

All children and parents who were approached during consultation received verbal information about the study by their GP during this regular consultation. If child and parent were interested in participation, height, weight and waist circumference of the child were measured and contact information was sent to the researcher. Written study information and informed consent forms were then sent to the participant by the research team (children of age 12 and older also received an informed assent form), where after the researcher contacted the family to answer any questions about the study and to investigate if they were willing to participate. The child was formally included in the study when the informed consent (and informed assent form when needed) was received. While participating in the study, children received usual care from their GP.

Data collection

At baseline, after formal inclusion, a questionnaire was sent to the GP to collect data on the child's height, weight, waist circumference and to collect the reason for consultation at baseline. The parents of the included children also received a questionnaire at baseline to collect data on demographics of parent and child. After inclusion, the participants were asked to fill out a questionnaire at 6, 12 and 24 months. If one of these questionnaires was not completed after one week, a reminder was sent, which was repeated for eight weeks. If after these eight weeks the questionnaire was still unanswered, the research assistant contacted the participant to remind him or her. After two years follow-up, the research assistant retrieved the medical file records of all children who completed the two year follow-up (as covered by informed consent) or who gave permission to search their file even after drop-out. For every consultation during the two year-follow up period, the GP recorded reason for consultation by the international classification of primary care (ICPC-coding) (16) (APPENDIX 1) and the corresponding explanatory text was extracted. Any correspondence between the GP and other health professionals during the two year follow-up was also extracted.

Measures

For the present study, the GP questionnaire was used to extract the child's age and gender. Height and weight were measured by the GP or the research assistant, who received the same instructions and followed an identical protocol (15). From height and weight measures taken after formal inclusion, baseline BMI-z scores were calculated and weight status was determined using the international age and gender specific cut-off points (17, 18). Since only a small percentage of the included children was obese, overweight and obese children were combined into one category called the 'overweight' category. Parent's questionnaires were used to extract general information. Ethnicity (both parents born in the Netherlands, at least one parent born in another country), socio-economic status based on net household income using monthly general labor income of 2014 as cut-off point(19) (<2000 euros/month, ≥2000 euros/month), and marital status reported by parents (parents living together, parents separated) were dichotomized. Highest level of education in the household was categorized into three levels (up to lower secondary level, upper secondary level, at least bachelor level), based on the international standard classification of education (20).

Medical files were used to determine the frequency of all consultations. The ICPC-letter 'L' (corresponding to musculoskeletal complaints) and the explanatory text were used to determine the frequencies of musculoskeletal complaints. To further specify musculoskeletal complaints, the accompanying numbers were used and categorized into lower extremities, upper extremities and others (e.g. back, neck, thorax) (APPENDIX 2). Consultations with code L that could not be categorized, due to missing information on location, were defined as 'unclear'.

Primary outcome measures:

The primary outcome measures of this study were the frequency and type of musculoskeletal consultations during the two year follow-up. Secondary outcomes included the overall number of consultations.

Statistical analyses

Baseline demographics, frequencies of complaints and type of complaints among overweight and non-overweight children were described using means (sd) for continuous variables and frequencies (%) for dichotomous or categorical variables. To test whether weight status was associated with the frequency of musculoskeletal consultations and the frequency of consultations in general, Poisson regression was used. Logistic regression analysis was used to assess the association between weight status and the presence of musculoskeletal consultations during two-year follow-up time. Furthermore, the association between weight status and further specified musculoskeletal conditions denoting to specific body parts were tested separately using logistic regression analysis. Multivariable analysis was used to test for different predictors for musculoskeletal consultations during the two-year follow up. Complete case analysis was used.

All analyses were adjusted for potential confounders (age, gender, socio-economic status (ses), marital status), which were considered a confounder if the regression coefficient of the overweight status changed more than 10% after adding it to the model. We did not adjust for ethnicity and education level due to collinearity with ses. P-values <0.05 were considered statistically significant. The strength of associations were determined using Odds Ratios (OR) and Incidence Rate Ratios (IRR) with 95% Confidence Intervals (CI). IBM SPSS statistics 12.0 was used for statistical analyses.

RESULTS

General characteristics

Of the 1109 children that showed interest to their GP to participate, 733 gave written consent and were included. Baseline weight status was missing for 18 children due to missing weight and/or height measures at baseline. At two years follow up, medical records were not searched for 98 children due to drop out and/or no permission. A total of 28 children gave permission to search their medical file after drop-out. Therefore, a total of 617 children were included in the present study (Figure 1). Children excluded from analysis were significantly older (mean age 9.4 years sd (4.4) versus 8.0 (3.9), p=0.001) and had a higher BMI-z at baseline (mean 0.50 (1.3) versus 0.06 (1.344), p=0.003).

At baseline a total of 18% (n = 111) was overweight, of which 24 children (4% of total population) were obese, and 82% (n = 506) was non-overweight (Table 1). Overweight children were significantly older (mean age 9.8 years sd (3.6) versus 7.8 (4.0), p=0.004) and had significantly higher baseline BMI-z values (2.0 (0.7) versus -0.4 (1.1)). Most children came from families with a middle or high SES (78.6%) and high education level (83.5%), with both parents born in the Netherlands (84.8%) and with parents living together (84.0%).

Consultations during 2 year follow up

Overall, there was a mean of 6.8 (5.43) consultations during the 2-year follow up. Overweight children consulted the GP in general significantly more frequent than non-overweight children (mean 7.3 (5.7), and 6.7 (5.4) OR 1.09, 95%CI 1.01-1.18, adjusted p-value 0.03).

A total of 377 (61%) children went to see their GP at least once during follow up, and 260 (42.1%) children went for a musculoskeletal consultation (Table 2). After specifying into the different categories, 164 (26.6%) children consulted their GP for a lower extremity condition, 104 (16.9%) for an upper extremity condition, 65 (10.5%) for other body

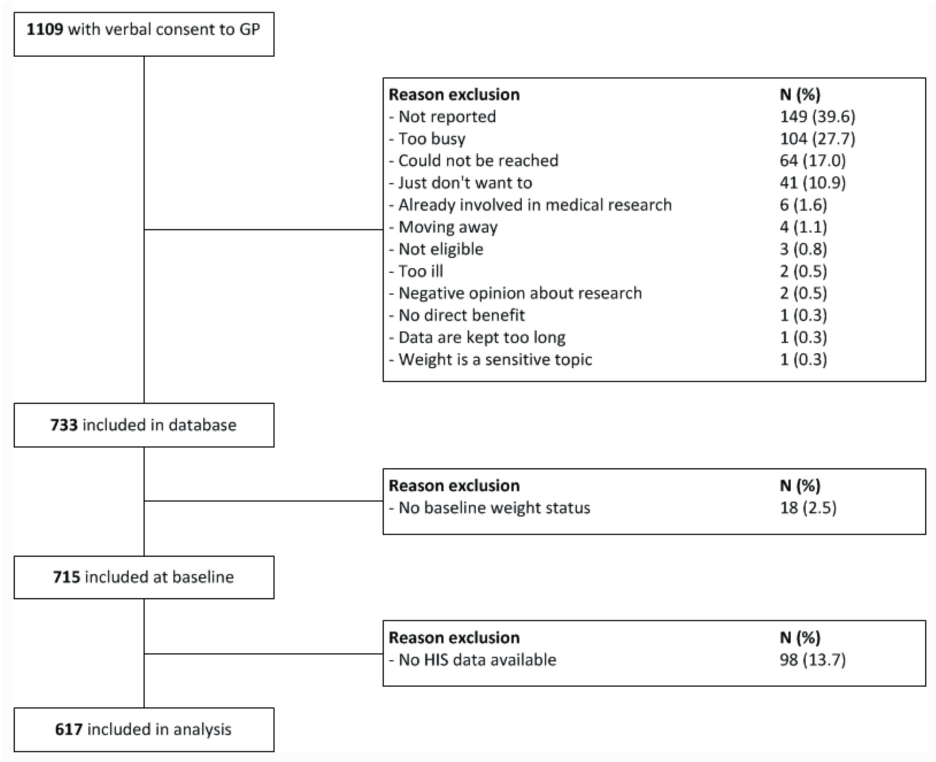


Figure 1 – Flow chart of inclusion

parts and in 42 (6.8%) the musculoskeletal localization was not registered. Since some children visited the GP for multiple musculoskeletal complaints of different categories, the sum of children with further specified consultations is greater than the number of children with consultations in the category 'any musculoskeletal consultation'. No significant difference was seen in the number of overweight and non-overweight children consulting their GP for any musculoskeletal complaints (56 (50.5%) versus 204 (40.3%), OR 1.36 (0.87 – 2.16)). After further specifying the musculoskeletal conditions into consultations for lower extremities, upper extremities, other body part, and miscellaneous, no significant differences in frequencies of visits were seen between children with and without overweight.

Number of musculoskeletal consultations (table 3)

During two-year follow-up, a child had a mean of 0.4 (sd 0.5) musculoskeletal consultations with the GP, which is equal to one musculoskeletal consult per five years. No significant difference was seen in the number of musculoskeletal consultations during two year follow-up between overweight (mean 0.5 (sd 0.5)) and non-overweight (0.4

(0.5)) children (OR 1.20, 95%CI 0.86-1.68). Additionally, no significant difference between overweight and non-overweight children was seen for the number of consultations for any of the further specified musculoskeletal conditions.

Finally, a multivariable regression was performed to test for predictors (besides overweight and/or obesity) for musculoskeletal consultations during two-year follow (Table 4). (Higher) age was significantly associated with a higher number of consultations for musculoskeletal complaints (OR 1.07 (95%C.I. 1.02-1.13).

Table 1 – Baseline characteristics.

	Study population N=617	Normal weight N=506	Overweight/ Obese N=111
Patient characteristics			
	N=617	**N=507**	**N=111**
Gender female, N (%)	321 (52.0)	260 (51.4)	61 (55.0)
	N=617	**N=507**	**N=111**
Age (years), mean (SD)	8.0 (3.9)*	7.76 (3.95)	8.9 (3.6)[¤]
	N=513	**N=421**	**N=92**
SES	**N (%)**	**N (%)**	**N (%)**
Low (<2000 euros)	110 (21.4)	88 (20.9)	22 (23.9)
Middle/High (>=2000 euros^)	403 (78.6)	333 (79.1)	70 (76.1)
	N=553	**N=450**	**N=103**
Highest education in household	**N (%)**	**N (%)**	**N (%)**
Low (up to lower secondary level)	91 (16.5)	75 (16.7)	16 (15.5)
Middle (upper secondary level)	222 (40.1)	176 (39.1)	46 (44.7)
High (at least bachelor level)	240 (43.4)	199 (44.2)	41 (39.8)
	N=540	**N=441**	**N=99**
Ethnicity	**N (%)**	**N (%)**	**N (%)**
Both parents born in Netherlands	458 (84.8)	379 (85.9)	79 (79.8)
At least one parent born in another country	82 (13.3)	62 (14.1)	20 (20.2)
	N=551	**N=449**	**N=102**
Marital status	**N (%)**	**N (%)**	**N (%)**
Parents separated	88 (16.0)	70 (15.6)	18 (17.6)
Parents together	463 (84.0)	379 (84.4)	84 (82.4)
	N=617	**N=507**	**N=111**
BMI-z score baseline, mean (sd)	0.06 (1.3)*	-0.36 (1.1)	1.98 (0.7) [¤]
	N=610	**N=500**	**N=110**
Waist circumference (cm), mean (sd)	60.33 (11.64)*	57.79 (8.76)	71.88 (15.54)[¤]

^more than 2000 euros monthly net income per household, * significantly different from whole sample (n=733), [¤]significantly different from normal weight

Table 2 – Number of patients with musculoskeletal consultations during 2 year follow-up.

	Total (n=617)	OW (n=111)	NW (n=506)	OR (95% C.I.)	Overall p-value	Adjusted OR+ (95% C.I.)	Adjusted p-value+
Any musculoskeletal consultation, # of patients (%)	260 (42.1)	56 (50.5)	204 (40.3)	1.51 (1.00-2.28)	0.05	1.36 (0.86-2.16)	0.19
Lower extremities consultation, # of patients (%)	164 (26.6)	36 (32.4)	128 (25.3)	0.71 (0.45-1.10)	0.12	0.77 (0.46-1.27)	0.30
Upper extremities consultation, # of patients (%)	104 (16.9)	20 (18.0)	84 (16.6)	0.91 (0.53-1.55)	0.72	0.95 (0.52-1.74)	0.88
Other body parts consultation (back, neck), # of patients (%)	65 (10.5)	13 (11.7)	52 (10.3)	0.86 (0.45-1.65)	0.66	0.76 (0.37-1.54)	0.44
Unclear/not registered where complaint is located, # of patients (%)	42 (6.8)	9 (8.1)	33 (6.5)	0.79 (0.37-1.70)	0.55	0.78 (0.32-1.91)	0.59

+adjusted for gender, age, marital status, ses. OW = overweight, NW = normal-weight, OR = odds ratio of overweight status compared to normal-weight

Table 3 – Number of musculoskeletal consultations during 2 year follow-up

	Total (n=617)	OW (n=111)	NW (n=506)	OR (95% C.I.)	Overall p-value	Adjusted OR+ (95% C.I.)	Adjusted p-value+
Any musculoskeletal consultation, mean (sd)	0.4 (0.5)	0.5 (0.5)	0.4 (0.5)	1.25 (0.93 – 1.25)	0.14	1.20 (0.86-1.68)	0.29
Lower extremities consultations, mean (sd)	0.4 (0.8)	0.5 (1.0)	0.4 (0.8)	1.31 (0.97-1.77)	0.08	1.15 (0.82-1.62)	0.43
Upper extremities consultations, mean (sd)	0.3 (0.7)	0.3 (0.8)	0.2 (0.6)	1.21 (0.83-1.78)	0.32	1.11 (0.73-1.69)	0.64
Other body parts consultations (back, neck), mean (sd)	0.1 (0.5)	0.2 (0.6)	0.1 (0.4)	1.31 (0.79-2.19)	0.30	1.22 (0.69-2.15)	0.49
Unclear/not registered where complaint is located, mean (sd)	0.09 (0.4)	0.1 (0.5)	0.08 (0.4)	1.56 (0.85-2.86)	0.15	1.44 (0.72-2.89)	0.30

+adjusted for gender, age, marital status, and ses. OW = overweight, NW = normal-weight, OR = odds ratio of overweight status compared to normal-weight

Table 4 – Multivariable logistic regression for the presence of musculoskeletal consultations during two-year follow up.

	β	OR (95% C.I.)
Age	0.07	1.07 (1.02-1.12)**
Gender (male)	-0.04	0.96 (0.67-1.39)
Ethnicity (both Dutch)	-0.08	0.92 (0.55-1.55)
Marital status (parents together)	-0.03	1.03 (0.59-1.67)
SES (middle/high)	0.03	1.03 (0.62-1.71)
Weight status (normal weight)	-0.25	0.78 (0.49-1.24)

* p<0.05, **p<0.01

DISCUSSION

Main findings

Children with overweight or obesity consulted their GP more often than non-overweight children during a two year follow up period, but not for musculoskeletal problems. When further specifying the musculoskeletal consultations into lower and upper extremities, other body parts and a miscellaneous group, still no significant difference was seen for any of these subgroups in frequency of consultations between overweight and non-overweight children.

Our findings seem to be in contrast with published literature (2, 3, 21) showing more musculoskeletal complaints in overweight and obese children. These complaints were however mainly self-reported by means of questionnaires [8, 10]. These children may report complaints on questionnaires but may not find the complaints serious enough to consult the GP for. This could explain why we found no difference in frequency of musculoskeletal consultations between normal-weight and overweight children. Though, an earlier study performed in primary care did find a difference between overweight and obese children and normal-weight children in experiencing musculoskeletal problems (21). However, the authors did not adjust the analyses for important confounders including socio-economic status and ethnicity, while these factors are known confounders for the frequency of GP consultations (22, 23). This is confirmed by the current study where the positive trend between overweight/obesity and musculoskeletal consultations ($p=0.05$) changes to being not significant ($p=0.19$) after adjusting for confounders (Table 2). Furthermore, our study population is relatively young compared to other literature. It is known that the frequency of musculoskeletal complaints seen in primary care especially increases around the age of ten (24). This is strengthened by the fact that we found a positive association between age and musculoskeletal consultations during follow-up. This might explain that studies with an older age group will find more musculoskeletal complaints.

Strengths and limitations

This is, to our knowledge, the first prospective cohort study comparing overweight and non-overweight children in general practice with a two year follow-up. Calibrated scales were used to measure height and weight for BMI calculation, consultations were recorded from medical files and GP trainees were trained on the reliability of measurement. This all implies that the main outcomes of this paper are based on valid data.

By instructing the GP trainees to invite every child visiting the GP to participate in the study, we tried to minimize selection bias. However, when we compare our study population to the overall Dutch population, parents from children in our cohort were more often both born in the Netherlands (84% vs. 79%) and highly educated (43% vs.

32%). Therefore, our cohort might not be completely representative of all children in general practices, which could lead to an underestimation of the percentage overweight and obese. Furthermore, since we recruited our patients at the GP, our study population only reflects a sample of all children living in the Netherlands. However, since in the current study we are primarily interested in children visiting the GP, we believe this did not impact our results.

Children who completed the two year follow-up or who gave permission for their medical files to be used were included in the analyses. Children excluded from analysis were significantly older and had a higher BMI-z at baseline. Therefore, an underestimation of the percentage overweight could be the result of this selection bias.

The size of our study sample was smaller than intended (15). The smaller sample size may have introduced a power problem. We were able to show a significant difference in visits to the GP in general, indicating that this difference could be even more profound if more children were included.

Furthermore, there was a significant difference in age and BMI between the included and excluded children, which could bias the results. Excluded children were significantly older and had a significantly higher BMI. Since an earlier study found that overweight children of older age had more consultations at the GP than overweight children of younger age (25), the exclusion of these children could have led to an underestimation of the amount of GP consultations.

Finally, we did not take possible changes in weight status during the two year follow up into consideration which may have had impact on the consultations during the 2-year follow-up.

Conclusion

Overweight and obese children visited the GP significantly more often than normal-weight children during a two year follow up. However, no association was seen between childhood overweight and obesity and the frequency and type of musculoskeletal consultations at the GP.

REFERENCES

1. James PT, Leach R, Kalamara E, Shayeghi M. The worldwide obesity epidemic. *Obes Res* 2001;**9 Suppl 4:** 228S-233S.
2. 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.
3. 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.
4. Kemler E, Vriend I, Paulis WD, Schoots W, van Middelkoop M, Koes B. Is overweight a risk factor for sports injuries in children, adolescents, and young adults? *Scand J Med Sci Sports* 2015;**25:** 259-264.
5. Wearing SC, Hennig EM, Byrne NM, Steele JR, Hills AP. The impact of childhood obesity on musculoskeletal form. *Obes Rev* 2006;**7:** 209-218.
6. Lerner ZF, Browning RC. Compressive and shear hip joint contact forces are affected by pediatric obesity during walking. *J Biomech* 2016;**49:** 1547-1553.
7. Lerner ZF, Board WJ, Browning RC. Pediatric obesity and walking duration increase medial tibiofemoral compartment contact forces. *J Orthop Res* 2016;**34:** 97-105.
8. Shultz SP, D'Hondt E, Fink PW, Lenoir M, Hills AP. The effects of pediatric obesity on dynamic joint malalignment during gait. *Clin Biomech (Bristol, Avon)* 2014;**29:** 835-838.
9. Widhalm HK, Seemann R, Hamboeck M, Mittlboeck M, Neuhold A, Friedrich K*, et al.* Osteoarthritis in morbidly obese children and adolescents, an age-matched controlled study. *Knee Surg Sports Traumatol Arthrosc* 2016;**24:** 644-652.
10. Wluka AE, Lombard CB, Cicuttini FM. Tackling obesity in knee osteoarthritis. *Nat Rev Rheumatol* 2013;**9:** 225-235.
11. Pottie P, Presle N, Terlain B, Netter P, Mainard D, Berenbaum F. Obesity and osteoarthritis: more complex than predicted! *Ann Rheum Dis* 2006;**65:** 1403-1405.
12. Gegout PP, Francin PJ, Mainard D, Presle N. Adipokines in osteoarthritis: friends or foes of cartilage homeostasis? *Joint Bone Spine* 2008;**75:** 669-671.
13. Carolan E, Hogan AE, Corrigan M, Gaotswe G, O'Connell J, Foley N*, et al.* The impact of childhood obesity on inflammation, innate immune cell frequency, and metabolic microRNA expression. *J Clin Endocrinol Metab* 2014;**99:** E474-478.
14. Pomerantz WJ, Timm NL, Gittelman MA. Injury patterns in obese versus nonobese children presenting to a pediatric emergency department. *Pediatrics* 2010;**125:** 681-685.
15. Paulis WD, van Middelkoop M, Bueving H, Luijsterburg PAJ, van der Wouden JC, Koes BW. Determinants of (sustained) overweight and complaints in children and adolescents in primary care: the DOERAK cohort study design. *Bmc Fam Pract* 2012;**13**.
16. World Health Organization. International Classification of Primary Care. *Family practice: OUP* 2003.
17. 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.
18. 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.
19. Centraal Bureau voor de Statistiek. Average income; particular households on different characteristics 2015. Available from: http://statline.cbs.nl/StatWeb/publication/?DM=SLNL&PA=70843ned&D1=a&D2=0&D3=0&D4=a&HDR=G1,G2,G3&STB=T&VW=T.
20. CBS. International Standard Classification of Education: Inpassen van het Nederlandse onderwijs in ESCED 2011. *Voorburg* 2011;**Netherlands**.

21. 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.
22. Hetlevik O, Gjesdal S. Does socioeconomic status of list populations affect GP practice? A register-based study of 2201 Norwegian GPs. *Eur J Gen Pract* 2012;**18:** 212-218.
23. Hull S, Mathur R, Boomla K, Chowdhury TA, Dreyer G, Alazawi W*, et al.* Research into practice: understanding ethnic differences in healthcare usage and outcomes in general practice. *Br J Gen Pract* 2014;**64:** 653-655.
24. van der Linden MW vS-SL, Schellevis FG, van der Wouden JC. *Tweede nationale studie naar ziekten en verrichtingen in de huisartsenpraktijk*, 2005.
25. Doherty E, Queally M, Cullinan J, Gillespie P. The impact of childhood overweight and obesity on healthcare utilisation. *Econ Hum Biol* 2017;**27:** 84-92.

Appendix 1 - ICPC coding system

ICPC letter	Body system
A	General
B	Blood, blood-forming organs, immunity system
D	Gastro-intestinal
F	Eye
H	Ear
K	Cardiovascular
L	Musculoskeletal
N	Nervous system
P	Psychological problems
R	Airway
S	Skin
T	Endocrine glands, metabolism, nutrition
U	Urinary tract
W	Pregnancy, giving birth
X	Female genitals
Y	Male genitals
Z	Social problems

Appendix 2 – ICPC codes for musculoskeletal complaints

L01 Neck symptom/complain
L02 Back symptom/complaint
L03 Low back symptom/complaint
L04 Chest symptom/complaint
L05 Flank/axilla symptom/complaint
L07 Jaw symptom/complaint
L08 Shoulder symptom/complaint
L09 Arm symptom/complaint
L10 Elbow symptom/complaint
L11 Wrist symptom/complaint
L12 Hand/finger symptom/complaint
L13 Hip symptom/complaint
L14 Leg/thigh symptom/complaint
L15 Knee symptom/complaint
L16 Ankle symptom/complaint
L17 Foot/toe symptom/complaint
L18 Muscle pain
L19 Muscle symptom/complaint NOS
L20 Joint symptom/complaint NOS
L26 Fear of cancer musculoskeletal
L27 Fear musculoskeletal disease other
L28 Limited function/disability (l)
L29 Sympt/complt. Musculoskeletal other
L70 Infections musculoskeletal system
L71 Malignant neoplasm musculoskeletal
L72 Fracture: radius/ulna
L73 Fracture: tibia/fibula
L74 Fracture: hand/foot bone
L75 Fracture: femur
L76 Fracture: other
L77 Sprain/strain of ankle
L78 Sprain/strain of knee
L79 Sprain/strain of joint NOS
L80 Dislocation/subluxation
L81 Injury musculoskeletal NOS
L82 Congenital anomaly musculoskeletal
L83 Neck syndrome
L84 Back syndrome w/o radiating pain
L85 Acquired deformity of spine
L86 Back syndrome with radiating pain
L87 Bursitis/tendinitis/synovitis NOS
L88 Rheumatoid/seropositive arthritis
L89 Osteoarthrosis of hip
L90 Osteoarthrosis of knee
L91 Osteoarthrosis other
L92 Shoulder syndrome
L93 Tennis elbow
L94 Osteochondrosis
L95 Osteoporosis
L96 Acute internal damage knee
L97 Neoplasm benign/unspec musculo.
L98 Acquired deformity of limb
L99 Musculoskeletal disease, other

Chapter 5

Differences in respiratory consultations in primary care between underweight, normal-weight, and overweight children.

Janneke van Leeuwen, Zoubeir El Jaouhari, Winifred D. Paulis, Patrick J.E. Bindels, Bart W. Koes, Marienke van Middelkoop

NPJ Prim Care Respir Med. 2019 May 3;29(1):15

ABSTRACT

Aim

This prospective cohort study investigates whether the suggested association between weight status and respiratory complaints in open populations is also reflected in the frequency of consultations for respiratory complaints at the general practice.

Methods

Children aged 2-18 years presenting at one of the participating general practices in the Netherlands could be included. Electronic medical files were used to extract data on consultations. Logistic regression- and negative binomial regression analyses were used to assess the associations between weight status and the presence-, and frequency of respiratory consultations respectively during 2-year-follow-up. Subgroup analyses were performed in children aged 2-6 years, 6-12 years, 12-18 years old.

Findings

Of the 617 children, 115 (18.6%) were underweight, 391 (63.4%) were normal-weight and 111 (18%) were overweight. Respiratory consultations were not more prevalent in underweight - compared to normal-weight- (OR 0.87, 95%CI 0.64-1.10), and in overweight- compared to normal-weight children (OR 1.33, 95%CI 0.99-1.77). Overweight children aged 12-18 years had more respiratory consultations (OR 2.14, 95%CI 1.14-4.01), more asthma-like consultations (OR 3.94, 95%CI 1.20-12.88), and more respiratory allergy related consultations (OR 3.14, 95%CI 1.25-7.86) than normal-weight children.

Conclusions

General practitioners should pay attention to weight loss as part of the treatment of respiratory complaints in overweight and obese children.

INTRODUCTION

Pediatric underweight, overweight and obesity are, among other diseases, associated with respiratory diseases and symptoms, like asthma and allergic rhinitis (1-5). Previous studies have shown a u-shaped association between weight status and prevalence of asthma (3, 5). Several underlying mechanisms have been suggested for the higher prevalence of asthma in obese children. (6, 7). One of these include that high body weight may exacerbate airway inflammation, which may also contribute to the development of asthma (8). Symptoms of asthma in overweight and obese children are also partly due to the excess weight itself, and its accompanying fat deposition in the upper body, abdomen and upper airways (9). Besides asthma, obesity is also linked to atopy, like allergic rhinitis, however the evidence for this association is contradicting (8, 10, 11).

In 2016, worldwide 14% of children under the age of 5 years was underweight, and just over 18% of children aged 5-19 years was overweight or obese (12, 13). In 2016, in the Netherlands, 7.4% of children aged 4-12 years was underweight (14), 13.6% of children aged 4-17 years was overweight and 2.7% was obese (15). Although the prevalence of underweight has slowly declined in the past decennia, the prevalence of overweight and obesity has steadily increased over the past years both worldwide and in the Netherlands (13, 15, 16).

Asthma is among the top two diseases in the Netherlands for which children consult the general practitioner (GP) the most (17). In the Netherlands, the GP is responsible for primary care and therefore the first doctor to assess a symptom or health complaint. Up to now, studies that stated that weight status is associated with different kind of respiratory diseases and symptoms, were all conducted in open-based or school-based populations and used questionnaires to gather data on symptoms and diseases (1-5). Therefore, the question arises whether the suggested association between weight status and respiratory complaints in an open population is reflected in the frequency of consultations for respiratory complaints at the GP by underweight-, normal-weight- and overweight children.

This study investigated the association between weight status and the number of respiratory consultations in general, and specific respiratory consultations at the GP, which include asthma-like -, respiratory inflammatory -, and respiratory allergy related consultations. Since the prevalence of asthma and other respiratory symptoms in children varies between different ages, the current study also investigated the beforementioned associations in different age categories (18).

METHODS

Study design

This study was a prospective cohort study with a follow-up of two years; data from the DOERAK (Determinants of (sustained) Overweight and complaints; Epidemiological Research among Adolescents and Kids in general practice) study were used (28). The Institutional Review Board of the Erasmus University Medical Centre has approved the DOERAK study (MEC-2010-092).

Participant selection

GPs, and GP trainees in their last year of education (from now on both GP), invited all children who consulted the GP between December 2010 and April 2013 for any type of complaint to participate in the study. These children could be invited at 71 participating GP offices located in various socio-economic regions in the South-West of the Netherlands. Children had to be aged 2-18 years and both children, depending on their age, and their parent(s) had to have at least a basic understanding of the Dutch language to be able to give informed consent and understand the questionnaires. Children who were disabled, had serious comorbidities affecting weight or consulted the GP for an emergency were excluded.

Eligible children and their parents received verbal information from their GP during consultation. If they were interested to participate in the study, the child's height and weight were measured by the GP. Hereafter, written information and an informed consent form was provided to the parents, and an informed assent form was provided to children aged 12 years and older. Within two weeks, the family was contacted by the research assistant to answer any remaining questions and to examine their interest to participate in the study. Once the signed informed consent forms (and if applicable, assent forms) were received, the child was officially included in the study. During the study period, children received usual care from their GP.

Data collection

Height and weight were measured by the GP at baseline and an online questionnaire with questions about, among other things, sociodemographic information was sent to parents and, if at least nine years old, to the child. Families without access to internet received paper copies of the questionnaires via post. If the questionnaires were not completed one week after the participant received the questionnaire, weekly reminders were sent to the child and/or parents.

Information regarding the frequencies and types of consultations of the children at the GP during the 2-year follow-up was registered in the electronic medical files at the GP office. In these medical files, reasons for consultation and the accompanying diagnoses were recorded by the GP using the International Classification of Primary Care (ICPC) (Supplementary Table 1) (29). These ICPC-codes, together with possible explanatory comments, were extracted for analysis from the electronic medical files.

Measures

Age and gender were extracted from the GPs' baseline questionnaires. Weight status was determined based on Body Mass Index (BMI) z-scores, which were calculated using BMI (bodyweight in kilograms divided by height in meters squared) and age-specific and gender-specific cut-off points(30, 31). Due to the small number of obese children in the cohort (n=24), both obese and overweight children were merged into the overweight group, classified as BMI >85th percentile.

Ethnicity, parental education, socio-economic status (SES), marital status, the child's birth weight and information on breastfeeding were extracted from the parent's questionnaires. SES was based on net household income, and was dichotomized into 'low SES'(<2000 Euros/month) and 'middle/high SES'(≥2000 Euros/month) using the mean monthly general labor income of 2014 as the cut-off point (32). Ethnicity ('both parents born in the Netherlands' and 'at least one parent not born in the Netherlands'), marital status ('parents are together' and 'parents separated') and breastfeeding ('breastfed' and 'not breastfed') were also dichotomized. Parental education was categorized into three classes: 'up to lower level secondary education', 'higher level secondary education' and 'at least a bachelor diploma'.

In order to analyze the frequency and type of consultations, respiratory consultations in general were defined as all ICPC codes with the letter 'R'. Asthma-like consultations were defined as ICPC codes R02 (shortness of breath), R03 (wheezing) and R96 (asthma). Respiratory allergy related consultations were defined as ICPC code R02, R03, R96 and R97 (allergic rhinitis). Respiratory inflammatory consultations were defined as ICPC codes R05 (cough), and R71 up to R83 (respiratory inflammatory codes).

Outcome measures

The primary outcome measures in this study were the frequency and type of (specific) respiratory consultations during the 2-year follow-up in underweight, normal-weight, and overweight children. Secondary outcome measure was the overall number of consultations.

Sample size calculation

The incidence of self-reported respiratory diseases in children with overweight is 0.311, and in children of normal-weight the incidence is 0.217 (33). When using the formula of Fleiss with a two-sided significance level of 0.05 and a power of 90%, the sample size is 461 children in each group (28, 34). Taking about 10% of drop-outs into account the number of participants in each group is 500.

Statistical analysis

The independent T-test was used to test for differences in baseline characteristics between the included and excluded children. The ANOVA test was used to compare baseline characteristics between the three different weight status groups. Analysis for collinearity between potential confounders showed no collinearity between confounders, therefore all analyses were adjusted for gender, age, ethnicity, SES and breastfeeding. Missing data on confounders (8.5%) were handled using multiple imputation with 10 iterations. Logistic regression analyses were used to assess the association between weight status and the presence of respiratory consultations, asthma-like consultations, respiratory inflammatory consultations, and respiratory allergy related consultations during the 2-year follow-up. Negative binomial regression was used to test the association between weight status and the frequency of respiratory consultations, asthma-like consultations, respiratory inflammatory consultations, and respiratory allergy related consultations during the 2-year follow-up. Subgroup analyses were performed in three different age categories: 2 to 6 years old, 6 to 12 years old, 12 to 18 years old. Sensitivity analyses were performed to test for differences in frequencies of respiratory consultations between normal-weight and underweight children, using a stricter cut-off for underweight status so that the 7.4% underweight prevalence in the Netherlands was simulated (14).

P values <0.05 were considered statistically significant. Adjusted odds ratio's (OR) with a 95% confidence interval (CI) were used to determine the strength of associations. Data were analyzed using IBM SPSS Statistics 21/24.

RESULTS

General characteristics

Of the 1109 children who initially gave verbal consent to participate in the study, 733 gave written consent and were included in the database (Figure 1). Children with missing baseline weight status (n=18) and/or children who did not give permission to review their medical files (n=98) were excluded from the analysis, therefore 617 children were included in the analyses. The excluded children were significantly older (mean 9.45(SD 4.4) vs 7.96(3.9), p=0.001)) and had a higher BMI z-score at baseline (0.49(1.3) vs 0.06(1.3), p=0.003) compared to included children.

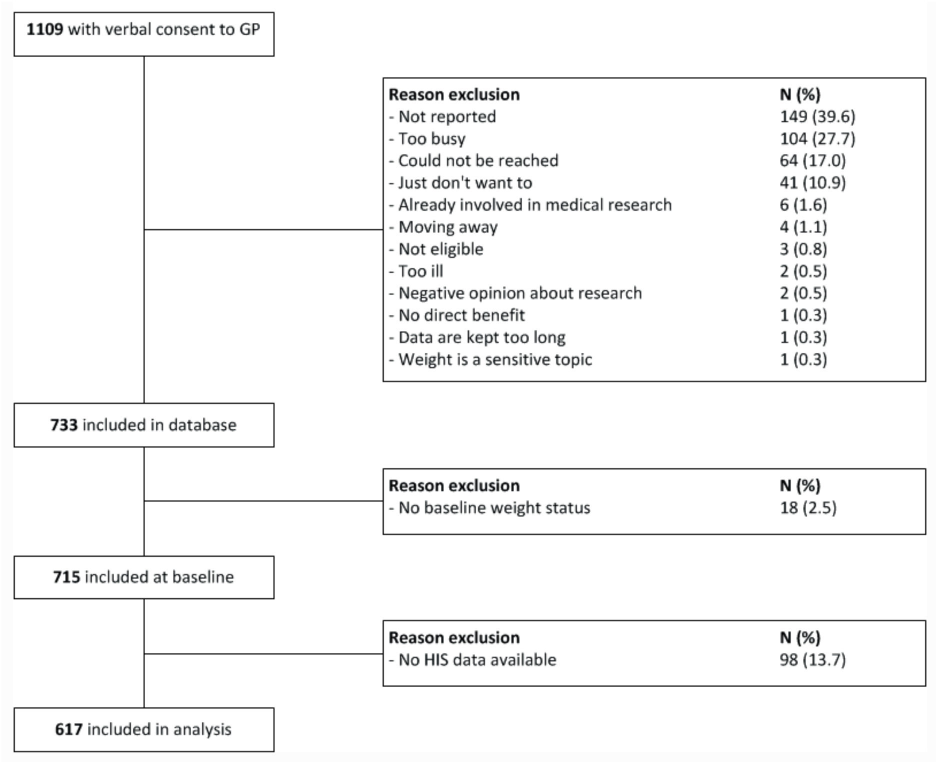


Figure 1 – Flowchart of inclusion

At baseline 115 (18.6%) children were underweight, 391 (63.4%) were of normal-weight and 111 (18.0%) were overweight (Table 1). Underweight children were younger (6.77(3.8) vs 8.05(4.0), p=0.017) and more often breastfed (85.4% vs 68.6%, p=0.025) than normal-weight children. Parents of overweight children were less often from Dutch descent compared to parents of normal-weight children (79.8% vs 86.3%, p=0.006).

Overall prevalence of consultations

Children had a mean of 6.9 (SD 5.6) consultations of any type during the 2-year follow up. No significant differences were seen in the number of consultations between underweight (6.8 (5.1)) and normal-weight (6.7 (5.7)) children (OR 1.04, 95%CI 0.83-1.31), and between overweight (7.3 (5.7)) and normal-weight children (OR 1.10, 95%CI 0.88-1.39).

Presence of respiratory consultations during 2-year follow-up (Table 2)

During the 2-year follow-up, 570 (92.4%) children consulted the GP at least once for any type of complaint and 279 (45.2%) children consulted the GP at least once for a respiratory complaint. For asthma-like complaints, respiratory inflammatory complaints, and

Table 1 - Baseline characteristics

Patient characteristics	Study population (n=617)	Underweight (n=115; 18.6%)	Normal-weight (n=391; 63.4%)	Overweight (n=111; 18.0%)
Gender, female (n; %)	321 (52.0)	61 (53.0)	199 (50.9)	61 (55.0)
Age (mean; SD)	7.96 (3.9)*	6.77 (3.8) #	8.05 (4.0)	8.87 (3.6)
Ethnicity (n; %)				
- **Both parents born in the Netherlands**	458 (84.8)	90 (84.9)	289 (86.3)	79 (79.8) +
- **At least one parent not born in the Netherlands**	82 (15.2)	16 (15.1)	46 (13.7)	20 (20.2)
SES (n; %)				
- **Low (<2000 euros)**	110 (21.4)	19 (19.4)	69 (21.4)	22 (23.9)
- **Middle/high (≥2000 euros)**	403 (78.6)	79 (80.6)	254 (78.6)	70 (76.1)
Marital status (n; %)				
- **Parents together**	463 (84.0)	90 (84.9)	289 (84.3)	84 (82.4)
- **Parents not together**	88 (16.0)	16 (15.1)	54 (15.7)	18 (17.6)
Education parents (n; %)				
- **Up to lower level secondary education**	91 (16.5)	19 (17.9)	56 (16.3)	16 (15.5)
- **Higher level secondary education**	222 (40.1)	35 (33.0)	141 (41.0)	46 (44.7)
- **At least a bachelor diploma**	240 (43.4)	52 (49.1)	147 (42.7)	41 (39.8)
Breastfeeding (n; %)				
- **Breastfed**	352 (71.4)	82 (85.4)#	214 (68.6)	56 (65.9)
- **Not breastfed**	141 (28.6)	14 (14.6)#	98 (31.4)	29 (34.1)
Birth weight (mean; SD)	3421 (632)	3333 (550)	3413 (625)	3548 (725)
BMI z-score (mean; SD)	0.06 (1.3)*	-1.79 (0.9) #	0.06 (0.7)	1.98 (0.7) +

*Significant difference between analysis group and group excluded from analysis, $p<0.05$.

Significant difference between normal-weight and underweight, $p<0.05$.

+ Significant difference between normal-weight and overweight, $p<0.05$.

respiratory allergy related complaints, 47 (7.6%), 168 (27.2%), and 81 (13.1%) children respectively consulted the GP at least once during the 2-year follow-up. There were no significant differences in the number of children with respiratory consultations between underweight and normal-weight children (OR 1.06, 95%CI 0.68-1.63), and overweight and normal-weight children (OR 1.54, 95%CI 0.99-2.39). No significant differences between weight status groups were found for the number of children consulting the GP with asthma-like-, respiratory inflammatory-, and respiratory allergy related complaints.

Number of respiratory consultations (Table 2)

Children had a mean of 1.2 (2.0) respiratory consultations during the 2-year follow-up. No significant differences were seen in the number of respiratory consultations between underweight (1.0 (1.6)) and normal-weight (1.2 (2.0)) children (OR 0.87, 95%CI 0.64-1.10), and between overweight (1.4 (2.2)) and normal-weight children (OR 1.33, 95%CI

Table 2 - Number of children with at least one respiratory consultation during the 2-year follow-up, and number of respiratory consultations per child during 2-year follow-up

		Study population (n=617)	Normal-weight (n=391)	Underweight (n=115)	Adjusted OR (95% CI) [a]	Overweight (n=111)	Adjusted OR (95% CI) [b]
Number of children with respiratory consultations	Any respiratory consultation, n (%)	279 (45.2)	168 (43.0)	53 (46.1)	1.06 (0.68-1.63)	58 (52.3)	1.54 (0.99-2.39)
	Asthma-like consultations, n (%)	47 (7.6)	24 (6.1)	12 (10.4)	2.01 (0.94-4.30)	11 (9.9)	1.59 (0.74-3.42)
	Respiratory inflammatory consultations, n (%)	168 (27.2)	108 (27.6)	32 (27.8)	0.87 (0.53-1.42)	28 (25.2)	0.98 (0.59-1.63)
	Respiratory-allergy related consultations, n (%)	81 (13.1)	46 (11.8)	15 (13.0)	1.30 (0.98-2.49)	20 (18.0)	1.53 (0.84-2.77)
Number of respiratory consultations per child	Any respiratory consultation, mean (sd)	1.2 (2.0)	1.2 (2.0)	1.0 (1.6)	0.87 (0.64-1.1)	1.4 (2.2)	1.33 (0.99-1.77)
	Asthma-like consultations, mean (sd)	0.2 (0.8)	0.2 (0.7)	0.2 (0.7)	1.51 (0.85-2.69)	0.3 (1.0)	1.59 (0.94-2.68)
	Respiratory inflammatory consultations, mean (sd)	0.5 (1.1)	0.5 (1.1)	0.5 (1.1)	0.79 (0.54-1.16)	0.4 (0.9)	0.85 (0.57-1.27)
	Respiratory-allergy related consultations, mean (sd)	0.3 (0.9)	0.2 (0.8)	0.2 (0.7)	1.17 (0.70-1.97)	0.4 (1.1)	1.65 (1.06-2.57)*

* $P<0.05$, OR=odds ratio. CI=confidence interval. [a] OR between normal-weight and underweight, adjusted for gender, age, ethnicity, SES and breastfeeding. [b] OR between normal-weight and overweight, adjusted for gender, age, ethnicity, SES and breastfeeding.

0.99-1.77). Though, overweight children consulted the GP significantly more often for respiratory allergy related consultations (0.4 (1.1)) than normal-weight (0.2 (0.8)) children (OR 1.65, 95%CI 1.06-2.57). No significant differences between the weight status groups were found for asthma-like-, and respiratory inflammatory consultations.

Respiratory consultations per age category (Table 3)

The association between weight status and number of respiratory consultations during 2-year follow-up was investigated in three different age categories (2 to 6 years, 6 to 12 years, 12 to 18 years). This analysis revealed that overweight children aged 12-18 years had significantly more respiratory consultations at the GP (1.87 (3.06) vs. 0.93 (1.54)) than normal-weight children aged 12-18 years (OR 2.14, 95%CI 1.14-4.01).

Overweight children aged 12-18 years also had more asthma-related consultations (0.48 (1.50) vs 0.20 (1.00)) (OR 3.94, 95%CI 1.20-12.88), and more respiratory allergy related consultations (0.78 (1.68) vs 0.31 (1.05)) (OR 3.14, 95%CI 1.25-7.86) than normal-weight children aged 12-18 years.

No further significant differences were seen between weight status, specifically between underweight and normal-weight children, and the number of (further specified) respiratory consultations in the different age categories.

DISCUSSION

Overall, no significant differences were found in the number of children (aged 2-18 years) visiting the GP with at least one respiratory complaint between underweight and normal-weight, and overweight and normal-weight children during 2 years of follow-up. Overweight children of all ages consulted the GP more often than normal-weight children (0.4 vs 0.2) only for respiratory allergy related consultations. However, overweight children aged 12-18 years, had significantly more respiratory consultations in general (2.14 vs 0.93), asthma-like consultations (3.94 vs 0.20) and respiratory allergy related consultations (3.14 vs 0.31) than normal-weight children of this age.

We found that older overweight children had significantly more asthma-like consultations than their normal-weight peers. This is comparable with the results from a review, which supports the association between overweight and asthma as well (2). Moreover, two studies included in this review showed that with increasing age, the odds ratio between overweight and asthma increased, which is similar to what we found (19, 20). This may strengthen the suggestion that the relationship between obesity and asthma is dose-dependent, since older children who became overweight at an early age have been exposed to obesity for a longer period (8). They have also been exposed to metabolic

Table 3 - Number of respiratory consultation per child during 2-year follow-up per age category

	Age category	Normal-weight		Underweight		OR (95% CI) [a]	Overweight		OR (95% CI) [b]
		N(%)	Mean (SD)	N(%)	Mean (SD)		N(%)	Mean (SD)	
Any respiratory consultation	2-6 years	121 (30.9)	1.88 (2.73)	55 (47.8)	1.31 (1.85)	0.74 (0.48-1.16)	18 (16.2)	2.06 (2.34)	1.15 (0.61-2.14)
	6-12 years	190 (48.6)	0.81 (1.87)	45 (39.1)	0.69 (1.08)	0.87 (0.52-1.45)	70 (63.1)	1.09 (1.76)	1.30 (0.86-1.97)
	12-18 years	80 (20.5)	0.93 (1.54)	15 (13.1)	1.00 (1.96)	1.07 (0.45-2.54)	23 (20.7)	1.87 (3.06)	2.14 (1.14-4.01)*
Asthma-like consultations	2-6 years	121 (30.9)	0.12 (0.67)	55 (47.8)	0.20 (0.87)	1.91 (0.71-5.11)	18 (16.2)	0.06 (0.24)	0.57 (0.07-4.77)
	6-12 years	190 (48.6)	0.15 (0.64)	45 (39.1)	0.13 (0.40)	0.77 (0.29-2.10)	70 (63.1)	0.24 (0.95)	1.34 (0.62-3.55)
	12-18 years	80 (20.5)	0.20 (1.00)	15 (13.1)	0.27 (0.80)	3.17 (0.53-19.12)	23 (20.7)	0.48 (1.50)	3.94 (1.20-12.88)*
Respiratory inflammatory consultations	2-6 years	121 (30.9)	0.99 (1.52)	55 (47.8)	0.65 (1.31)	0.71 (0.42-1.19)	18 (16.2)	0.94 (1.76)	0.97 (0.46-2.01)
	6-12 years	190 (48.6)	0.31 (0.71)	45 (39.1)	0.33 (0.77)	1.08 (0.56-2.11)	70 (63.1)	0.33 (0.72)	1.13 (0.64-2.01)
	12-18 years	80 (20.5)	0.31 (0.80)	15 (13.1)	0.20 (0.56)	0.50 (0.12-2.09)	23 (20.7)	0.22 (0.52)	0.74 (0.24-2.32)
Respiratory-allergy related consultations	2-6 years	121 (30.9)	0.16 (0.70)	55 (47.8)	0.20 (0.87)	1.33 (0.53-3.34)	18 (16.2)	0.17 (0.71)	1.22 (0.31-4.83)
	6-12 years	190 (48.6)	0.23 (0.73)	45 (39.1)	0.20 (0.50)	0.79 (0.34-1.82)	70 (63.1)	0.34 (0.99)	1.21 (0.63-2.30)
	12-18 years	80 (20.5)	0.31 (1.05)	15 (13.1)	0.33 (0.82)	2.14 (0.47-9.77)	23 (20.7)	0.78 (1.68)	3.14 (1.25-7.86)*

* $p < 0.05$. OR=Odds Ratio. CI=Confidence Interval. [a] OR between normal-weight and underweight, adjusted for gender, ethnicity, SES and breastfeeding. [b] OR between normal-weight and overweight, adjusted for gender, ethnicity, SES and breastfeeding.

dysregulation and mechanical factors such as excess truncal adiposity for a longer period, and therefore may have more asthma complaints for which they consult the GP (6-8).

Another explanation for the fact that we only found an association between obesity and asthma in older children is that a recent review including 21130 children suggested that the association between asthma and obesity may be inverse, meaning that asthma may lead to obesity (21). This association may partially be explained by lifestyle factors, i.e. asthmatic children have lower levels of physical activity and less sleep than healthy children, both of which can lead to obesity (22). These processes may take a few years, which may explain that the association between obesity and asthma in our study is only found in older children.

The fact that that the association between obesity and asthma in our study was only found in older children may also be explained by the influence of hormonal factors on respiratory symptoms. It has been shown that obesity and early onset of puberty are independent risk factors for persistence of asthma after the onset of puberty in both boys and girls (23). Furthermore, early menarche at an age under 11.5 years predicts post-menarcheal incidence of asthma (24).

In addition to the higher percentage of asthma-like symptoms found in overweight children aged 12-18 years, significantly more respiratory and more respiratory allergy related consultations were seen in overweight children aged 12-18 years compared to their normal-weight peers. This difference was however not present in children aged 2 to 6 and 6 to 12 years old. This phenomenon may again be explained by the suggested dose-dependent relationship between obesity and asthma(8). It could also be suggested that the low percentage of overweight children aged 2-6 years in the study population (only 9%) introduced a statistical power problem. However, when looking at the OR's and the 95%CI of the associations between weight status and respiratory consultations in children aged 2 to 6 years old, they are not close to significance. Therefore, it does not seem that the fact that there were no differences in respiratory consultations between the young overweight and normal-weight children can be explained by lack of power.

It was notable that in our sample 18.6% of the children was underweight based on the age-specific and gender-specific cut-off scores from Cole et al., while in 2016 in the Netherlands 7.4% of children aged 4-12 years was underweight (14). We therefore wanted to investigate whether this large proportion of underweight children had an impact on our results. To approach the underweight percentage of 7.4% in the Netherlands, we manually adjusted the cut-off so that only the 7.5% most underweight children in our sample were marked as underweight. When re-running the analyses with this stricter cut-off, still no significant differences between underweight and normal-weight children for respiratory consultations were found. Therefore we believe that the results found in the underweight children are valid.

We earlier showed that overweight children consult their GP more often than normal-weight children (25). The current study found that this difference may partly be explained by the increased number of respiratory consultations seen in the older overweight children. However, the clinical relevance of this difference is questionable. Extrapolating the number of asthma-related consultations in the current study to the Dutch population, a GP in the Netherlands will have about four asthma-related consultations per year from 17 overweight children aged 12-18 years, compared to eleven consultations per year from 109 normal-weight children aged 12-18 years (14). On the other hand, in our cohort, 19% of all consultations were from children with overweight, while 35% of asthma-like consultations were from children with overweight. Thus, although the absolute number of normal-weight and overweight children consulting the GP for asthma complaints may not differ much, relatively, the percentage of respiratory consultations from children with overweight is much larger than the percentage of all type of consultations from children with overweight.

The asthma clinical guideline for GPs does not differentiate between the treatment of asthma in normal-weight or overweight children (26). There is some evidence that suggests that weight loss may lessen asthma symptom severity (2, 27). Therefore, it could be suggested that implementation of weight loss treatment for overweight and obese children in the asthma clinical guideline may be beneficial for the treatment of asthma. Though, more evidence on the effectiveness of weight loss is mandatory in order to implement these recommendations in clinical guidelines.

This study is the first to investigate the association between children's weight status and frequency and type of respiratory consultations at the GP. Weight and height of the children were measured by GPs, rather than using self-reported measures, which increases the reliability of these measures. Medical files to extract data on the number and type of consultations at the GP were used, instead of using questionnaires, which is an important strength of this study, as this means we are not confronted with recall bias.

One limitation is that the study population was smaller than initially anticipated (28), which may have introduced a power problem, especially in the younger children. By instructing the GPs to invite every child who presented him- or herself at the GP during the inclusion period to participate in the study, we tried to minimize selection bias. However, when we compare our study population to the overall Dutch population we found that our study population includes less families with an ethnic minority background (15.2% vs 22.6%), and more families with a high level of education (43% vs 32%). Therefore our cohort may not be completely representative of all children in general practices. Furthermore, the excluded children in our study were significantly older and had a significantly higher BMI z-score than included children. Since we found in the current study that it is mostly the older overweight children that consult the GP more often for different types of respiratory consultations, the exclusion of these children could have led to an underestimation of the amount of respiratory consultations at the GP.

In conclusion, overweight children aged 2-18 years consulted the GP more often than normal-weight children for respiratory allergy related consultations. Overweight children aged 12-18 years consulted the GP more often for respiratory, asthma-like, and respiratory allergy related symptoms than their normal-weight peers. Since evidence suggests that weight loss may lessen asthma symptom severity, there may be a place for weight loss treatment for overweight children in the asthma clinical guideline(2, 27). However, this effectiveness of weight loss on asthma symptoms should first be further investigated before these recommendations may be implemented.

REFERENCES

1. von Mutius E, Schwartz J, Neas LM, Dockery D, Weiss ST. Relation of body mass index to asthma and atopy in children: the National Health and Nutrition Examination Study III. *Thorax*; 2001;**56(11)**: 835-8.
2. 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.
3. 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**: 804-10.
4. 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.
5. Kwon HL, Ortiz B, Swaner R, Shoemaker K, Jean-Louis B, Northridge ME, et al. Childhood asthma and extreme values of body mass index: the Harlem Children's Zone Asthma Initiative. *J Urban Health.* 2006;**83**: 421-33.
6. Vijayakanthi N, Greally JM, Rastogi D. Pediatric Obesity-Related Asthma: The Role of Metabolic Dysregulation. *Pediatrics.* 2016;**137**.
7. Muc M, Mota-Pinto A, Padez C. Association between obesity and asthma- epidemiology, pathophysiology and clinical profile. *Nutr Res Rev.* 2016;**29**: 194-201.
8. Beuther DA. Recent insight into obesity and asthma. *Curr Opin Pulm Med.* 2010;**16**: 64-70.
9. Kasteleyn MJ, Bonten TN, de Mutsert R, Thijs W, Hiemstra PS, le Cessie S, et al. Pulmonary function, exhaled nitric oxide and symptoms in asthma patients with obesity: a cross-sectional study. *Respir Res.* 2017;**18**: 205.
10. Forno E, Acosta-Perez E, Brehm JM, Han YY, Alvarez M, Colon-Semidey A, et al. Obesity and adiposity indicators, asthma, and atopy in Puerto Rican children. *J Allergy Clin Immunol.* 2014;**133**: 1308-14, 14 e1-5.
11. Visness CM, London SJ, Daniels JL, Kaufman JS, Yeatts KB, Siega-Riz AM, et al. Association of childhood obesity with atopic and nonatopic asthma: results from the National Health and Nutrition Examination Survey 1999-2006*. J Asthma.* 2010;**47**: 822-9.
12. World Health Organization. Childhood overweight and obesity: WHO; 2018 [Available from: http://www.who.int/dietphysicalactivity/childhood/en/.
13. Prevalence of underweight, weight for age (% of children under 5) [Internet]. The World Bank Group,. 2016. Available from: https://data.worldbank.org/indicator/SH.STA.MALN.ZS?end=2016&start=1966&view=chart&year_high_desc=false.
14. Centraal Bureau voor de Statistiek. Lengte en gewicht van personen, ondergewicht en overgewicht; vanaf 1981: CBS, Nederland; 2017 [Available from: http://statline.cbs.nl/Statweb/publication/?DM=SLNL&PA=81565NED&D1=0-4&D2=a&D3=0,3-4&D4=0&D5=0,10,20,30,33-36&HDR=T&STB=G1,G2,G3,G4&VW=T.
15. Volksgezondheidszorg.info. Overgewicht kinderen: RIVM: Bilthoven; 2017 [Available from: https://www.volksgezondheidenzorg.info/onderwerp/overgewicht/cijfers-context/huidige-situatie#node-overgewicht-kinderen.
16. UNICEF. LEVELS AND TRENDS IN CHILD MALNUTRITION. World Bank Group, Washington DC: 2017.
17. Wijga AH, Beckers MC. [Complaints and illnesses in children in the Netherlands] Klachten en kwalen bij kinderen in Nederland. *Ned Tijdschr Geneeskd.* 2011;**155**: A3464.

18. Centers for Disease Control and Prevention. Most Recent Asthma Data: CDC, Washington, D.C., United States; 2018 [Available from: https://www.cdc.gov/asthma/most_recent_data.htm.
19. Okabe Y, Itazawa T, Adachi Y, Yoshida K, Ohya Y, Odajima H, et al. Association of overweight with asthma symptoms in Japanese school children. *Pediatr Int.* 2011;**53**: 192-8.
20. Ahmad N, Biswas S, Bae S, Meador KE, Huang R, Singh KP. Association between obesity and asthma in US children and adolescents. *J Asthma*. 2009;**46**: 642-6.
21. Contreras ZA, Chen Z, Roumeliotaki T, Annesi-Maesano I, Baiz N, von Berg A, et al. Does early-onset asthma increase childhood obesity risk? A pooled analysis of 16 European cohorts. *Eur Respir J.* 2018.
22. Ford ES. The epidemiology of obesity and asthma. *J Allergy Clin Immunol.* 2005;**115**: 897-909; quiz 10.
23. Guerra S, Wright AL, Morgan WJ, Sherrill DL, Holberg CJ, Martinez FD. Persistence of asthma symptoms during adolescence: role of obesity and age at the onset of puberty. *Am J Respir Crit Care Med.* 2004;**170**: 78-85.
24. Al-Sahab B, Hamadeh MJ, Ardern CI, Tamim H. Early menarche predicts incidence of asthma in early adulthood. *Am J Epidemiol.* 2011;**173**: 64-70.
25. van Leeuwen J, van Middelkoop M, Paulis WD, Bueving HJ, Bindels PJE, Koes BW. Overweight and obese children do not consult their general practitioner more often than normal weight children for musculoskeletal complaints during a 2-year follow-up. *Arch Dis Child.* 2018;**103**: 149-54.
26. Bindels PJ, van de Griendt EJ, Tuut MK, Steenkamer TA, Uijen JH, Geijer RM. [Dutch College of General Practitioners' practice guideline 'Asthma in children'] NHG-standaard 'Astma bij kinderen'. *Ned Tijdschr Geneeskd*. 2014;**158**: A7935.
27. Ulrik CS. Asthma and obesity: is weight reduction the key to achieve asthma control? *Curr Opin Pulm Med.* 2016;**22**: 69-73.
28. Paulis WD, van Middelkoop M, Bueving H, Luijsterburg PA, van der Wouden JC, Koes BW. Determinants of (sustained) overweight and complaints in children and adolescents in primary care: the DOERAK cohort study design. *BMC Fam Pract*. 2012; 13:70.
29. World Health Organization. International Classification of Primary Care. Oxford: Oxford University Press; 2003.
30. Cole TJ, Bellizzi MC, Flegal KM, Dietz WH. Establishing a standard definition for child overweight and obesity worldwide: international survey. *Bmj.* 2000;**320**: 1240-3.
31. 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.
32. Average income; particular households on different characteristics [Internet]. Centraal Bureau voor de Statistiek. 2014. Available from: http://statline.cbs.nl/StatWeb/publication/?DM=SLNL&PA=70843ned&D1=a&D2=0&D3=0&D4=a&HDR=G1,G2,G3&STB=T&VW=T.
33. Otters H. Childhood Morbidity in Dutch General Practice. Chapter 7, Thesis. Rotterdam, ErasmusMC2004.
34. Fleiss J. Statistical Methods for Rates and Proportions. 2nd ed. New York: Wiley; 1981.

Part III

Treatment

Chapter 6

The effect of a multidisciplinary intervention program for overweight and obese children on cardiorespiratory fitness and blood pressure

Janneke van Leeuwen, Eleni-Rosalina Andrinopoulou, Marleen Hamoen, Winifred D. Paulis, Jolande van Teeffelen, Kees Kornelisse, Kelly van der Wijst-Ligthart, Bart W Koes, Marienke van Middelkoop

Family Practice. 2019. 36(2): 147-153

ABSTRACT

Background

Multidisciplinary intervention programs for overweight and obese children mainly focus on reducing bodyweight and body mass index (BMI), but they may also positively impact blood pressure (BP), and cardiorespiratory fitness (CRF), which is a stronger predictor for all-cause mortality than BMI.

Objective

To evaluate whether Kids4Fit, a multidisciplinary weight reduction program, has a positive effect on CRF and BP in overweight and obese children in socially deprived areas.

Methods

A quasi-experimental study design with a waiting list control period including children who participated in a multidisciplinary intervention program of 12 weeks was set-up. BP measurements and shuttle-run test (SRT) were performed at baseline, at the start of the intervention, at the end of intervention and after 52 weeks. The effect of Kids4Fit on BP and on SRT-scores were analyzed using mixed models.

Results

A total of 154 children were included (mean age 8.5 years(SD 1.8)). No significant change was seen in systolic blood pressure percentiles at 52 weeks after start of the Kids4Fit intervention (β 0.08, (95%CI-0.06, 0.22)). Diastolic blood pressure percentiles increased significantly over time (β 0.20 (0.08, 0.31)). Effect plots showed an initial significant increase of the SRT-scores but this effect diluted after the intervention.

Conclusion

A local multidisciplinary intervention program in deprived areas had a significant positive effect on cardiorespiratory fitness, but this effect diluted after the intervention. Diastolic blood pressure percentiles significantly increased over time. However, systolic blood pressure did not change over time.

INTRODUCTION

Childhood obesity is a global health issue and its prevalence increases every year (1). The prevalence of childhood obesity is especially high in children living in deprived areas, who are often of ethnic minorities and have low socioeconomic status (2). According to several studies, multidisciplinary interventions show effective results in reducing obesity and overweight amongst children (3, 4). However, most of these interventions did not focus on children in deprived areas.

Multidisciplinary intervention programs mainly focus on reducing bodyweight and body mass index (BMI), though recent studies have shown that cardiorespiratory fitness (CRF) is a stronger predictor for all-cause mortality than BMI (5, 6, 7). CRF is an objective measure of habitual physical activity, and defined as the ability of the circulatory, respiratory, and muscular systems to apply oxygen during sustained physical activity (8). Improving CRF may be more important than lowering the BMI in order to reduce the risk of cardiovascular disease and all-cause mortality, and is therefore an important outcome measure of multidisciplinary intervention programs.

Elevated blood pressure in childhood is related to a variety of diseases in adulthood, including type 2 diabetes mellitus, left ventricular hypertrophy, dyslipidemia, nonalcoholic steatohepatitis and obstructive sleep apnea (9). Overweight and obesity increase the risk of high blood pressure in children (10).Therefore, not only CRF, but also blood pressure levels are important outcome measures of multidisciplinary weight reduction intervention programs.

Recently, it has been shown that Kids4Fit, a multidisciplinary intervention program in deprived areas of Rotterdam, The Netherlands, has a non-significant positive effect towards a lower BMI-z, and is effective in reducing waist circumference (WC) in overweight and obese children (4). However, no previous research has studied the effects of a multidisciplinary intervention program for overweight and obese children in deprived areas on CRF and blood pressure. Therefore, the current study aims to evaluate whether Kids4Fit also has a positive effect on CRF and blood pressure in overweight and obese children in socially deprived areas. Secondary aims include the description of blood pressure status and the level of physical fitness during and after Kids4Fit.

METHODS

Study design

A quasi-experimental study design study, with a waiting list control period, with a follow-up of one year was performed. Children who were admitted to the Kids4Fit multidisciplinary intervention program were eligible for inclusion. The study protocol was approved by Medical Ethics Review Committee (METC-2012-479) of the Erasmus MC in Rotterdam, the Netherlands.

Intervention

Kids4Fit is an ongoing multidisciplinary intervention program of 12 weeks for overweight and obese children, which runs in four locations in deprived areas of Rotterdam, The Netherlands.

Children admitted to the Kids4Fit program have to be aged 6-12 years and have to be overweight or obese according to the International Obesity Task Force Body Mass Index (BMI) cut-off points (11). Children with co-morbidities, underlying medical pathologies as a cause of the excess weight, and children with an inability to function in a group cannot participate in the program. Eligible children can be referred to Kids4Fit by general practitioners, pediatricians, youth health care workers or dieticians, or can subscribe to Kids4Fit on their own initiative.

After signing up for Kids4Fit, children are placed on a waiting list until there is a group of 8-12 children to start the intervention program. Before the start of the intervention, each child and his/her parent(s) have an intake appointment of 20 minutes with each of the treatment providers present, to receive more information about the intervention. The program consists of group sessions led by a physiotherapist, a dietitian and a child psychologist.

The physiotherapist leads the exercise component of the program, which consists of 18 group sessions. During the first six weeks, children have 2-weekly 1-hour indoor sport sessions. The last six weeks consists of a 1-weekly 1-hour session and children are stimulated to combine this with a sport in their neighborhood outside of the program. The training sessions focus on fitness and strength and includes different types of sport. Parents are invited to join four of these sessions to increase their involvement in the program. The primary aim of Kids4Fit is to activate the child and to stimulate the child to join a sports club during or at the end of the intervention.

All children participate in four 1-hour group sessions led by the dietitian, in which healthy eating behavior and physical activity are the topics. Special attention is given to having breakfast, to avoid sugared drinks, to limit the use of television or computer and to stimulate daily physical activity. Parents are also educated on the points mentioned above and attention is given to parents being a role model for their children.

The third part of the program consists of four 1-hour group sessions with a child psychologist, which aims to support the nutritional and exercise advice and to improve the child's self-image. Parents also attend four 1-hour group sessions with the child psychologist, during which they receive information on a healthy lifestyle and how to incorporate this in daily family life, and on their position as a role model.

At the end of the 12-week intervention, GP's are informed with the results by a report. GP's are expected to follow-up the child.

Subjects

In order to evaluate the effect of this multidisciplinary intervention, children participating in Kids4Fit between October 2012 and August 2014 were asked to join the current study. After subscription, parents received information from the research team about the study. If interested, the research team sent them information and scheduled an appointment for the first measurements. Written informed consent by parents (and children aged 12 years and older) was provided before the first measurements took place.

Data collection

Data was collected after children signed up for Kids4Fit (baseline), at the start of the intervention (T1), at the end of the intervention (T2), and 52 weeks after the start of the intervention (T3).

At baseline, all parents filled in a questionnaire including sociodemographic characteristics (ethnicity, highest level of education), weight and height of both parents, information on how the child became aware of Kids4Fit (self-referred or referred by health care provider), and information on whether or not the child was a member of a sports club.

Anthropometric measurements, blood pressure measurements and the SRT were performed at all time points. The child's height was measured to the nearest 0.1 cm (SECA 217 freestanding mobile stadiometer) and weight to the nearest 0.1 kg (SECA 716 weighing scale). From height and weight measures, BMI-z scores were calculated using the World Health Organization reference data (12).

Blood pressure was measured twice (OMRON M5-I) before the SRT, on the left arm with an interval of at least two minutes. Before measuring, children were instructed to sit down and relax. The second blood pressure measurements were converted to percentiles based on gender, age and height, using the blood pressure percentiles calculator constructed by the National High Blood Pressure Education Program (13); these were consequently used for the primary analyses.

Children were also categorized into a hypertensive (SBP ≥ 95th percentile or diastolic blood pressure (DBP) ≥95th percentile), prehypertensive (SBP 90-94th percentile or DPB 90-94th percentile) or normotensive (SBP and DBP <90th percentile) group according to the Fourth Report on the Diagnosis, Evaluation, and Treatment of High Blood Pressure in Children and Adolescents (13). CRF was tested using the shuttle run test (SRT) (14). A 10-meter SRT was used since this distance was available in all Kids4Fit locations. The running pace was given by an audio-tape and started at 5km/h and increased by 0,25 km/h every minute. Each increase of speed level was equal to one stage, therefore every stage of the SRT matches one minute of running. The test was stopped when the child stopped running or when the child was unable to reach the 1.5m zone placed ahead of each 10m line at the moment of the audio signal, two times consecutively. The results were recorded with an accuracy of half a stage and were used for primary analyses.

Children were also categorized as 'low fit' (least fit 20%; boys SRT≤2.5, girls SRT≤4), 'moderately fit' (middle 40%; boys SRT >2.5 and ≤7.5, girls SRT >4 and ≤6.5) and 'high fit' children (most fit 40%; boys SRT>7.5, girls SRT>6.5) (15).

Children's and parent's attendance to all group sessions during the intervention were registered, and children with ≥75% attendance rate were considered compliant to the intervention.

Statistics

Data were analyzed using the statistical software package R (free download from www.rproject.org). Baseline demographics were described using means and standard deviations (sd) for continues variables and frequencies with proportions (%) for dichotomous or categorical variables.

Linear mixed-effects models with random intercept and random slope were used to analyze the effect of the multidisciplinary intervention up to 52 weeks on SBP and DBP percentiles, and on SRT-scores. Linear mixed-effect models were also used to analyze the effect of being a member of a sports club at T3 on SBP and DBP percentiles, and on SRT-scores. A mixture of chi-squared distributions for likelihood ratio testing was applied to investigate whether random intercept and slope were needed. The maximum likelihood test was used to determine whether the outcomes were non-linear over time. Since SRT-scores were nonlinear over time, the splines approach was used for the random intercept and random nonlinear slope. In this model, age, gender, the waiting list period and compliance were used as covariates. For the models with SBP and DBP percentiles as outcome measures, the waiting list period and compliance were used as covariates and a random intercept was assumed. Correction for multiple testing was not applied and statistical significance was set at $p<0.05$.

Graphics to visualize the blood pressure status and the level of physical fitness at the four different measurement times were constructed using Microsoft Excel 2010.

RESULTS

A total of 154 children were included in the study. Baseline measurements were performed in 132 children, and 22 children entered the study at T1, without a waiting list control period. The mean duration of the waiting list period was 23.3 (sd 10.9) weeks. At 52 weeks after the start of the intervention, measurements could be performed for 89 children. No significant differences in baseline demographics were present between children who completed the study and children who were lost to follow-up.

Data of all 154 children were used for analyses and consisted of 66 (42.9%) boys, and the mean (SD) age was 8.5 (sd 1.9) years (Table 1). 77.9% of the children had at least one parent that was born outside the Netherlands, and 84.4% of the children had parents of which the highest level of education was in the category 'low'. Mean parental BMI (maternal BMI or, if not available, paternal BMI) was 30.7 (SD 6.3). Of all participants, 68 (56.2%) were compliant to the intervention.

Table 1 – Baseline characteristics of included children (N = 154)

	N	%
Gender (male)	66	42.9
Age in years [mean (sd)]	8.5 (1.9)	
Ethnicity		
Both parents born in the Netherlands	21	13.7
At least one parent born outside the Netherlands	120	77.9
Unknown	13	8.5
Parental education		
High (at least bachelor level)	21	13.7
Low (up to secondary level)	130	84.4
Unkown	3	1.9
Signed up for Kids4Fit on own initiative	31	20.1
Referred to Kids4Fit by health care provider	114	74.0
BMI-z child [mean (sd)]	2.7 (0.8)	
BMI parent (mother, or if not available father) [mean (sd)]	30.7 (6.3)	

Table 2 shows the mean blood pressure percentiles and the mean SRT-scores at all four measurement time points. Baseline SBP and DBP percentiles, and SRT-scores of children who were lost to follow-up were not significantly different from those of children who completed the study.

Linear mixed-effect model analyses showed no significant change in SBP percentiles at 52 weeks after the start of Kids4Fit intervention (β 0.07%, (95%CI -0.07, 0.21)), expressed as the effect of the intervention per week.

DBP percentiles increased significantly over time (β 0.19% (0.08, 0.31)). However, Table 2 shows that both SBP and DBP percentiles decrease during the intervention period. The percentages of participants with a normotensive, prehypertensive and hypertensive blood pressure at the four different measurement times are presented in Figure 1.

At T0, 24.8% of the children were member of a sports club, at T1 this was 27.9%, at T2 32.7% and at T3 this was 35.4%. At the end of the study period, children who were a member of a sports club did not have a lower SBP and DBP than children who did not participate in sports outside of Kids4Fit.

Table 2 – Blood pressure percentiles at all time points [mean (sd)]

	Baseline (n=129)	Pre-intervention (n=125)	Post-intervention (105)	52 weeks after start intervention (89)
Systolic blood pressure percentile	51.9 (26.9)	48.9 (28.0)	47.1 (27.8)	52.7 (26.6)
Diastolic blood pressure percentile	60.3 (23.3)	64.0 (22.6)	59.9 (21.2)	69.0 (20.2)
Shuttle run test score	6.4 (2.8)	7.8 (2.8)	8.1 (3.1)	7.5 (2.6)

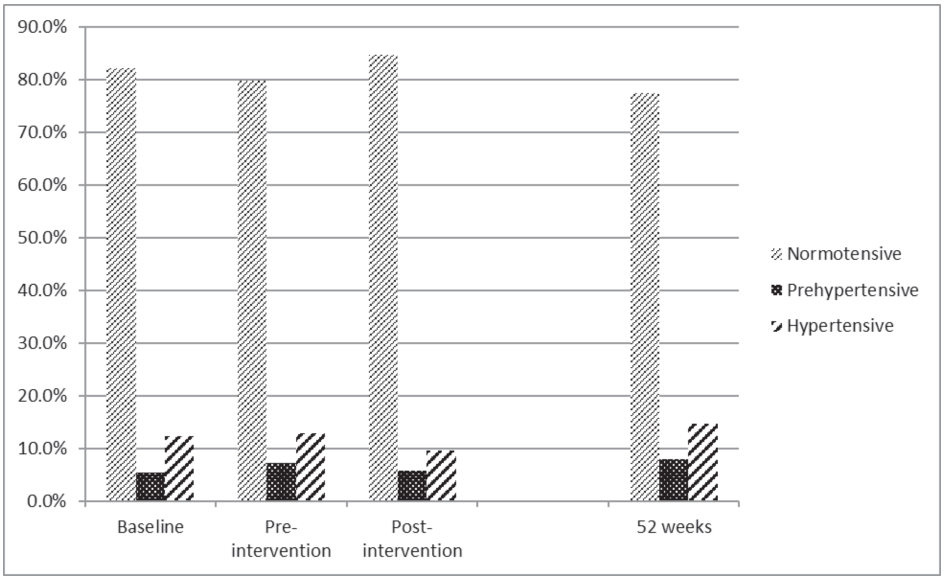


Figure 1 – Percentage of participants with a normotensive, pre-hypertensive or hypertensive blood pressure at the 4 different measurement times.

The effect of the intervention on the SRT-scores are shown in Figure 2. Figure 2a presents the effect plot of average aged (8.5 years), male participants who were compliant to the intervention. The horizontal axis denotes the time in weeks from baseline up to 52 weeks after intervention. Because of the varying waiting list period, the x-axis goes up to 80 weeks. The y-axis presents the SRT-scores. The figure shows that from baseline up to 30 weeks, which is equal to the mean waiting list period plus intervention period, the SRT scores improved significantly. After these 30 weeks, the effect on SRT-scores diluted. Since gender and compliance were non-significant confounders, the effect plot would look identical for female participants who were not compliant to the intervention. An increase in age significantly increased the SRT scores. Figure 2b presents the effect plots of 'Young' (5 years) participants and 'Old' (12 years) participants. The percentages of low fit, moderately fit, and high fit participants at the four different measurement times are presented in Figure 3. At the end of the study period, children who were member of a sports club had a significantly higher srt-score than children who were not a member of a sports club.

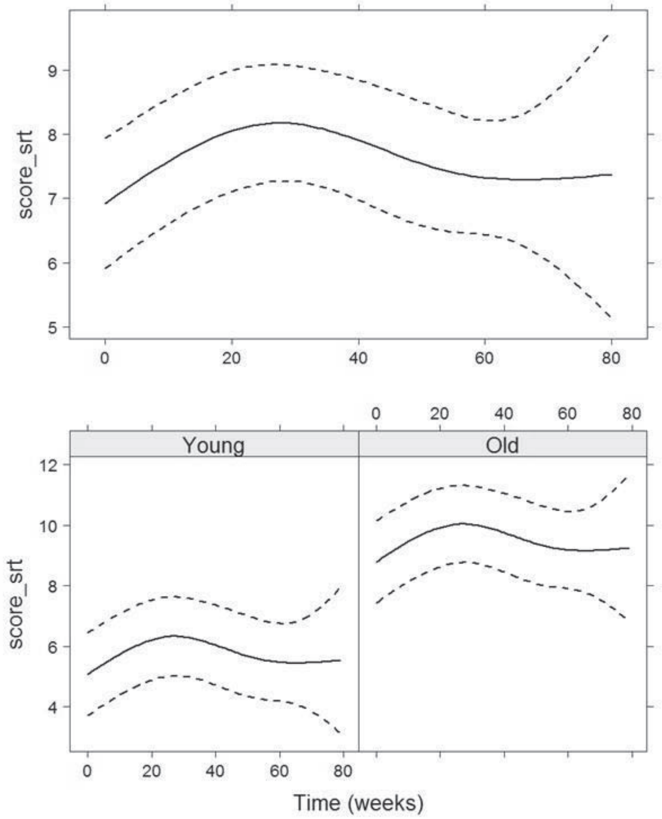


Figure 2 – (A) Effect plot based on mixed-effect model analyses for shuttle run test scores over time. The 8.5-year-old boys who were compliant to the intervention are presented. (B) Effect plot based on mixed-effect model analyses for shuttle run test scores over time. Boys of 5-year old (Young) and 12-year old (Old) who were compliant to the intervention are presented.

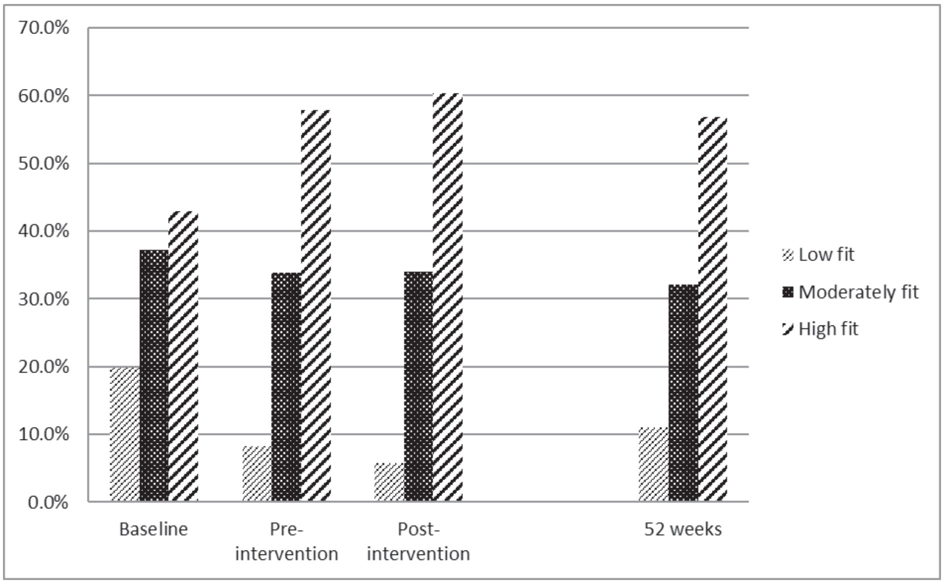


Figure 3 – Percentages of low fit, moderately fit, and high fit participants at the 4 different measurement times.

DISCUSSION

Main findings

A multidisciplinary intervention program for overweight and obese children in socially deprived areas has a significant positive effect on CRF. Furthermore, a non-significant trend towards improved physical fitness was seen over the total follow-up period of 52 weeks. The level of fitness improved from 20% of children being low fit at baseline to 11% being low fit at 52 weeks after intervention. SBP percentiles did not change, while DBP percentiles significantly increased up to 52 weeks after the intervention. Though, SBP has a stronger association with risk of coronary heart disease and better predicts coronary heart disease risks than DBP and therefore seems of less importance (16, 17). Of all children, 82.2% had a normotensive blood pressure at baseline, while 77.5% were normotensive 52 weeks after the start of the intervention. It is known that high blood pressure during childhood predicts hypertension into adulthood, which is associated with cardiovascular diseases. However, it remains unclear what the effects of childhood hypertension are during childhood and adolescence.

It has been shown that children with high CRF have less central and total obesity (7), and lower blood pressure levels (18). This is supported by the current study, where at 52 weeks after intervention, 22.2% of the low fit children was hypertensive, while of the high fit children, only 8.7% was hypertensive (data not presented).

The effect of the Kids4Fit intervention on CRF is comparable to three previous studies (19, 20, 21). They found that physical fitness improved during an intervention for overweight and obese children, but this effect was not maintained after the intervention. Our study findings are similar to these three studies, which show that SRT-scores improve during an intervention, but decrease after the intervention (19, 20, 21). Though, in the current study, a non-significant trend towards improved physical fitness was seen over the total follow-up period.

The results of our study with regard to blood pressures are in contrast with the results from a review by Garcia-Hermoso et al., that showed that exercise interventions for obese children significantly decrease both SBP and DBP (22). The duration of the included interventions ranged between 8 and 24 weeks (median 12 weeks), with no follow-up time after the intervention (22). This may well explain the difference between our results and the results of Garcia-Hermoso et al., since our results show that it is exactly in the period following the intervention that blood pressure percentiles increased, after an initial decrease during the intervention period.

Hofsteenge et al. investigated the long term effects of a 3-month multidisciplinary treatment for obese adolescents, including seven educational sessions on healthy dietary, sedentary and physical activity behavior (23). The intervention also included four booster sessions at 6, 14, 26 and 36 weeks after the intervention(23). In contrast to our study, they found a significant reduction on both BMI-sds and SBP and DBP at 18 months, but only for obese adolescents from western descent and not from non-western descent. This suggests that ethnicity may play a role in the change in blood pressure levels of children and may also explain why we did not find a reduction on SBP and DBP percentiles as 80% of the included children of the present study were from non-western descent. Furthermore, the effect found by Hofsteenge et al. on blood pressure at 18 months (23) could partly be the result of the booster sessions provided after the intervention. As mentioned before, our results show a decrease in blood pressure during the intervention, however in the period after the intervention the blood pressure levels start rising again. Booster sessions could have possibly played a role in preventing this rise from happening.

We earlier showed that the intervention studied had a positive trend towards a lower BMI-z at 52 weeks after the start of Kids4Fit, and a significant reduction in waist circumference (4). These results, in combination with a significantly improved CRF immediately after the intervention period, which is a stronger predictor for all-cause mortality than BMI (5-7), and a positive effect on blood pressure during the intervention period, indicate that a multidisciplinary intervention in deprived areas for overweight and obese children has potential to improve different health outcomes. However, more attention should be paid to maintain the effects of intervention programs right after the intervention and throughout children's life.

Providing booster sessions in the period following an intervention may be one option to maintain the positive effects of an intervention program. However, this may only postpone the deterioration of health outcomes until after the booster sessions, when the participants become completely dependent on their own decisions. Besides focusing on improving intervention programs, it is also important to consider environmental factors that can either facilitate or hinder maintenance of health benefits of such interventions. People have personal responsibilities for their health, but environmental factors, such as increasing the accessibility to safe and secure playgrounds, and promoting the consumption of healthy food, can affect the ability of people to make healthy choices (24, 25). Therefore it could be argued that, in addition to the personal guidance as in multidisciplinary intervention programs, it is especially the environmental factors that should be tackled in order to maintain the health benefits of an intervention.

Strength and limitations

A strength of this study is that we made use of an existing intervention program in deprived areas, and therefore did not intervene with existing health pathways. As a consequence, we did not apply a randomized controlled trial design, but applied an observational study design. By using the waiting list period before the intervention, children formed their own controls.

The number of children included in our analyses was 129 at baseline, and 89 at follow up. Since at follow-up only a small number of children was labeled as unfit, we lacked power to test for statistical differences in blood pressure status between the unfit and fit children. If our sample size would have been larger, the non-statistical trend that unfit children have a higher blood pressure than fit children, which we saw in our data, may have become statistically significant.

Children (and their parents) admitted to the Kids4Fit intervention had to be highly motivated for the intervention program in order to be eligible to participate. As a consequence, the results of this study are applicable to a selected group of children.

Conclusions

A local multidisciplinary intervention program for overweight and obese children in deprived areas had a significant positive effect on cardiorespiratory fitness, but this effect diluted after the intervention. SBP and DBP percentiles improved during the intervention-period. However, over the whole study period (i.e. waiting-, intervention-, and follow-up period) , SBP percentiles did not change, while DBP percentiles slightly increased.

REFERENCES

1. Commission on Ending Childhood Obesity. Ending Childhood Obesity. World Health Organization; 2016 [cited 2017]; Available from: http://apps.who.int/iris/bitstream/handle/10665/204176/9789241510066_eng.pdf;jsessionid=D6D910CE16D6DD1C75DEFFF89F745084?sequence=1.
2. Gishti O, Kruithof CJ, Felix JF, Raat H, Hofman A, Duijts L, et al. Ethnic disparities in general and abdominal adiposity at school age: a multiethnic population-based cohort study in the Netherlands. *Ann Nutr Metab* 2014;**64**:208-17.
3. 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 Aug;**13**:294-302.
4. 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. *Family Practice* 2017;**34**:702-7.
5. 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**:327-32.
6. 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**:382-90.
7. Nassis GP, Psarra G, Sidossis LS. Central and total adiposity are lower in overweight and obese children with high cardiorespiratory fitness. *Eur J Clin Nutr* 2005;**59**:137-41.
8. Lee DC, Artero EG, Sui X, Blair SN. Mortality trends in the general population: the importance of cardiorespiratory fitness. *J Psychopharmacol* 2010;**24(4 Suppl)**:27-35.
9. 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.
10. 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**:110-5.
11. Cole TJ, Lobstein T. Extended international (IOTF) body mass index cut-offs for thinness, overweight and obesity. *Pediatr Obes* 2012;**7**:284-94.
12. 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.
13. National High Blood Pressure Education Program Working Group on High Blood Pressure in C, Adolescents. The fourth report on the diagnosis, evaluation, and treatment of high blood pressure in children and adolescents. *Pediatrics* 2004;**114**:555-76.
14. Mayorga-Vega D, Aguilar-Soto P, Viciana J. Criterion-Related Validity of the 20-M Shuttle Run Test for Estimating Cardiorespiratory Fitness: A Meta-Analysis. *J Sports Sci Med* 2015;**14**:536-47.
15. Blair SN, Kampert JB, Kohl HW, 3rd, Barlow CE, Macera CA, Paffenbarger RS, Jr., et al. Influences of cardiorespiratory fitness and other precursors on cardiovascular disease and all-cause mortality in men and women. *Jama* 1996;**276**:205-10.
16. Kannel WB, Gordon T, Schwartz MJ. Systolic versus diastolic blood pressure and risk of coronary heart disease. The Framingham study. *Am J Cardiol* 1971;**27**:335-46.
17. Onat A, Ceyhan K, Erer B, Basar O, Uysal O, Sansoy V. Systolic, diastolic, and pulse pressures as coronary risk factors in a population with low cholesterol levels: a prospective 10-year evaluation. *Clin Cardiol* 2003;**26**:91-7.

18. Klasson-Heggebo L, Andersen LB, Wennlof AH, Sardinha LB, Harro M, Froberg K, et al. Graded associations between cardiorespiratory fitness, fatness, and blood pressure in children and adolescents. *Br J Sports Med* 2006;**40**:25-9.
19. Eliakim A, Kaven G, Berger I, Friedland O, Wolach B, Nemet D. The effect of a combined intervention on body mass index and fitness in obese children and adolescents- a clinical experience. *Eur J Pediatr* 2002;**161**:449-54.
20. Sandercock GR, Cohen DD, Griffin M. Evaluation of a multicomponent intervention to improve weight status and fitness in children: Upstarts. *Pediatr Int* 2012;**54**:911-7.
21. Nemet D, Barkan S, Epstein Y, Friedland O, Kowen G, Eliakim A. Short- and long-term beneficial effects of a combined dietary-behavioral-physical activity intervention for the treatment of childhood obesity. *Pediatrics* 2005;**115**:e443-9.
22. Garcia-Hermoso A, Saavedra JM, Escalante Y. Effects of exercise on resting blood pressure in obese children: a meta-analysis of randomized controlled trials. *Obes Rev* 2013;**14**:919-28.
23. Hofsteenge GH, Chinapaw MJ, Delemarre-van de Waal HA, Weijs PJ. Long-term effect of the Go4it group treatment for obese adolescents: a randomised controlled trial. *Clin Nutr* 2014;**33**:385-91.
24. Roberto CA, Swinburn B, Hawkes C, Huang TT, Costa SA, Ashe M, et al. Patchy progress on obesity prevention: emerging examples, entrenched barriers, and new thinking. *Lancet* 2015;**385**:2400-9.
25. Active Living Research. The Potential of Safe, Secure and Accessible Playgrounds to Increase Children's Physical Activity. Active Living Research; 2011 [cited 2017]; Available from: https://activelivingresearch.org/sites/default/files/ALR_Brief_SafePlaygrounds_0.pdf.

Chapter 7

Children with overweight are not less physically active than children of normal-weight

Janneke van Leeuwen, Bart W. Koes, Winifred D. Paulis,
Patrick J.E. Bindels, Marienke van Middelkoop

Under review: BMC Pediatrics

ABSTRACT

Background

The aim of this study was to investigate the differences in objectively measured physical activity and in self-reported physical activity between overweight and normal-weight children.

Methods

Data from a prospective cohort study including children, presenting at the participating general practices in the south-west of the Netherlands, were used. Children (aged 4-15 years) were categorized as normal-weight or overweight using age- and sex specific cut-off points. They wore an ActiGraph accelerometer for one week to register physical activity, and filled out a diary for one week about physical activity.

Results

A total of 57 children were included in this study. Overweight children spent significantly less percentage time per day in sedentary behavior (β-1.68 (95%CI-3.129,-0.07)). There were no significant differences in percentage time per day spent in light to moderate physical activity (β 1.52 (-0.01, 3.04)), and in moderate to vigorous physical activity (β 0.33 (-0.11, 0.78)). No significant differences were found between children of normal-weight and overweight in self-reported measures of physical activity.

Conclusions

Overweight children are not less physically active than normal-weight children, which may be associated with the risen awareness towards overweight/obesity and with implemented interventions for children with overweight/obesity.

BACKGROUND

Childhood obesity is one of the most serious public health challenges of the 21st century, according to the World Health Organization (1). It can, among other diseases, lead to pulmonary complaints, diabetes, and cardiovascular diseases like hypertension (2). Besides reducing sedentary time, and promoting a healthy diet, increasing physical activity is another strategy to address childhood obesity. Therefore, to fight the childhood obesity epidemic, and promote other health benefits, children are advised to be moderately to vigorously physically active for at least 60 minutes each day (1).

Previous literature states that children with overweight and obesity are less physically active than children of normal-weight based on objective data of accelerometers (3, 4). However, these studies are conducted over 10 years ago, while since then several initiatives have been launched to reduce overweight and obesity. In the Netherlands (in 2010), the 'covenant healthy weight', promoting healthy lifestyle for children, was introduced (5). The covenant healthy weight aimed to increase awareness on the health risks of overweight and obesity, and consequently decrease the prevalence of overweight and obesity in the Netherlands. Therefore, it is interesting to investigate whether children with overweight and obesity in today's society are as active, or even more active as their normal-weight peers.

Physical activity and sedentary behavior can be measured objectively with accelerometers or inclinometers, but the usage of diaries and questionnaires is also often used. This way of data collection is subjective and the validity of self-reported physical activity by children and parents is controversial (6). Moreover, it has been shown that parents of children with overweight overestimate their child's physical activity (7). Though, self-reported questionnaires are a valid methodological approach to measure sedentary behavior in adolescents (8).

The aim of this study is to describe potential differences between children with overweight and children of normal-weight in objectively measured and self-reported physical (in)activity.

METHODS

Study Design

This study is a longitudinal cohort study with a follow-up of one week using a subsample from the DOERAK study (9). The DOERAK study is a prospective cohort study including 733 children with a two-year follow-up, that studied differences between children with and without overweight that consulted the general practitioner (GP) (10). The DOERAK study was primarily designed to study differences between with- and without overweight, in the number of consultations at the GP, the type of complaints, quality of life, and levels of physical activity. The study has been approved by the Institutional Review Board of the Erasmus University Medical Center, Erasmus MC (MEC-2010-092).

Participant selection for DOERAK database

Children aged 2-18 years, visiting one of the 71 participating GP practices located in various socio-economic regions in the South-West of the Netherlands between December 2010 and April 2013 with any type of complaint were invited to participate in the study. They, or their parents, had to have at least a basic understanding of the Dutch language. Children with mental or physical disabilities, children with serious co-morbidities affecting weight and children consulting their GP with emergency problems were not invited to participate in the study. If children showed interest to participate in the study and after verbal consent, height, weight and waist circumference of the child were measured by the GP, and contact information of the parents was gathered. For assessing height and weight, calibrated height and weight measures were used. Waist circumference was measured midway between the lowest rib and the top of the iliac crest, at the end of gentle expiration. Parents then received written study information and an informed consent form (children aged 12 years and older also received an informed assent form). The child was formally included in the study when the signed informed consent (and signed informed assent form when needed) was received by the research team.

Subsample selection for current study

From the 733 included children in the DOERAK cohort, it was aimed to ask every fifth child with overweight and fifteenth child of normal-weight aged 4-18 years to wear an accelerometer for one week (ActiGraph, GT3X, Pensacola, Florida) to provide objective information about sedentary time and physical activity (11). These 65 children were used for the current study.

Data collection

After formal inclusion, the researcher sent a questionnaire to the GP to collect data on the child's age and sex, and the GP measured height, weight and waist circumference during consultation. Parents of included children received a questionnaire to collect data on demographics (i.e. socio-economic status, highest education in household, ethnicity, marital status) of parents and child. Children aged 9 years and older received an online diary which had to be filled out once each day in the same week the ActiGraph was worn. For younger children (aged 4-9 years), parents were asked to fill out the diary. The diary contained open questions on how many hours were spent on sleeping, watching tv, playing sports, outdoor play, and using the computer. There was also room for comments about taking off the ActiGraph during sports/showering. Children had to wear the

ActiGraph at the waist at the right side of the body for seven days; five weekdays and two weekend days. Epoch length was set at 10 seconds. The measurement started at 7am and ended 8 days later at 7am. Children were instructed to take off the ActiGraph when going to bed and with activities involving water. The first full seven days of recording were used for the analysis. The child received the activity monitor the day before the measurements started in order to become familiar with the device. The researcher or research assistant who delivered the ActiGraph to the participants gave instructions to children and their parents on how to wear the ActiGraph. Children and parents were asked to put on the accelerometer as soon as the child woke up.

Measures

The GP questionnaire was used to extract child's age and sex and from height and weight measurements, BMI-z scores were calculated and weight status was determined using the international age and sex specific cut-off points (12). Since only a small percentage of the included children was obese (n=3), children with overweight (n=19) and obesity were combined into one category called the 'overweight' category. Parent's questionnaires were used to extract information on baseline demographics. Socio-economic status (SES) was based on net household income, and was dichotomized into 'low SES'(<2000 Euros/month) and 'middle/high SES'(≥2000 Euros/month). Ethnicity ('both parents born in the Netherlands' and 'at least one parent not born in the Netherlands'), and marital status ('parents are together' and 'parents separated') were also dichotomized. Parental education was categorized into three levels: 'up to lower level secondary education', 'higher level secondary education' and 'at least a bachelor diploma'.

The diary was used to extract data on the amount of hours per day spent on watching TV, using the computer, outdoor play and playing sports. The outcome measures were categorized into: 0=not applicable, 1=30 minutes or less, 2=30 minutes - 1 hour, 3=1-2 hours, 4=2-4 hours, 5 >4 hours.

Data from the ActiGraphs were extracted using ActiLife (v.5.4.0.0). Non-wearing time was defined as a period of at least 20 minutes of consecutive zero counts (14). ActiGraph data were considered valid when daily wearing time was at least 8 hours a day and if there were at least 3 valid weekdays and 1 valid weekend day. Children who wore the ActiGraph less than this predetermined amount of days were excluded from analyses (n=6). For children with valid ActiGraph data, all valid weekdays and weekend days were used in the analyses. The chosen cut-off points in counts per minute (cpm) for the various activity levels were <100 cpm for sedentary behavior, <2220 cpm for light, <4136 cpm for moderate and ≥4136 cpm for vigorous activity (15). The amount of time spent in each level of activity per day, and the percentage of time spent in each activity level per day (time spent per day in level of activity/total wear time of that day) were extracted from ActiLife (v5.4.0.0).

The percentage of time spent per day in light and moderate activity were clustered into 'light to moderate physical activity' (LMPA). Additionally, the percentage of time spent per day in moderate and vigorous activity were clustered into 'moderate to vigorous physical activity' (MVPA).

Sample size calculation

Based on the formula of Fleiss [34] with a two-sided significance level of 0.05 and a power of 90% and the median result of 580 counts/min in a day from Riddoch et al [37], 50 participants in both the normal-weight- and the overweight group are needed to find a difference of 10% between the groups (9, 16, 17).

Statistical analysis

Descriptive statistics were used to describe baseline demographics. Potential differences between children of normal-weight and with overweight were tested using independent t-tests.

In order to account for differences between children in total wear time of the ActiGraph per day, percentages of time spent in the different activity levels were used. Potential differences in sedentary behavior and physical activity between children with overweight and children of normal-weight were tested using linear mixed models. Effects of mixed model analyses were expressed as the percentages of time spent in activity level per day of children with overweight compared to children of normal-weight; expressed as beta (β), with accompanying 95% confidence intervals (CI). Generalized estimating equations (GEE) were used to test for differences between children with overweight and of normal-weight for self-reported time spent on watching TV, using the computer, playtime outside and playing sports. To examine differences between percentage of children with overweight and of normal-weight meeting the WHO guidelines of 60 minutes of MVPA per day, GEE was used. Effects were expressed in β, with 95%CI. All analyses were adjusted for sex, age and ethnicity. The significance level was set at $p<0.05$.

RESULTS

General characteristics

Of the 65 children with ActiGraph data, six were excluded from the analyses due to invalid wear time. Weight status was missing for two children because of missing height and/or weight at baseline. Therefore, 57 children were included in the current study, of which the characteristics are presented in Table 1. The average age of the participating children was 8.7 (3.2) years and 60% was female. Of the participating children, 24% had a family with a low socio-economic status and in 19% of the children, at least one parent was born in another country than the Netherlands. In 19% of the families, the parents were separated and in 15% of the families, the highest level of education from the parents was up to lower secondary level. In families of the children with overweight, compared to children of normal-weight, significantly more often one parent was born in another country.

Table 1 - Participant characteristics

	Study population N=57	Normal-weight N=35	Overweight N=22
Age, mean (SD), y	8.7 (2.5)	8.4 (2.7)	9.1 (2.2)
Sex: female, N (%)	34 (59.6)	20 (57.1)	14 (63.6)
Socio-economic status	**N(%)**	**N(%)**	**N(%)**
Low (<2000)	12 (23.5)	8 (25.0)	4 (21.1)
Middle/High (>=2000^)	39 (76.5)	24 (75)	15 (78.9)
Highest education in household	**N(%)**	**N(%)**	**N(%)**
Low (up to lower secondary level)	8 (15.1)	5 (15.6)	3 (14.3)
Middle (upper secondary level)	21 (39.6)	10 (31.3)	11 (52.4)
High (at least bachelor level)	24 (45.3)	17 (53.1)	7 (33.3)
Ethnicity	**N(%)**	**N(%)**	**N(%)**
Both parents born in Netherlands	43 (81.1)	28 (87.5)	15 (71.4)
At least one parent born in another country	10 (18.9)	4 (12.5)	6 (28.6)
Marital status	**N(%)**	**N(%)**	**N(%)**
Parents separated	11 (19.3)	8 (25.0)	3 (14.3)
Parents together	42 (73.7)	24 (75.0)	18 (85.7)
Time per day in sedentary behavior, mean (SD), Hours:Minutes:Seconds	08:19:18 (03:07:40)	08:17:50 (03:07:38)	08:37:44 (03:02:19)
Time per day in light activity, mean (SD), Hours:Minutes:Seconds	03:43:10 (00:55:07)	03:38:10 (00:56:02)	03:48:38 (00:53:53)
Time per day in moderate activity, mean (SD), Hours:Minutes:Seconds	00:36:44 (00:18:38)	00:35:24 (00:19:21)	00:37:38 (00:17:10)
Time per day in vigorous activity, mean (SD), Hours:Minutes:Seconds	00:16:22 (00:16:20)	00:14:46 (00:14:01)	00:16:18 (00:13:37)

Actigraph-data

On average, children had 4.7 valid weekdays and 1.9 valid weekend days on which they wore the ActiGraph for at least 8 hours. The average total wear time per day was 12 hours, 51 minutes and 4 seconds (sd 02:48:24). Children with overweight spent significantly less percentage time per day in sedentary behavior (β-1.68 (95%CI-3.29,-0.07)). There were no significant differences between children of normal-weight and overweight in percentage time per day spent in light activity (β 1.26 (-0.06, 2.59)), in LMPA (β 1.52 (-0.01, 3.04)) and in MVPA (β 0.33 (-0.11, 0.78)) (Table 2). No significant difference between children of normal-weight and with overweight was found in percentage time per day spent.

The number of children meeting the WHO guidelines of at least 60 minutes of MVPA per day based on objective measured data ranged per day from 24.1%- 39.3%. On average per week, 27% of children of normal-weight and 37% of children with overweight met the WHO guidelines on physical activity, based on objectively measured data (APPENDIX 1). No significant difference was seen between the number of children of normal-weight and with overweight meeting the WHO guidelines (β-0.56 (-1.18, 0.07)).

Table 2 - Results of the linear mixed model analyses on the influence of weight status on % of time spent per day in each level of activity.

	Beta	95% C.I.	P-value
% time in sedentary			
Normal-weight	Ref		
Overweight	-1.68	-3.29--0.07	0.04*
% time in light activity			
Normal-weight	Ref		
Overweight	1.26	-0.06 – 2.59	0.06
% time in light to moderate activity			
Normal-weight	Ref		
Overweight	1.52	-0.01 – 3.04	0.05
% time in moderate to vigorous activity			
Normal-weight	Ref		
Overweight	0.33	-0.11 – 0.78	0.14

All analyses were adjusted for sex, age and ethnicity. *p<0.05.

Self-reported physical activity

No differences were seen between children of normal-weight and children with overweight for self-reported time spent on watching TV, using the computer, playtime outside and playing sports which was gathered from the diaries (Table 3).

Table 3 – The average time per week spent on different types of physical activity.

	Study Population (N=57)	Normal-weight (N=35)	Overweight (N=22)
Time spent watching TV			
Not Applicable	14.3%	17.2%	10.3%
1/2 hour or less	22.2%	18.3%	26.5%
½ - 1 hour	26.0%	28.5%	23.9%
1-2 hours	26.7%	24.2%	30.8%
2-4 hours	9.5%	10.2%	7.7%
>4 hours	1.3%	1.6%	0.9%
Time spent on the computer			
Not Applicable	44.5%	45.0%	46.6%
1/2 hour or less	24.5%	24.1%	19.8%
½ - 1 hour	17.2%	16.8%	19.0%
1-2 hours	11.3%	11.0%	12.9%
2-4 hours	1.9%	2.1%	1.7%
>4 hours	0.6%	1.0%	0%

Table 3 – The average time per week spent on different types of physical activity. (*continued*)

	Study Population (N=57)	Normal-weight (N=35)	Overweight (N=22)
Time spent on playing outside			
Not Applicable	9.0%	9.3%	8.5%
1/2 hour or less	11.6%	8.3%	17.1%
½ - 1 hour	16.8%	18.7%	13.7%
1-2 hours	23.2%	26.4%	17.9%
2-4 hours	23.5%	24.4%	22.2%
>4 hours	15.8%	13.0%	20.5%
Time spent on playing sports			
Not Applicable	60.9%	62.1%	58.8%
1/2 hour or less	5.9%	5.3%	7.0%
½ - 1 hour	12.8%	11.6%	14.9%
1-2 hours	15.8%	15.3%	16.7%
2-4 hours	3.0%	5.3%	1.8%
>4 hours	0.5%	0.5%	0.9%

DISCUSSION

Children with overweight spent less percentage time per day in sedentary behavior (-1,68%)compared to children of normal-weight. The magnitude of this difference is small, which is characterized by the following calculation: if a child of normal-weight would spent 6 hours (=360 minutes) in sedentary behavior per day, a child with overweight would spend on average-1.68% * 360 = 6.05 minutes less in sedentary behavior per day. Even though this difference is small, it indicates that children with overweight are certainly not less physically active, than children of normal-weight. Furthermore, no differences were seen in percentage time per day spent in light activity, LMPA and MVPA between children of normal-weight and overweight. Self-reported data on physical activity, which was measured with a diary, also showed no differences in physical activity between children of normal-weight and overweight. On average, 73.3% of children of normal-weight and 63.2% of children with overweight, did not meet the WHO guidelines on daily physical activity based on objectively measured data.

In contrast with the current study, others found that children with overweight are less physically active than children of normal-weight, based on objective measurements (3, 4). The finding of the present study, i.e. children with overweight are not less physically active than children of normal-weight may be associated with the risen awareness and implemented interventions for children with overweight and obesity. In the Netherlands, the 'covenant healthy weight' has resulted, among other things, in special health programs at schools and after-school physical activity intervention programs (5). These implementations and the improved awareness may have resulted in higher activity rates in children with overweight. Though, it remains unclear whether these intervention programs affected the physical activity rates of the children included in this study.

National data from the Netherlands, based on online- and paper questionnaires, found that in 2015, 48% of Dutch children, aged 4-12 years met the WHO guideline on physical activity (20). This number is slightly higher than the number found in the current study (24.1% - 39.3%) which used objective measures (rather than questionnaires) to measure physical activity. It could be suggested that questionnaires are less accurate than objectively measured data, due to, among other things, recall bias. A study by Verloigne et al. conducted in 2010 also used accelerometers to measure levels of physical activity in 10-12 year old children (21). They found that 2.1% of the girls and 15.8% of the boys in the Netherlands met the WHO guidelines on physical activity (21). These numbers indicate that even though many interventions promoting physical activity in children (with overweight) are present these days, the number of children meeting the physical activity guideline are not sufficient yet.

There may also be other explanations for the fact that the children with overweight of the current cohort are not less physically active than children of normal-weight. The children with overweight in this cohort may be more focused on their weight and perhaps already motivated to change their lifestyle, since they were willing to participate in a study focused on overweight and obesity. The included children with overweight may have started to increase their level of physical activity as soon as the study started. Additionally, wearing an ActiGraph for a week is an intervention in itself, which could have resulted in higher physically active children with overweight compared to their normal-weight peers.

Strength and limitations

By assigning every fifth child with overweight and every fifteenth child of normal-weight to the subsample used in the current study, we tried to minimize selection bias. The subsample did not differ from the DOERAK cohort in basic demographics (10). However, when we compare our subsample to the most recent numbers of the overall Dutch population, parents from our cohort were more highly educated (45.3% vs 32%) (22). Furthermore, it could be suggested that the parents and children participating in the DOERAK study are more motivated to lose weight compared to the overall Dutch population, since the DOERAK study is a study about overweight and obesity. Therefore, our cohort might not be completely representative for all Dutch children, and it could have led to an overestimation of physical activity levels in the Dutch population.

The size of our study sample was smaller than intended (9). The smaller sample size may have introduced a power problem. We found a difference in time spent on physical activity, but a larger sample size, introducing more variation in the demographics, could have had an impact on the effect we found in the current study. Therefore we believe that our results should be handled with care and further research with larger sample sized populations should be performed.

CONCLUSIONS

In our study, children with overweight are not less physically active than children of normal-weight. However, the majority of both children of normal-weight and with overweight do not meet the guidelines of 60 minutes of MVPA per day. Therefore, promoting physical activity in all children should remain an important topic for today's society.

REFERENCES

1. World Health Organization. Childhood overweight and obesity: WHO; 2017 [Available from: http://www.who.int/dietphysicalactivity/childhood/en/.
2. Daniels SR. Complications of obesity in children and adolescents. Int J Obes (Lond). 2009;33 Suppl 1:S60-5.
3. Haerens L, Deforche B, Maes L, Cardon G, De Bourdeaudhuij I. Physical activity and endurance in normal weight versus overweight boys and girls. J Sports Med Phys Fitness. 2007;47(3):344-50.
4. Dorsey KB, Herrin J, Krumholz HM. Patterns of moderate and vigorous physical activity in obese and overweight compared with non-overweight children. Int J Pediatr Obes. 2011;6(2-2):e547-55.
5. Jongeren op Gezond Gewicht. Convenant Gezond Gewicht 2010-2014 2010 [Available from: https://extranet.who.int/nutrition/gina/sites/default/files/NLD%202010-2014%20Covenant%20on%20healthy%20weight.pdf.
6. 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(1):2-27.
7. 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(5):638-54.
8. Nascimento-Ferreira MV, Moraes ACF, Rendo Urteaga T, Oliveira PVT, Moreno LA, Barbosa Carvalho H. Impact of methodological approaches in the agreement between subjective and objective methods for assessing screen time and sedentary behavior in pediatric population: a systematic review. Nutr Hosp. 2019.
9. Paulis WD, van Middelkoop M, Bueving H, Luijsterburg PA, van der Wouden JC, Koes BW. Determinants of (sustained) overweight and complaints in children and adolescents in primary care: the DOERAK cohort study design. BMC Fam Pract. 2012;13:70.
10. van Leeuwen J, van Middelkoop M, Paulis WD, Bueving HJ, Bindels PJE, Koes BW. Overweight and obese children do not consult their general practitioner more often than normal weight children for musculoskeletal complaints during a 2-year follow-up. Arch Dis Child. 2018;103(2):149-54.
11. De Vries SI, Van Hirtum HW, Bakker I, Hopman-Rock M, Hirasing RA, Van Mechelen W. Validity and reproducibility of motion sensors in youth: a systematic update. Med Sci Sports Exerc. 2009;41(4):818-27.
12. Cole TJ, Bellizzi MC, Flegal KM, Dietz WH. Establishing a standard definition for child overweight and obesity worldwide: international survey. Bmj. 2000;320(7244):1240-3.
13. 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(7612):194.
14. Yildirim M, Verloigne M, de Bourdeaudhuij I, Androutsos O, Manios Y, Felso R, et al. Study protocol of physical activity and sedentary behaviour measurement among schoolchildren by accelerometry--cross-sectional survey as part of the ENERGY-project. BMC Public Health. 2011;11:182.
15. Trost SG, Loprinzi PD, Moore R, Pfeiffer KA. Comparison of accelerometer cut points for predicting activity intensity in youth. Med Sci Sports Exerc. 2011;43(7):1360-8.
16. Fleiss J. Statistical Methods for Rates and Proportions. 2nd ed. New York: Wiley; 1981.
17. Riddoch CJ, Mattocks C, Deere K, Saunders J, Kirkby J, Tilling K, et al. Objective measurement of levels and patterns of physical activity. Arch Dis Child. 2007;92(11):963-9.
18. Dyrstad SM, Hansen BH, Holme IM, Anderssen SA. Comparison of self-reported versus accelerometer-measured physical activity. Med Sci Sports Exerc. 2014;46(1):99-106.

19. Ottevaere C, Huybrechts I, De Bourdeaudhuij I, Sjostrom M, Ruiz JR, Ortega FB, et al. Comparison of the IPAQ-A and actigraph in relation to VO2max among European adolescents: the HELENA study. J Sci Med Sport. 2011;14(4):317-24.
20. VeiligheidNL and CBS. Bewegen en Ongevallen: RIVM; 2015 [Available from: https://www.volksgezondheidenzorg.info/onderwerp/sport-en-bewegen/cijfers-context/huidige-situatie#node-beweeggedrag-kinderen.
21. Verloigne M, Van Lippevelde W, Maes L, Yildirim M, Chinapaw M, Manios Y, et al. Levels of physical activity and sedentary time among 10- to 12-year-old boys and girls across 5 European countries using accelerometers: an observational study within the ENERGY-project. Int J Behav Nutr Phys Act. 2012;9:34.
22. Centraal Bureau voor de Statistiek. Bevolking; onderwijsniveau; geslacht, leeftijd en migratieachtergrond: CBS; 2017 [Available from: http://statline.cbs.nl/StatWeb/publication/?VW=T&DM=SLnl&PA=82275NED&LA=nl.

APPENDIX 1 - The number of children meeting the WHO guidelines of 60 minutes MVPA per day.

Day	Weight status	MVPA ≥ 60 minutes	N	%
Monday	Normal-weight	Yes	7	21.2
	(2 missing)	No	26	78.8
	Overweight	Yes	9	45.0
	(2 missing)	No	11	55.0
Tuesday	Normal-weight	Yes	8	25.0
	(3 missing)	No	24	75.0
	Overweight	Yes	8	38.1
	(0 missing)	No	13	61.9
Wednesday	Normal-weight	Yes	10	29.4
	(1 missing)	No	24	70.6
	Overweight	Yes	7	36.8
	(3 missing)	No	12	63.2
Thursday	Normal-weight	Yes	7	20.0
	(0 missing)	No	28	80.0
	Overweight	Yes	6	28.6
	(1 missing)	No	15	71.4
Friday	Normal-weight	Yes	11	31.4
	(0 missing)	No	24	68.6
	Overweight	Yes	5	23.8
	(1 missing)	No	16	76.2
Saturday	Normal-weight	Yes	11	33.3
	(2 missing)	No	22	66.7
	Overweight	Yes	9	42.9
	(1 missing)	No	12	57.1
Sunday	Normal-weight	Yes	9	26.5
	(1 missing)	No	25	73.5
	Overweight	Yes	8	42.1
	(3 missing)	No	11	57.9

Chapter 8

General discussion

Childhood overweight and -obesity are a public health problem and its prevalence has increased worldwide over the past decades (1). Overweight and obesity are defined as abnormal or excessive fat accumulation that presents a risk to health (1). The childhood obesity prevalence has increased from 13.9% in 1999-2000 to 18.5% in 2015-2016, in the United States (2). In the Netherlands, between 1981 and 2015 the obesity prevalence fluctuated between 2.1% and 2.8%. However, the prevalence of overweight in children in the Netherlands increased from 10.1% to 21.1% during this same time period (3).

Children with overweight and obesity have a high risk of developing diseases during childhood and adulthood targeting almost every organ system (4, 5, 6, 7). For instance, it has been shown that for each one-half unit increase in BMI-z score, there is a 50% increase in the risk of metabolic syndrome for children with overweight (4). Furthermore, the relative risk of hypertension in children associated with childhood overweight ranges from 2.5 to 3.7 (4).

Since 2010 there is a Dutch clinical guideline on obesity for general practitioners in the Netherlands, which states that the general practitioner should play a role in signaling and treating obesity (8). To be able to do this, the general practitioner should recognize overweight and obesity in children, and the general practitioner should be able to discuss the weight status of a child during consultation, irrespective of the reason for encounter. Furthermore, giving advice about the treatment of obesity and knowledge on reasons for referral are other important roles of the general practitioner according to the guideline (8).

The first part of this thesis aimed to study the accuracy of self-reported weight and height, since these measures are needed to determine the weight status of a child. In part two, the associations between weight status and bone mineral density, and between weight status and the frequencies of musculoskeletal and respiratory consultations in general practice were studied. Lastly, part three described the effects of a multidisciplinary intervention program on cardiorespiratory fitness and blood pressure, and presented the differences in (in)activity between children with overweight and normal-weight.

In the current chapter, the key findings of this thesis are presented and discussed in comparison to other relevant studies. Finally, recommendations for clinical practice and future research will be addressed.

Key findings

In ***part one*** of this thesis, **Chapter 2,** we showed that in the age group 2–8 years, parents of children with underweight reported a significantly higher weight than the actual measured weight, whereas parents of children with overweight reported a significantly lower weight. In the age group 9–17 years, children with normal-weight- and-overweight reported a significantly lower weight than measured weight. Of all children who were classified as overweight by the GP (N=116), 17% was misclassified as normal-weight and

4% as underweight when self-reported measurements were used. Therefore, it can be concluded that general practitioners cannot fully rely on reported weight and height of parents and children.

In ***part two*** of this thesis the associations between childhood overweight and medical consequences are described. By means of a meta-analysis, moderate and high quality of evidence showed (**Chapter 3**) that children with overweight and -obesity have a significantly higher bone mineral density compared to normal-weight children. In **chapter 4**, using the DOERAK database, we showed that children with overweight consulted the general practice significantly more often during the 2-year follow up compared to normal-weight children (mean 7.3 (5.7) vs 6.7 (5.4), odds ratio (OR) 1.09; 95%CI 1.01-1.18). However, no differences were seen in the number of children with overweight and -normal-weight who consulted the general practice for a musculoskeletal complaint (OR 1.20; 95%CI 0.86 – 1.68). Moreover, no differences between children with normal-weight and children with overweight in the number of musculoskeletal consultations in general and musculoskeletal consultations of the upper- and lower extremities during two-year follow-up were found. In **chapter 5** we studied the association between children's weight status in the age group 2-18 years and respiratory consultations at the general practice. Overall, respiratory consultations were not more prevalent in children with underweight compared to normal-weight children (OR 0.87; 95%CI 0.64-1.10), and in children with overweight compared to normal-weight children (OR 1.33; 95%CI 0.99-1.77). Though, children aged 12-18 years with overweight had significantly more respiratory consultations (mean 1.87 (3.06) vs. 0.93 (1.54), OR 2.14; 95%CI 1.14-4.01), more asthma-like consultations (mean 0.48 (1.50) vs 0.20 (1.00), OR 3.94; 95%CI 1.20-12.88), and more respiratory allergy-related consultations (mean 0.78 (1.68) vs 0.31 (1.05), OR 3.14; 95%CI 1.25-7.86) than normal-weight children aged 12-18 years. However, in children aged 2-6, and 6-12 years old, no associations were found between weight status and respiratory complaints.

Part three of this thesis consists of two chapters that focused on physical activity and the treatment of childhood obesity. In **chapter 6,** we demonstrated that a multidisciplinary intervention program for children with obesity in deprived areas resulted in a significant positive effect on cardiorespiratory fitness, but this effect was diluted one year after the intervention. Diastolic blood pressure percentiles were significantly higher at 52 weeks after intervention (β 0.20; 95%CI 0.08, 0.31). However, systolic blood pressure percentiles did not differ 52 weeks after the intervention, compared to baseline (β 0.08; 95%CI -0.06, 0.22). In **chapter 7**, a subsample (n=65) of the DOERAK database of children aged 4-18 years who wore an ActiGraph for one week was used. We showed that children with overweight spent significantly less time per day in sedentary behavior (β -1.65; 95%CI -3.12, -0.18), more time in light to moderate physical activity (β 1.48; 95%CI 0.07, 2.89), and more time in moderate to vigorous physical activity than normal-weight children (β 0.45; 95%CI 0.02, 0.87). We found no significant difference between the number of normal-weight children and children with overweight meeting the WHO guidelines of 60 minutes of moderate to vigorous physical activity each day. Self-reported values of physical activity did not correlate well with objectively measured values.

Recognizing childhood overweight and obesity

This thesis showed that self-reported weight and height of children is not fully accurate, which is in line with what previous studies have found (9). Children with overweight (and their parents) underestimate their weight, and as a consequence, the general practitioner cannot only rely on self-reported weight and height of children. Therefore, general practitioners should measure the child him- or herself when the child visits the practice, to prevent misclassification of weight status from happening. This is in agreement with the Dutch clinical guideline on obesity, which recommends general practitioners to measure height and weight of each child they believe to be overweight or obese. However, this entails that general practitioners are able to recognize overweight and obesity in children. Unfortunately, research showed that although most general practitioners are able to identify children at the end of the spectrum (i.e. underweight or obese), many are not able to correctly identify the weight status of children who are at the category margins (10). This means that many children who are only slightly overweight and who do not bring up their weight for discussion themselves, will be missed by the general practitioner. This would be a missed opportunity to discuss the weight of the child and consequently give advice about a healthy lifestyle in order to prevent future obesity and morbidity. Besides the fact that general practitioners are not able to recognize all children with overweight, if recognized, general practitioners still find it difficult to start the conversation about weight if this is not the complaint the child consulted the general practitioner for (11). General practitioners seem to be reluctant to engage in weight-related discussions. This is primarily due to expected negative responses from parents, but also to a lack of time (11, 12, 13, 14).

One solution that may overcome the above described issues of not recognizing overweight and not starting the conversation about weight, is to improve the collaboration and communication between the Youth Health Care (JGZ), primary schools and general practices. In the Netherlands, the JGZ screens children on their health and development (15). They physically examine each child regularly from birth up to the age of four, once at the age of five and once at age eleven. During these examinations, children's weight and height are measured. The outcomes of these physical examinations are only issued to parents and not to the general practice of the child. If a child is overweight or obese, the JGZ has a treatment protocol which entails that the JGZ gives advice about a healthy lifestyle and that the JGZ has two follow-up appointments with the child (16). If after these advices, the child is still overweight or obese, the JGZ recommends the parents to contact the general practice regarding the results of the examination. However it is still up to the parent to contact the general practice, and the question arises how often the parents actually contact the general practice in these cases.

If a better collaboration between JGZ and general practice is established, abnormal examination results and progress of children with overweight and obesity during follow-up at the JGZ would be communicated directly with the general practice. This way the general practitioner is aware of the weight problem and he or she can discuss the weight status when the child is coming for a next visit to the general practice. The general practitioner would also be up to date on the actions of the JGZ regarding the weight status, and can evaluate these actions with the child during consultations.

One major limitation of the JGZ screening program is that there are no routine examinations between ages 5-11, while this is a vulnerable period for children to become overweight or obese. It would be ideal if children of these ages were measured annually too so that children who are slightly overweight would be recognized, and general practitioners would be able to observe trends, such as (rapidly) increasing BMI. Especially since children with overweight who do not visit the general practice because they do not experience health problems would otherwise be missed. However, since there are 934.593 children between ages 5-11, implementing this extended screening program seems impossible due to the extra costs and extra workload that would be put both on the JGZ and on general practices (17).

Therefore, other solutions to get a better grip on the group of children in this age-range, in regards to recognizing overweight and obesity, have to be proposed. Formerly, children aged 8 years were also included in the JGZ program for routine examination. Since the Dutch government has recently become more active in fighting childhood obesity (i.e. the National Prevention Agreement), perhaps it is a possibility to re-introduce the measurement of 8 year old children (total of 188.580 children) by the JGZ screening program (17). However, the extra costs of this measurement could be a barrier for implementation. Furthermore, primary schools could play a more pronounced role in recognizing overweight and obesity during a children's life, especially since teachers see children from ages 4-11 almost daily. Not only could they recognize overweight and obesity at an early stage, primary schools also play a role in teaching children about healthy lifestyles. Thus, collaboration between general practice, JGZ and primary schools to recognize and attack childhood overweight and obesity at an early stage is crucial. With this collaboration, childhood overweight would be recognized at an earlier stage and early intervention could be initiated when weight management efforts may be more likely to be successful. All three parties can collectively play a role in trying to prevent childhood obesity progress into adult obesity, and prevent childhood overweight to turn into childhood obesity. However, the willingness of schools to have an additional signaling role should be investigated.

Other important parties in this collaboration are the government and townships. They should initiate this collaboration by bringing all parties together and they should be the leading party and make sure the collaboration is well organized. The government should also take other actions to fight childhood obesity such as promoting healthy foods and physical activity, creating healthy environments, etc.. The role of the government in these actions will be discussed later on in this discussion. Health insurance companies should also get involved in this collaboration, since prevention of childhood obesity is also of interest for them, because in it the end it would lead to lower medical costs.

The above proposed collaboration between all these parties would be very useful to attack childhood obesity, however some barriers are to overcome in order to implement this collaboration. First of all, the government should make clear rules and regulations about this collaboration so that everyone is involved. They should delegate that all townships organize meetings with the local JGZ, general practices and schools to explain and carry out this new collaboration. Moreover, the collaboration between all parties cannot be established without better communication between JGZ, general practices and schools. The development of one electronic medical record in which all information from JGZ and general practice can be safely shared or a way to safely exchange data is an important next step that should be facilitated by the government taking into account legal barriers.

Musculoskeletal complaints

This thesis showed that children with overweight and obesity do not consult the general practitioner more often for musculoskeletal complaints than children of normal-weight. We also showed that there is no association between weight status and musculoskeletal complaints of the lower- or upper extremities in particular. Our findings are not in line with what was expected from previous studies, which showed that childhood overweight and obesity was associated with musculoskeletal complaints, injuries and fractures (18, 19). Our finding, that we found no association between weight status and complaints of the lower extremities, was also unexpected since several studies have found more complaints of the lower extremities in children with overweight than in children of normal-weight (18, 19, 20, 21). Moreover, some of the theories about why children with overweight have more complaints of lower extremities are well substantiated. A few of these proposed theories are 1) obesity changes the biomechanical alignment and function of the joints, 2) being overweight or obese puts a greater load on bones and joints, and 3) changes in gait and balance are common in overweight and obese people (21, 22, 23, 24).

The discrepancy between previous literature and the findings in this thesis could however be due to the fact that previous literature mainly based their findings on questionnaires in open populations, rather than from medical files (18, 20). It could therefore be suggested that the complaints reported in these questionnaires by children with overweight and obesity are only temporarily present and/or not severe, or at least not relevant enough, to consult the general practitioner. Another explanation may be that children with overweight at the age of eight, which was the average age of the children in our cohort, do not experience more musculoskeletal complaints (yet) than normal-weight children. However, when we compared the older children with overweight to older normal-weight children in our cohort, still no differences were found in musculoskeletal consultations. Though, the average age of the children included in the studies that did find an association between being overweight and having musculoskeletal complaints was higher (mean age 10.5-17.8 years) than our cohort (mean 8 years) (18, 20). Perhaps these children have been exposed to excess weight for a longer period of time and therefore experience more musculoskeletal complaints.

We also found no association between weight status and complaints of the upper extremities such as pain or injury of the shoulder or arm. A large study by Adams et al. including 913.178 children aged 2-18, using data from medical files, found similar results as us regarding the association between weight status and complaints of the upper extremities (19). This may be explained by the fact that the joints in the upper extremities are not exposed to the extra load from the excess weight compared to the lower extremities, and therefore are not more prone to injuries than normal-weight children.

One association that has frequently been shown to exist is the association between obesity and osteoarthritis in adults (25). Moreover, it has already been shown that children with morbid obesity show early signs of osteoarthritis (26). The children in our cohort however, were younger than the children in the study by Widhalm et al. (26). It is also known that injury risk in overweight, obese and extremely obese children increases in a linear fashion (19). Moreover, a recent study by Kelly et al. about the association between BMI and primary health care use in childhood showed that children with obesity had significantly higher rates of appointments at the general practice than normal-weight children, while this difference was not found in children with overweight compared to normal-weight children (27). The children in our cohort were not in the range of morbid obesity (only 3% was obese), which may explain why no association was found between overweight and musculoskeletal complaints in our cohort.

Although our study on musculoskeletal complaints in children with overweight and obesity did not find an association between the two, the published literature does give indication that there is an association (18, 19, 20, 21, 22, 23, 24). Based on published literature, general practitioners should be aware of the consequences of childhood obesity, and more importantly, should make their young patients and their parents aware of the potential consequences, even when they are not apparent yet.

Respiratory complaints

Since the prevalence of both asthma and obesity have increased over the past decades, researchers have increasingly investigated the (causal) relationship between these two diseases (28). According to this thesis, children with overweight aged 12-18 years had significantly more respiratory-, asthma-like, and respiratory allergy related consultations than normal-weight peers. In children aged 2-6, and 6-12 years old, no association was found between weight status and respiratory complaints. This may be explained by the suggestion that the relationship between obesity and asthma might be dose-dependent, since the children aged 12-18 years could have been exposed to obesity for a longer period of time (29).

No conclusions could be drawn about the causal relationship between obesity and asthma, since we did not have data starting at birth, and therefore did not know which disease started first. There are, however, other convincing studies showing that childhood obesity increases the risk of asthma (30, 31, 32, 33). Besides the finding that obesity increases the risk of asthma, it has also been found that obesity is associated with worse asthma-related health outcomes (34, 35). A large study in adults showed a 10% increase in asthma prevalence per unit of increase in BMI in men, and a 7% increase in prevalence per unit increase in BMI in women, which strengthens the suggestion that the relationship between obesity and asthma is dose-dependent (29, 35).

A recent review including 21.130 children suggested that the association between asthma and obesity may be inverse, meaning that asthma may lead to obesity (36). The authors showed that children with physician-diagnosed asthma had a 66% higher risk of incident obesity than those without asthma (36). The association between asthma and obesity may be caused by different factors, such as biological and lifestyle factors. Some hypothesized pathways underlying both asthma and obesity are systemic inflammation, adipokine dysregulation and shared genetics (37). The association may also partially be explained by lifestyle factors, i.e. asthmatic children have lower levels of physical activity and less sleep than healthy children, both of which can lead to obesity (38). Furthermore, asthma medication use (inhalation corticosteroid) also increases the risk of obesity (36). However, the association between asthma and obesity cannot be fully explained by medication use only (36).

Regardless of whether asthma causes obesity, or obesity causes asthma, the two often coexist. This has consequences for the treatment of asthma in children with overweight and obesity, since it is known that children with overweight and obesity require increased amounts of B-agonists and higher oral steroid use (39). Therefore, weight reduction in children with overweight and obesity with asthma may improve asthma related symptoms and may improve response to medication. A Cochrane review including a total of 197 adults showed that weight loss may be beneficial for improving asthma control in adults with overweight and obesity. However, all included studies were of high risk of bias (40). Another review found that all 15 included studies showed an improvement of at least one asthma outcome variable after weight loss in adults (41). Though research in children on the effects of weight loss on asthma symptoms is limited, a small randomized controlled trial by Jensen et al. including 28 children showed that weight loss in children with obese improved the static lung function and asthma control (42). Moreover, a recently published cohort study including 507.496 children that compared asthma incidence among children with overweight and obesity found that 10% of clinically diagnosed asthma among all children in the population could be prevented with weight reduction (43).

Even though the evidence is still limited, it does suggest that weight loss leads to improved asthma symptoms and decreased exacerbations in children- and adults with overweight, and can even decrease asthma incidence in children. Therefore, more research should be done to provide stronger evidence on the effectiveness of weight loss on asthma symptoms in children and adults. Though, with this limited evidence, the GP can already discuss weight loss when a child with overweight or obesity with asthma consults him or her, not only to improve asthma, but also for general health reasons. Up to now, no guidelines are available on how to integrate weight loss into asthma treatment. If future research confirms that weight loss is an effective intervention to improve asthma symptoms and reduce the need for asthma medication and may improve the response to medication, weight loss should be implemented as part of the treatment of asthma in asthma guidelines, both for children and adults. By doing so, patients will be treated as a whole and better health outcomes may be reached.

Treatment

Obesity is a complex disease. Some predisposing factors for obesity are genetics, prenatal factors (such as an overweight mother during pregnancy), parent feeding behaviors (i.e. restriction, food prompting and pressuring), increased sedentary behavior, decreased physical activity, increased caloric sweeteners (i.e. sweetened beverages, snacks), decreased child nighttime sleep duration, increased parent BMI, and chronic stress (44, 45, 46, 47). Since obesity is such a complex disease, the Dutch clinical guideline on obesity states that multidisciplinary intervention programs are the first choice of treatment for obesity (8).

The health outcomes of the intervention program Kids4Fit presented in chapter 6 in this thesis showed that during the intervention period beneficial health effects are reached, such as better cardiorespiratory fitness. However, one year after the intervention, the positive effects of the program have diluted. Three Cochrane reviews have investigated the effect of diet, physical activity and behavioral interventions for the treatment of overweight or obesity in children up to 6 years of age, children aged 6 to 12 years and adolescents aged 12 to 17 years (48, 49, 50). These reviews found that multidisciplinary intervention programs may be beneficial for children with overweight and obesity in all age categories, but the evidence is mostly of low quality due to limited confidence on how the studies were performed, inconsistent results between studies, and the low number of included children in some studies (48, 49, 50). Furthermore, long-term follow-up after the interventions was rarely performed, while it is known that maintenance of weight-loss after an intervention is the main challenge. Therefore, it is important to investigate which maintenance interventions are successful for long-term weight loss. A review on maintenance interventions in children with overweight or obesity by van der Heijden et al. showed a favorable effect of maintenance interventions with stable BMI-z scores in the maintenance intervention patients, compared to a slight increase in BMI-z scores in control patients (51). They also showed that 'face-to-face' interventions were more effective than 'on distance' interventions, and that continuous motivation was the strongest predictor for weight maintenance (51). Though, these conclusions should be handled with care, since the studies included in this review had considerable clinical and methodological heterogeneity, with limitations in the quality of the studies such as small sample sizes and risk of bias (51). Another study in children with obesity found a positive effect of motivational interviewing on BMI and on obesity-related behavior outcomes (52). Therefore, to maintain long-term weight loss, booster sessions with face-to-face contact and motivational interviewing should play a role in multidisciplinary intervention programs for children with overweight and obesity. However, since the literature for this group of patients is still scarce and mainly of low quality, further research should focus on the most appropriate forms of post-intervention maintenance in order to ensure intervention benefits are sustained over the longer term.

Since multidisciplinary intervention programs are the preferred non-invasive treatment for obesity, and the obesity prevalence is still rising, the minister of medical care and the state secretary of public health of the Netherlands announced that certified multidisciplinary intervention programs will be included in the basic health insurance package of adults from January 2019 (53). This means that adults with obesity can be referred to intervention programs by the general practice, and the health insurance covers the costs. This decision to include intervention programs for adults with obesity in the basic health insurance package is a step in the right direction to attack the obesity epidemic. However, this policy change only affects obese adults, but should also be introduced for children. Furthermore, since it is known that childhood obesity increases the risk of staying obese in adulthood, and since prevention is better than cure, the focus should be on preventing obesity in children in the first place (1).

Prevention

We live in an obesogenic environment that promotes unhealthy eating habits and unhealthy lifestyle and by doing so, this contributes to the development of overweight and obesity in children and adults. An important point of discussion is who takes responsibility for the increase and treatment of obesity. Is it the individual consumer who decides what lifestyle to adapt, or is it the general practice, the food industry or the government who should take responsibility? In my opinion, since obesity is so complex, many different disciplines need to work together to prevent the obesity epidemic to rise even further and this is not something the general practitioner can solve by him- or herself. I believe the food industry and the government should take further actions to fight the obesity epidemic, just like the concerted actions that are initiated to curb the smoking prevalence especially among adolescents (i.e. increasing the price of cigarettes, making smoking prohibited in most public places, etc.) and alcohol consumption (i.e. increasing the legal drinking age to 18). Recently, in November 2018, the Dutch government and secretary of state presented a ‘National Prevention Agreement’ which focuses on reducing smoking, alcohol consumption and overweight prevalence (54). The three pillars for reducing overweight are: 1) promoting healthy foods, 2) increasing physical activity, and 3) improving a healthy environment and healthcare (54). These pillars will be further discussed and referred to below.

Promoting healthy foods

The food industry is responsible for commercials about sugary beverages, snacks and sweets. In the US, children view 15 television food advertisements per day on average, and 98% of these commercials viewed by children aged 2-11 years promote products high in fat, sugar and/or sodium (55). In these commercials, positive emotions are often evoked by making an association with sports, and by associating food with fun and good times, and being hip or cool (56). Research has shown that there is a direct causal link between food advertising and greater snack consumption and that over-consumption of sugar is a major contributor to obesity (57, 58). Not only commercials, but also the abundance of sugary snacks offered at the cash registry of every supermarket and gas station seduce people to buy unhealthy food. Research showed that by reducing unhealthy food advertisement exposure of children to zero, 14%-33% of children with obesity in the USA might not have been obese (59). The Dutch government is in the position to make rules and regulations about food advertisement, such as putting restrictions on the amount and type of commercials during children’s television programs. Even though the National Prevention Agreement does not make a statement on restrictions on the amount and type of commercials during children’s television programs, it does state that the use of licensed media characters aimed at children under the age of 13 must be limited (54). It also states that during sport events, no food commercials should be aimed at children under the age of 13, unless they are about healthy foods. These new rules seem to be small steps to the right direction to attack childhood obesity, although rules and regulations on TV-advertisement are lagging behind.

Besides the excessive advertising of unhealthy foods, the healthy food choices are often more expensive than the unhealthy foods, making it more expensive for people to eat healthy (60). Moreover, in the Netherlands the price for unhealthy food (ice cream, sugar, candy) have dropped the past year, while the prices of healthy products (milk, eggs, fruit, nuts) have increased (61). The WHO has composed fiscal policies for diet and the prevention of non-communicable diseases and it proposes that "as appropriate to national context, countries consider the use of economic tools that are justified by evidence, and may include taxes and subsidies, to improve access to healthy dietary choices and create incentives for behaviors associated with improved health outcomes and discourage the consumption of less healthy options" (62). It has been shown that putting a tax on sugary drinks that increases prices by 20% can lead to a reduction in consumption by 20%, thus preventing obesity (63). Furthermore, in the UK, the USA and New Zealand, fruits and vegetable subsidies that reduces prices by 10-30% are effective in increasing fruit and vegetable consumption (62, 64). It seems logical to think that these measures would also be effective in The Netherlands. However, rather than providing subsidies on fruit and vegetables, the cabinet decided to increase the tax rate on these products from 6% to 9% in 2019 (65). On the other hand, much attention in the National Prevention Agreement has been given to promote healthy diets. It states that, among other things, consumers must be tempted to buy healthy foods, employers in supermarkets will be educated on healthy eating to better advice their customers who have questions regarding healthy foods, and sports clubs and hospitals must provide healthier foods (54). However, based on what has been shown in previous research, it may have been more effective if the government introduced tax on sugary drinks and other products high in fat and sugar, and subsidies on fruits and vegetables (62, 63, 64).

Besides the role of the government, other parties should take part in promoting healthy foods as well. First off, schools are in a great position to teach children about healthy foods and drinks. An example of schools where this is already successfully carried out are the 'Lekker Fit' schools in Rotterdam (66). At these schools a healthy lifestyle is promoted by, for instance, having children engage in physical activity three set times during the school day, and by stimulating the children to eat healthy treats and to drink water (66). General practices are also in the position to give advices about healthy foods to children and parents. Physician assistants working in general practices can educate children with overweight and their parents on healthy foods. Another possibility is to include a dietician in the general practice who is easily accessible for children with overweight or obesity and their parents. This would especially be beneficial in areas where obesity is more prevalent. Furthermore, multidisciplinary intervention programs to treat childhood obesity, such as Kids4Fit which was discussed in chapter 6 of this thesis, should involve a dietician to educate children and their parents about a healthy diet.

Physical activity

The second pillar in the National Prevention Agreement is the increase of physical activity. Besides the changes in the food industry over the past years, there has also been a change in the lifestyle of people. Children (and adults) are more sedentary, screen time has increased and time spent on physical activity has decreased (67, 68). Research conducted in 2007-2012, showed that children spent on average about 2,2-2,5 hours per day on screen time (67, 69, 70, 71). Of children aged 4-11 years, 55.5%, and only 31% of children aged 12-17 years, meet the guideline of 60 minutes of moderate to vigorous physical activity (MVPA) per day (72). In line with that, Chapter 7 of this thesis investigated the physical activity behavior in children with normal-weight and-overweight and studied if children met the WHO guidelines of 60 minutes of MVPA per day (1). The findings of that study showed that there is no difference in level of physical activity between children with normal-weight and children with overweight, and of the normal-weight children, only 20% - 33% met the MVPA guidelines and for children with overweight this ranged from 24% - 45%. Because of the increased inactivity in children, children are not developing motor coordination, or motor competence. It is known that motor competence is positively associated with physical activity, cardiorespiratory endurance, and perceived motor competence, while it is inversely correlated with weight status (73, 74, 75). Furthermore, motor competence is an important predictor for physical activity in childhood and adolescence, and it is a step toward lifelong commitment to physical activity (76). Since motor competence is inversely associated with weight status and positively associated with health related fitness and a lifelong commitment to physical activity, it is important that children at a young age are already put in the position to develop these movement skills (74).

Both screen time and physical (in)activity are modifiable behaviors that may be tackled in childhood obesity prevention efforts. Similar as with promoting healthy foods, increasing physical activity and teaching about the importance of physical activity can also be carried out by many different parties, such as schools, general practices and the JGZ. These different parties should be adequately informed about the importance of physical activity at a young age, so that they can better educate parents and children about this. Educating parents and children about the importance of physical activity would then hopefully lead to better involvement in physical activity. A great example of where physical activity is integrated in daily school life is Finland. After every 45 minutes of class time, children get 15 minutes of playtime outside (77). In comparison to other European countries the Finnish children spend the least time in class, and have the least amount of homework, and they still are at the top of the Programme for International Student Assessment (PISA) list each year (77, 78). Therefore, primary schools in the Netherlands should spend more time on physical activity as well. In The Netherlands, there is a guideline on movement education for primary schools (79). Even though there is no lawful norm on the amount of time that has to be spent on movement education by schools, the guideline does state that children in primary schools are advised to get 2 x 45 minutes of movement education per week (79). The previous cabinet in the Netherlands even stated that there should be at least 3 hours per week of movement education in primary schools. However, according to a recent report (2017) by the Mulier Institute for sport research, children in primary schools are only physically active for 89 minutes per week (80). Thus, to increase levels of physical activity, to improve motor competence, and to improve weight status, primary schools should be imposed to meet the requirement of (at least) 3 hours of physical activity per week. The National Prevention Agreement makes a few statements on how to increase levels of physical activity in children and adults: 1) sport providers will be locally supported to offer sports which are more suitable for inactive children and adults, and to make sure that attending these sports leads to structural physical activity; 2) it will be stimulated to bike to school and work; 3) extra attention will be given on how to improve the development of motor skills in children and extra attention will be given to children with motor development problems (54). If these three measures are executed, the levels of physical activity throughout the Dutch population will hopefully increase.

Role of parents in stimulating physical activity

Parents are essential in determining the amount of screen time and physical activity of their children. Parents are the ones that can put restrictions on the amount of time children spend on their tablet, phones, and watching television. Moreover, reducing parents' own screen time can lead to a decreased child screen time (81). It has also been found that children whose parents encourage and support their child's physical activity are more likely to have higher levels of physical activity. Also parents' physical activity was positively associated with children's' levels of physical activity (81). This highlights the importance of involving parents in multidisciplinary intervention programs, as has been done in the Kids4Fit intervention (Chapter 6). Educating (future) parents in the role they play in their children's activity life as stated above should be emphasized during interventions. The JGZ and the general practices can also play a role in giving information to parents about physical activity during consultations of children with overweight or obesity.

Improving healthy environment

Lastly, pillar three of the National Prevention Agreement is about creating healthy schools, and a healthy environment and healthcare (54). It states that in 2020, 25% of all schools should be a 'healthy school', which entails extra education on obesity, having a healthy environment, healthy food choices etc. They also state that schools should have a healthy playground at school, and that children daycares should have a pedagogical professional who is trained in nutrition, physical activity, playtime outside and socio-emotional development of children. Healthy townships and districts are also promoted in the National Prevention Agreement, especially since the environment has a strong influence on the behavior and health of children and adults (54). It has been shown that low levels of green space, no access to a garden and no access to a run-down area are associated with childhood overweight and obesity (82). Furthermore, poor neighborhood conditions increased the probability of overweight or obesity significantly (82). Therefore, improving these conditions are crucial in the fight of obesity and the government should play a central role in this.

I believe that all the actions described in the National Prevention Agreement on promoting healthy food, increasing physical activity, and improving healthy schools and a healthy environment would lead to a more healthy lifestyle of parents and children now, and in the future and would lead to a decrease of the obesity prevalence. (54). However, many different parties are involved in taking these actions which makes it very complex. Moreover, implementing all these actions throughout the country will cost a lot of money and will take a lot of time. Therefore, whether the National Prevention Agreement will indeed deliver positive results on lifestyle changes is still to be expected.

Implications for the general practice

The role for the general practitioner in the signaling and treatment of obesity has been stated in the clinical guideline on obesity, but is now mainly demand-driven. This makes it hard since there are only 4.6, 2.9 and 2.7 consultation per year at the general practitioner for children aged 0-4, 4-12, and 12-16 years respectively (83, 84). Only this small amount of children who visit the general practice for any type of complaint are exposed to the possibility that the general practitioner brings up their weight (8). Moreover, it is even questionable how many general practitioners bring up weight problems during consultations, since it has been shown that only 53.8% of the general practitioners agreed that they should discuss weight, even if the obese patient has another reason for the consultation (14). It has also been found that weight problems were less frequently discussed by younger general practitioners (14). Therefore, (future) general practitioners should be educated on different communication techniques and ways to start the conversation about weight.

With the previously mentioned collaboration between general practices, JGZ and schools, general practices would be better aware of which children in their practice are overweight or obese which would make it easier to reach out to these children and discuss their weight status during consultations. General practices can, together with the JGZ and schools, discuss topics like diet, screen-time, and physical activity, which are all mentioned in the obesity guideline. General practices can also refer to a dietician to help the child and parent with a healthy diet, or they can include a dietician in their general practice to make it easier to access.

If a child already has an obese weight status, the general practice can refer to a multidisciplinary intervention program such as Kids4Fit. It is important for general practices to be aware of the available intervention programs in their area, so it is easier to refer the children with obesity. The general practitioner or physician assistant should stay in contact with the children with obesity and their parents during the intervention to check the progress every 3 months, as stated in the obesity guideline (8). It would also be recommended to follow-up the child after the intervention, so that children do not regain their weight.

Lastly, from this thesis we know that children with overweight and obesity consult the general practice more often in general and more for respiratory symptoms. From other literature we know that obesity is associated with comorbidities in every organ system. Therefore, if a child with overweight or obesity consults the general practice, the general practitioner should approach the child as a whole, rather than just the one complaint, and make both the child and parents aware of the different health consequences associated with overweight and obesity.

It is, however, important to keep in mind that the general practitioner cannot stop the childhood obesity epidemic in their consultations rooms (85). Schools, families, and especially the government should take their combined responsibilities in fighting the obesity epidemic. All disciplines should work together to aim for the best results.

Future research

There are some important suggestions for future research as a results of the studies presented in this thesis. To begin with it would be interesting to investigate the barriers and facilitators of a collaboration between the JGZ, schools and general practices. Hereafter, a pilot study could research the effects of such a collaboration on overweight and obesity prevalence. If this collaboration proves to be successful, it should be implemented throughout the country.

Furthermore, more research should be done to investigate how to improve the role of the general practice in the obesity epidemic, especially since the majority (83%) of the general practitioners in the Netherlands agreed that weight management of their patients is part of their responsibility (14). Wageningen University has performed a pilot study on a minimal intervention strategy (MIS) to treat adults with overweight and obesity in the general practice (86). It is a hands-on method, with flowcharts describing different steps in the treatment process, which helps the general practitioner to find out if the patient is motivated, and it helps the general practitioner to set up a treatment plan and to evaluate the progress (86). Both the general practitioners and the patients who worked with the MIS were enthusiastic about the method. It would be interesting to perform a similar pilot study on a MIS for the treatment of children with overweight or obesity. The MIS could also involve the role of a physician assistant and of a dietician in the general practice, so that there is a multidisciplinary approach.

To get a better understanding of the effects of childhood overweight or obesity on physical (and mental) complaints in general practice, general practitioners should be more consequent in reporting weight status in the medical files. By improving this reporting, future research can better investigate the effects of overweight and obesity, but also of weight loss, on different health outcomes such as musculoskeletal complaints in children with overweight and obesity of all ages. Furthermore, more research should be done to investigate the effects of weight loss on asthma, in order to optimize the treatment for children with overweight and obesity with asthma. If weight loss in children with overweight and obesity proves to be effective in reducing asthma symptoms, weight loss strategies can be added to the clinical guideline on asthma in children.

The long-term effects of multidisciplinary intervention programs on the health outcomes of children should be further investigated, since as of today, mainly the short term effects are studied. It is however, interesting and important to know what happens with the health outcomes after the intervention is completed. Furthermore, it would be helpful to investigate which measures (i.e. booster sessions) would be effective to maintain the health effects of intervention programs for children with overweight and obesity after the intervention has finished.

Lastly, it will be very important to see what the effects of the National Prevention Agreement will be throughout the next few years on the incidence and severity of overweight and obesity rates in the Netherlands. It does seem like a good start has been made, although I wonder whether the plans are effective enough.

REFERENCES

1. World Health Organization. Childhood overweight and obesity: WHO; 2017 [cited 2017 26-10-2017]. Available from: http://www.who.int/dietphysicalactivity/childhood/en/.
2. 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.
3. Volksgezondheidenzorg.info. Overgewicht kinderen - trends: RIVM; [cited 2018]. Available from: https://www.volksgezondheidenzorg.info/onderwerp/overgewicht/cijfers-context/trends#node-trend-overgewicht-kinderen .
4. Daniels SR. Complications of obesity in children and adolescents. *Int J Obes (Lond)* 2009;**33 Suppl 1:** S60-65.
5. 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.
6. Dietz WH. Health consequences of obesity in youth: childhood predictors of adult disease. *Pediatrics* 1998;**101:** 518-525.
7. Wallace WJ, Sheslow D, Hassink S. Obesity in children: a risk for depression. *Ann N Y Acad Sci* 1993;**699:** 301-303.
8. 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.
9. 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.
10. Gage H, Erdal E, Saigal P, Qiao Y, Williams P, Raats MM. Recognition and management of overweight and obese children: a questionnaire survey of general practitioners and parents in England. *J Paediatr Child Health* 2012;**48:** 146-152.
11. Dettori H, Elliott H, Horn J, Leong G. Barriers to the management of obesity in children- A cross sectional survey of GPs. *Aust Fam Physician* 2009;**38:** 460-464.
12. Banks J, Shield JP, Sharp D. Barriers engaging families and GPs in childhood weight management strategies. *Br J Gen Pract* 2011;**61:** e492-497.
13. Larsen LM, Ledderer L, Jarbol DE. Management of Overweight during Childhood: A Focus Group Study on Health Professionals' Experiences in General Practice. *Int J Family Med* 2015;**2015:** 248985.
14. Kloek CJ, Tol J, Veenhof C, van der Wulp I, Swinkels IC. Dutch General Practitioners' weight management policy for overweight and obese patients. *BMC Obes* 2014;**1:** 2.
15. Nederlands Centrum Jeugdgezondheid. Richtlijn: Overgewicht. Meten van gewicht en lengte. 2012 [cited 2018 23-10-2018]. Available from: https://www.ncj.nl/richtlijnen/alle-richtlijnen/richtlijn/?richtlijn=10&rlpag=689.
16. Kist-van Holthe JEB, M.; Bulk-Bunschoten, A.M.W.; L'Hoir, M.; Kuijpers, T.; Pijpers, F.; Renders, C.M.; Timmermans-Leenders, E.P.; Blok, D-I.J.; van de Veer, M.; HiraSing, R.A.. Overgewicht. Preventie, signalering, interventie en verwijzing. Nederlands Centrum Jeugdgezondheid: Utrecht, 2012.
17. Centraal Bureau voor de Statistiek. Bevolking; geslacht, leeftijd en burgerlijke staat, 1 januari 2018 [cited 2019]. Available from: https://statline.cbs.nl/StatWeb/publication/?VW=T&DM=SLNL&PA=7461BEV&D1=0&D2=a&D3=1-27,101-105,121-123,131&D4=l&HD=110621-1139&HDR=T,G3,G1&STB=G2.
18. 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.
19. 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.

20. Deere KC, Clinch J, Holliday K, McBeth J, Crawley EM, Sayers A*, et al.* Obesity is a risk factor for musculoskeletal pain in adolescents: findings from a population-based cohort. *Pain* 2012;**153:** 1932-1938.
21. Mesquita PR, Neri SGR, Lima RM, Carpes FP, de David AC. Childhood obesity is associated with altered plantar pressure distribution during running. *Gait Posture* 2018;**62:** 202-205.
22. Lerner ZF, Board WJ, Browning RC. Pediatric obesity and walking duration increase medial tibiofemoral compartment contact forces. *J Orthop Res* 2016;**34:** 97-105.
23. Shultz SP, D'Hondt E, Fink PW, Lenoir M, Hills AP. The effects of pediatric obesity on dynamic joint malalignment during gait. *Clin Biomech (Bristol, Avon)* 2014;**29:** 835-838.
24. Chan G, Chen CT. Musculoskeletal effects of obesity. *Curr Opin Pediatr* 2009;**21:** 65-70.
25. Blagojevic M, Jinks C, Jeffery A, Jordan KP. Risk factors for onset of osteoarthritis of the knee in older adults: a systematic review and meta-analysis. *Osteoarthritis Cartilage* 2010;**18:** 24-33.
26. Widhalm HK, Seemann R, Hamboeck M, Mittlboeck M, Neuhold A, Friedrich K*, et al.* Osteoarthritis in morbidly obese children and adolescents, an age-matched controlled study. *Knee Surg Sports Traumatol Arthrosc* 2016;**24:** 644-652.
27. Kelly B, West J, Yang TC, Mason D, Hasan T, Wright J. The association between body mass index, primary healthcare use and morbidity in early childhood: findings from the Born In Bradford cohort study. *Public Health* 2019;**167:** 21-27.
28. Eder W, Ege MJ, von Mutius E. The asthma epidemic. *N Engl J Med* 2006;**355:** 2226-2235.
29. Beuther DA. Recent insight into obesity and asthma. *Curr Opin Pulm Med* 2010;**16:** 64-70.
30. Chen YC, Liou TH, Chen PC, Chiang BL, Yang YH, Fan HY*, et al.* Growth trajectories and asthma/rhinitis in children: a longitudinal study in Taiwan. *Eur Respir J* 2017;**49**.
31. Gilliland FD, Berhane K, Islam T, McConnell R, Gauderman WJ, Gilliland SS*, et al.* Obesity and the risk of newly diagnosed asthma in school-age children. *Am J Epidemiol* 2003;**158:** 406-415.
32. Gold DR, Damokosh AI, Dockery DW, Berkey CS. Body-mass index as a predictor of incident asthma in a prospective cohort of children. *Pediatr Pulmonol* 2003;**36:** 514-521.
33. Rzehak P, Wijga AH, Keil T, Eller E, Bindslev-Jensen C, Smit HA*, et al.* Body mass index trajectory classes and incident asthma in childhood: results from 8 European Birth Cohorts--a Global Allergy and Asthma European Network initiative. *J Allergy Clin Immunol* 2013;**131:** 1528-1536.
34. Manion AB. Asthma and obesity: the dose effect. *Nurs Clin North Am* 2013;**48:** 151-158.
35. Hjellvik V, Tverdal A, Furu K. Body mass index as predictor for asthma: a cohort study of 118,723 males and females. *Eur Respir J* 2010;**35:** 1235-1242.
36. Contreras ZA, Chen Z, Roumeliotaki T, Annesi-Maesano I, Baiz N, von Berg A*, et al.* Does early-onset asthma increase childhood obesity risk? A pooled analysis of 16 European cohorts. *Eur Respir J* 2018.
37. Litonjua AA, Gold DR. Asthma and obesity: common early-life influences in the inception of disease. *J Allergy Clin Immunol* 2008;**121:** 1075-1084; quiz 1085-1076.
38. Ford ES. The epidemiology of obesity and asthma. *J Allergy Clin Immunol* 2005;**115:** 897-909; quiz 910.
39. Quinto KB, Zuraw BL, Poon KY, Chen W, Schatz M, Christiansen SC. The association of obesity and asthma severity and control in children. *J Allergy Clin Immunol* 2011;**128:** 964-969.
40. Adeniyi FB, Young T. Weight loss interventions for chronic asthma. *Cochrane Database Syst Rev* 2012**:** CD009339.
41. Eneli IU, Skybo T, Camargo CA, Jr. Weight loss and asthma: a systematic review. *Thorax* 2008;**63:** 671-676.
42. Jensen ME, Gibson PG, Collins CE, Hilton JM, Wood LG. Diet-induced weight loss in obese children with asthma: a randomized controlled trial. *Clin Exp Allergy* 2013;**43:** 775-784.
43. Lang JE, Bunnell HT, Hossain MJ, Wysocki T, Lima JJ, Finkel TH*, et al.* Being Overweight or Obese and the Development of Asthma. *Pediatrics* 2018;**142**.

44. Vos MB, Welsh J. Childhood obesity: update on predisposing factors and prevention strategies. *Curr Gastroenterol Rep* 2010;**12:** 280-287.
45. Dev DA, McBride BA, Fiese BH, Jones BL, Cho H, Behalf Of The Strong Kids Research T. Risk factors for overweight/obesity in preschool children: an ecological approach. *Child Obes* 2013;**9:** 399-408.
46. Magee C, Caputi P, Iverson D. Lack of sleep could increase obesity in children and too much television could be partly to blame. *Acta Paediatr* 2014;**103:** e27-31.
47. Wilson SM, Sato AF. Stress and paediatric obesity: what we know and where to go. *Stress Health* 2014;**30:** 91-102.
48. Al-Khudairy L, Loveman E, Colquitt JL, Mead E, Johnson RE, Fraser H*, et al.* Diet, physical activity and behavioural interventions for the treatment of overweight or obese adolescents aged 12 to 17 years. *Cochrane Database Syst Rev* 2017;**6:** CD012691.
49. Colquitt JL, Loveman E, O'Malley C, Azevedo LB, Mead E, Al-Khudairy L*, et al.* Diet, physical activity, and behavioural interventions for the treatment of overweight or obesity in preschool children up to the age of 6 years. *Cochrane Database Syst Rev* 2016;**3:** CD012105.
50. Mead E, Brown T, Rees K, Azevedo LB, Whittaker V, Jones D*, et al.* Diet, physical activity and behavioural interventions for the treatment of overweight or obese children from the age of 6 to 11 years. *Cochrane Database Syst Rev* 2017;**6:** CD012651.
51. van der Heijden LB, Feskens EJM, Janse AJ. Maintenance interventions for overweight or obesity in children: a systematic review and meta-analysis. *Obes Rev* 2018;**19:** 798-809.
52. Borrello M, Pietrabissa G, Ceccarini M, Manzoni GM, Castelnuovo G. Motivational Interviewing in Childhood Obesity Treatment. *Front Psychol* 2015;**6:** 1732.
53. Schaars D. Gecombineerde Leefstijl Interventies (GLI) in de basiszorgverzekering. *Alles over Sport*, 2018.
54. RIVM. Nationaal Preventieakkoord, naar een Gezonder Nederland. 2018, pp 34-50.
55. Powell LM, Szczypka G, Chaloupka FJ, Braunschweig CL. Nutritional content of television food advertisements seen by children and adolescents in the United States. *Pediatrics* 2007;**120:** 576-583.
56. Folta SC, Goldberg JP, Economos C, Bell R, Meltzer R. Food advertising targeted at school-age children: a content analysis. *J Nutr Educ Behav* 2006;**38:** 244-248.
57. Harris JL, Bargh JA, Brownell KD. Priming effects of television food advertising on eating behavior. *Health Psychol* 2009;**28:** 404-413.
58. World Health Organization. Taxes on sugary drinks: Why do it? : World Health Organization; 2017 [cited 2018 06-11-2018]. Available from: http://apps.who.int/iris/bitstream/handle/10665/260253/WHO-NMH-PND-16.5Rev.1-eng.pdf;jsessionid=60ACAA64D35685218AB08DC0DC329856?sequence=1.
59. Veerman JL, Van Beeck EF, Barendregt JJ, Mackenbach JP. By how much would limiting TV food advertising reduce childhood obesity? *Eur J Public Health* 2009;**19:** 365-369.
60. Rao M, Afshin A, Singh G, Mozaffarian D. Do healthier foods and diet patterns cost more than less healthy options? A systematic review and meta-analysis. *BMJ Open* 2013;**3:** e004277.
61. NOS. Ongezond eten opnieuw goedkoper, gezond weer duurder: NOS; 2018 [cited 2018 06-11-2018]. Available from: https://nos.nl/artikel/2212497-ongezond-eten-opnieuw-goedkoper-gezond-weer-duurder.html.
62. World Health Organization. Fiscal policies for diet and the prevention of noncommunicable diseases: World Health Organization; 2015 [cited 2018 06-11-2018]. Available from: http://apps.who.int/iris/bitstream/handle/10665/250131/9789241511247-eng.pdf?sequence=1.
63. Powell LM, Chriqui JF, Khan T, Wada R, Chaloupka FJ. Assessing the potential effectiveness of food and beverage taxes and subsidies for improving public health: a systematic review of prices, demand and body weight outcomes. *Obes Rev* 2013;**14:** 110-128.

64. Thow AM, Downs S, Jan S. A systematic review of the effectiveness of food taxes and subsidies to improve diets: understanding the recent evidence. *Nutr Rev* 2014;**72:** 551-565.
65. Winterman P. Kabinet houdt vast aan hogere btw op groente en fruit. *Algemeen Dagblad*, 2018.
66. Lekker Fit. Lekker Fit: Gemeente Rotterdam; 2016 [cited 2019]. Available from: http://www.rotterdam-lekkerfit.nl/.
67. Rideout V FU, Roberts D. Generation M2: Media in the Lives of 8- to 18-Year-Olds. The Henry J. Kaiser Family Foundation: Menlo Park, CA, 2010.
68. Committee on Physical Activity and Physical Education in the School Environment; Food and Nutrition Board; Institute of Medicine; Kohl HW III CH, editors. *Educating the Student Body: Taking Physical Activity and Physical Education to School.* . National Academies Press (US): Washington (DC), 2013.
69. Bornhorst C, Wijnhoven TM, Kunesova M, Yngve A, Rito AI, Lissner L*, et al.* WHO European Childhood Obesity Surveillance Initiative: associations between sleep duration, screen time and food consumption frequencies. *BMC Public Health* 2015;**15:** 442.
70. nu.nl. Kinderen besteden meer tijd aan smartphone dan aan buiten spelen. *NU.nl*, 2018.
71. Ahluwalia N, Frenk SM, Quan SF. Screen time behaviours and caffeine intake in US children: findings from the cross-sectional National Health and Nutrition Examination Survey (NHANES). *BMJ Paediatr Open* 2018;**2:** e000258.
72. Rijksinstituut voor Volksgezondheid en Milieu. Bewegen: RIVM; 2018 [cited 2018 06-11-2018]. Available from: https://www.rivm.nl/Onderwerpen/L/Leefstijlmonitor/Cijfers/Bewegen.
73. Lopes VP, Stodden DF, Bianchi MM, Maia JA, Rodrigues LP. Correlation between BMI and motor coordination in children. *J Sci Med Sport* 2012;**15:** 38-43.
74. Hardy LL, Barnett L, Espinel P, Okely AD. Thirteen-year trends in child and adolescent fundamental movement skills: 1997-2010. *Med Sci Sports Exerc* 2013;**45:** 1965-1970.
75. Luz C, Rodrigues LP, Meester A, Cordovil R. The relationship between motor competence and health-related fitness in children and adolescents. *PLoS One* 2017;**12:** e0179993.
76. Barnett LM, van Beurden E, Morgan PJ, Brooks LO, Beard JR. Childhood motor skill proficiency as a predictor of adolescent physical activity. *J Adolesc Health* 2009;**44:** 252-259.
77. Oude Avenhuis E. Finland: onderwijsparadijs waar bewegen op school centraal staat: Alles over sport; 2017 [updated 28-06-2017; cited 2018 07-11-2018]. Available from: https://www.allesoversport.nl/artikel/finland-onderwijsparadijs-waar-bewegen-op-school-centraal-staat/.
78. Organization for Economic Cooperation and Development. Programme for International Student Assessment: OECD; 2018 [cited 2018 07-11-2018]. Available from: http://www.oecd.org/pisa/data/.
79. Koninklijke Vereniging voor Lichamelijke Opvoeding. Wettelijke richtlijnen voor bewegingsonderwijs van basisschool tot mbo: Alles over Sport; 2016 [updated 28-03-2018; cited 2018 24-10-2018]. Available from: https://www.allesoversport.nl/artikel/wettelijke-richtlijnen-voor-bewegingsonderwijs-van-basisschool-tot-mbo/.
80. Keultjes H. Minimaal drie uur gymles? Bijna geen school die het haalt. *Algemeen Dagblad*, 2017.
81. Xu H, Wen LM, Rissel C. Associations of parental influences with physical activity and screen time among young children: a systematic review. *J Obes* 2015;**2015:** 546925.
82. Schalkwijk AAH, van der Zwaard BC, Nijpels G, Elders PJM, Platt L. The impact of greenspace and condition of the neighbourhood on child overweight. *Eur J Public Health* 2018;**28:** 88-94.
83. O'Donnell JE, Foskett-Tharby R, Gill PS. General practice views of managing childhood obesity in primary care: a qualitative analysis. *JRSM Open* 2017;**8:** 2054270417693966.
84. Centraal Bureau voor de Statistiek. Gezondheid en zorggebruik; persoonskenmerken 2018 [updated 16-03-2018; cited 2019 07-01-2019]. Available from: http://statline.cbs.nl/Statweb/publication/?DM=SLNL&PA=83005ned&D1=61-89&D2=0-13&D3=0&D4=l&VW=T.

85. Bindels P. Huisartsenzorg heeft grensen. *Ned Tijdschr Geneeskd* 2017;**161:** D2416.

86. Fransen GAJ, Hiddink, G.J., Koelen, M.A., van Dis, S.J., Drenthen, A.J.M., van Binsbergen, J.J., van Woerkum , J.M.J. Minimale interventie strategie voor Volwassenen met Overgewicht en Obesitas. Wageningen University, 2008.

Chapter 9

Summary

SUMMARY

The aim of this thesis was to describe: 1) the accuracy of self-reported weight and height of children at the general practitioner; 2) the associations between childhood weight status and its medical consequences such as the frequency of musculoskeletal and respiratory consultations at the general practitioner; 3) the effect of a multidisciplinary intervention program for children with obesity on different health outcomes; 4) the physical activity behavior of normal-weight children and children with overweight.

PART I:

In **chapter 2**, the aim was to investigate the differences between self-reported weight and -height, and measured weight and-height for children with underweight,-normal-weight and-overweight in a general practice setting. Data from the DOERAK database was used to investigate these differences. The DOERAK database was set up to investigate potential differences between normal-weight children and children with overweight in general practice and consisted of 733 children aged 2-18 years. Means of reported and measured weight and height were compared using the paired T-test. Of the 715 included children, 17.5% were defined as underweight, 63.2% as normal-weight and 19.3% as overweight according to measured weight and height. In the age group 2-8 years, parents of children with underweight reported a significantly higher weight than measured weight (mean difference (MD) 0.32kg; 95%CI 0.02, 0.62), while parents of children with overweight reported a significantly lower weight (MD -1.08kg; 95%CI -1.77, -0.39). In the age group 9-17 years, normal-weight children (MD -0.51kg; 95%CI -0.79 ,-0.23) and children with overweight (MD -1.28kg; 95%CI -2.08, -0.47) reported a significantly lower weight than measured weight. Therefore, general practitioners cannot rely on self-reported weight and height measures from children and their parents, and should measure children themselves to prevent any misclassification of weight status from happening.

PART II:

The review in **chapter 3** examined the differences in bone mineral density (BMD) between children of normal-weight and children with overweight or obesity. Medline (OVID), Embase, Cochrane, Web of Science (WoS), Cinahl ebsco, Pubmed publisher and Google scholar were systematically reviewed for articles providing data on differences in BMD between children with normal-weight and-overweight and/or children with normal-weight and-obesity. Twenty-seven studies, with a total of 5958 children, were included.

There was moderate and high quality of evidence that children with overweight (MD 213 grams; 95%CI 166, 261) and children with obesity (MD 329 grams; 95%CI 229, 430) have a significantly higher whole body bone mineral content than normal-weight children. Similar results were found for whole body bone mineral density. Sensitivity analysis showed the association was stronger in girls. In conclusion, children with overweight and -obesity have a higher BMD than normal-weight children, however since only one study with a longitudinal design was included in this review, the long-term impact of childhood overweight and obesity on bone health at adulthood remains unclear.

Chapter 4 studied the association between weight status and the frequency and type of musculoskeletal consultations at the general practice during a two-year follow up. Similar to chapter 2, data from the DOERAK database were used. Poisson regression and logistic regression analyses were applied to test whether weight status was associated with the presence, the frequency and type of musculoskeletal consultations at the general practice. Multivariable analysis was used to test for different predictors for musculoskeletal consultations during the two-year follow up. Children with overweight consulted the general practitioner in general significantly more frequent during the 2-year follow up than normal-weight children (mean 7.3 (5.7) vs 6.7 (5.4), odds ratio (OR) 1.09; 95%CI 1.01-1.18). No significant difference was seen in the number of normal-weight children compared to children with overweight consulting their general practitioner for musculoskeletal complaints (OR 1.20; 95%CI 0.86 – 1.68). Additionally, no significant difference between normal-weight children and children with overweight was seen for the number of consultations for further specified musculoskeletal disorders. Thus, children with overweight do consult the general practitioner more often than normal-weight children, but not for musculoskeletal complaints.

In **chapter 5** the associations between weight status and the frequency and type of respiratory consultations were investigated. Data from the DOERAK database was used. Logistic regression analyses and negative binominal regression analyses were applied to test the associations between weight status and the presence, the frequency and the type of respiratory consultations during a two year follow-up. Respiratory consultations were not more prevalent in children aged 2-18 years with underweight compared to normal-weight children aged 2-18 (OR 0.87; 95%CI 0.64-1.10). Respiratory consultations were also not more prevalent in children aged 2-18 years with overweight compared to normal-weight children (OR 1.33; 95%CI 0.99-1.77). Though, children with overweight aged 12-18 years had significantly more respiratory consultations at the general practice than normal-weight children aged 12-18 years (OR 2.14; 95%CI 1.14-4.01). Children with overweight aged 12-18 year also had more asthma-like consultations (OR 3.94; 95%CI 1.20-12.88), and more respiratory allergy related consultations (OR 3.14; 95%CI 1.25-7.86) than normal-weight children aged 12-18 years. In younger children, no associations were found between weight status and respiratory consultations. Thus, children with overweight aged 12-18 years consult the general practitioner more often for respiratory consultations, asthma-like consultations and respiratory allergy related consultation than their normal-weight peers.

PART III:

In **chapter 6**, a study is presented that aimed to investigate the effects of a multidisciplinary intervention program, for children with obesity in socially deprived areas, on blood pressure and cardiorespiratory fitness.

Children with obesity who signed-up for the 12-week intervention program 'Kids4Fit' were eligible to participate in this study. After signing-up for Kids4Fit, children were placed on a waiting list, which was used as a control period, until there was a group of 8-12 children signed-up to start the intervention. Cardiorespiratory fitness was assessed by using the shuttle-run-test (SRT). Blood pressure measurements and SRT were performed at baseline, at the start of the intervention, at the end of intervention and at 52 weeks after the start of the intervention. The effect of Kids4Fit on blood pressure and on SRT scores were analyzed using mixed models and effectplots. A total of 154 children were included with a mean age of 8.5 years (standard deviation 1.8). Effect plots showed an initial significant increase of the SRT-scores but this effect diluted after the intervention. No significant change was seen in systolic blood pressure percentiles at 52 weeks after start of the Kids4Fit intervention (β 0.08; 95%CI -0.06, 0.22). Diastolic blood pressure percentiles increased significantly over time (β 0.20; 95%CI 0.08, 0.31). Thus, a local multidisciplinary intervention program improves cardiorespiratory fitness, but the positive health effects of the intervention dilute after the intervention.

Chapter 7 examined the levels of physical activity in normal-weight children and children with overweight, and the accuracy of self-reported physical activity compared to objectively measured physical activity. This study used data from the DOERAK database, in which a subgroup (n=65) of the participants wore an ActiGraph for one week to objectively measure physical activity. During the same week, participants filled out a diary on physical activity. Linear mixed models and GEE were used to test for differences in objectively measured physical activity between children with normal-weight and-overweight. Generalized estimating equations (GEE) were applied to test for differences between children with normal-weight and-overweight for reported time spent on watching TV, using the computer, playtime outside and playing sports. Children with overweight spent significantly less percentage time per day in sedentary behavior (β -1.65; 95%CI -3.12,-0.18), significantly more percentage time in light to moderate physical activity (β 1.48; 95%CI 0.07, 2.89), and significantly more percentage time in moderate to vigorous physical activity (β 0.45; 95%CI 0.02, 0.87) than normal-weight children. No significant differences were seen between normal-weight children and children with overweight for reported time spent on watching TV, using the computer, playtime outside and playing sports. Self-reported values of physical activity do not correlate well with objectively measured values. Thus, children with overweight are not less physically active than normal-weight children. Furthermore, self-reported values of physical activity of children with normal-weight and with overweight should be handled with care.

Finally, in **chapter 8** the main results are discussed in a broader perspective, and implications for general practice and suggestions for future research are given.

Samenvatting

Het doel van dit proefschrift was het beschrijven van: 1) de nauwkeurigheid van zelf-gerapporteerde lengte en gewicht van kinderen bij de huisarts; 2) de associaties tussen de gewichtsstatus van kinderen en de medische consequenties hiervan, zoals het aantal consulten bij de huisarts voor musculoskeletale en respiratoire klachten; 3) het effect van een multidisciplinair interventie programma voor kinderen met obesitas op verschillende gezondheidsuitkomsten; 4) het beweeggedrag van kinderen met normaal gewicht en met overgewicht.

DEEL 1:

In **hoofdstuk 2** zijn de verschillen tussen zelf-gerapporteerde lengte en gewicht, en gemeten lengte en gewicht voor kinderen met ondergewicht, normaal gewicht en overgewicht in de huisartspraktijk onderzocht. Hiervoor is data uit de DOERAK database gebruikt. De DOERAK database is opgezet om potentiële verschillen tussen kinderen met- en zonder overgewicht in de huisartsenpraktijk te onderzoeken. De DOERAK database bestaat uit 733 kinderen tussen de 2 en 18 jaar. De gemiddelden van de zelf-gerapporteerde- en van gemeten lengte en gewicht zijn vergeleken met de gepaarde T-test. Van de 715 geïncludeerde kinderen had 17.5% ondergewicht, 63.2% normaal gewicht, en 19.3% overgewicht, op basis van gemeten lengte en gewicht. Bij kinderen van 2-8 jaar rapporteerden de ouders van kinderen met ondergewicht een significant hoger gewicht dan wat gemeten was (gemiddeld verschil(MD) 0.32kg; 95%Betrouwbaarheidsinterval(BI) 0.02, 0.62), terwijl de ouders van kinderen met overgewicht juist een significant lager gewicht rapporteerden dan het gemeten gewicht (MD -1.08kg; 95%BI -1.77, -0.39). Bij kinderen van 9-17 jaar rapporteerden de kinderen met normaal gewicht (MD -0.51kg; 95%BI -0.79 ,-0.23) en met overgewicht (MD -1.28kg; 95%BI -2.08, -0.47) een significant lager gewicht dan gemeten door de huisarts. Huisartsen kunnen daarom niet vertrouwen op zelf-gerapporteerde lengte en gewicht van kinderen en hun ouders, en zullen de kinderen zelf moeten meten om misclassificatie van gewichtsstatus te voorkomen.

DEEL 2:

In **hoofdstuk 3** zijn de resultaten van een literatuurstudie naar het verschil in botdichtheid tussen kinderen met normaal gewicht en overgewicht of obesitas weergegeven. Voor deze literatuurstudie werden Medline (OVID), Embase, Cochrane, Web of Science (WoS), Cinahl ebsco, Pubmed publisher and Google scholar systematisch doorzocht naar artikelen met data over verschillen in botdichtheid tussen kinderen met normaal gewicht en met overgewicht en/of tussen kinderen met normaal gewicht en obesitas. Er werden 27 studies in de literatuurstudie geïncludeerd, met in het totaal 5958 kinderen. Er was matige tot hoge kwaliteit van bewijs dat kinderen met overgewicht (MD 213 grams; 95%BI 166, 261) en met obesitas (MD 329 grams; 95%BI 229, 430) een significant hoger mineraalgehalte van het hele lichaam hebben dan kinderen met normaal gewicht. Vergelijkbare resultaten werden gevonden voor de botdichtheid van het hele lichaam. De sensitiviteitsanalyse liet zien dat deze associatie sterker was bij meisjes, in vergelijking met jongens. Concluderend hebben kinderen met overgewicht en obesitas een hogere botdichtheid dan kinderen met normaal gewicht. Echter, aangezien er maar één studie in deze literatuurstudie een longitudinale studieopzet had, kunnen er geen uitspraken worden gedaan over het lange-termijn effect van overgewicht en obesitas bij kinderen op de latere bot status als volwassene.

Hoofdstuk 4 bestudeerde de associaties tussen gewichtsstatus van kinderen en het aantal en type consulten voor musculoskeletale klachten bij de huisarts, tijdens een 2-jaar follow-up. Net als in hoofdstuk 2, werd ook hier gebruik gemaakt van data uit de DOERAK database. Poisson regressie en logistische regressie werden toegepast om de associaties te testen tussen de gewichtsstatus en de aanwezigheid van-, de frequentie- en de type consulten voor musculoskeletale klachten bij de huisarts. Een multivariabele analyse werd gebruikt om te testen of er voorspellers voor consulten voor musculoskeletale klachten bij de huisarts tijdens de follow-up van twee jaar waren. Kinderen met overgewicht consulteerden de huisarts vaker tijdens de 2-jaar follow-up dan kinderen zonder overgewicht (gemiddelde 7.3 (5.7) vs 6.7 (5.4), odds ratio (OR) 1.09; 95%BI 1.01-1.18). Er waren geen significante verschillen tussen het aantal kinderen met- en zonder overgewicht dat de huisarts bezocht voor alle musculoskeletale klachten (OR 1.20; 95%BI 0.86 – 1.68). Er werden ook geen verschillen gevonden tussen het aantal consulten voor musculoskeletale klachten van kinderen met- en zonder overgewicht. Tevens waren er geen verschillen tussen het aantal verder gespecificeerde consulten voor musculoskeletale klachten (zoals bovenste en onderste extremiteiten) van kinderen met- en zonder overgewicht. Kinderen met overgewicht consulteren de huisarts dus wel vaker dan kinderen zonder overgewicht, maar dit verschil wordt niet verklaard door een verschil in consulten voor musculoskeletale klachten.

In **hoofdstuk 5** werden de associaties bestudeerd tussen de gewichtsstatus van kinderen en het aantal en type consulten voor respiratoire klachten. Data uit de DOERAK database werden gebruikt. Logistische regressie analyses en negatieve binominale regressie analyses werden toegepast om de associaties tussen gewichtsstatus en de aanwezigheid-, de frequentie-, en de type respiratoire consulten tijdens een 2 jaar follow-up te testen. Kinderen tussen de 2 en 18 jaar met ondergewicht hadden niet meer consulten voor respiratoire klachten dan kinderen met normaal gewicht (OR 0.87; 95%BI 0.64-1.10). Ook kinderen van 2-18 jaar met overgewicht hadden niet meer consulten voor respiratoire klachten dan kinderen met normaal gewicht (OR 1.33; 95%BI 0.99-

1.77). Echter hadden kinderen tussen de 12-18 jaar met overgewicht significant meer consulten voor respiratoire klachten bij de huisarts dan kinderen van 12-18 jaar met normaal gewicht (OR 2.14; 95%BI 1.14-4.01). Kinderen van 12-18 jaar met overgewicht hadden ook meer consulten voor astma-gerelateerde klachten (OR 3.94; 95%BI 1.20-12.88), en meer consulten voor respiratoire allergie gerelateerde klachten (OR 3.14; 95%BI 1.25-7.86) dan kinderen van 12-18 jaar met normaal gewicht. Bij de jongere kinderen werden geen associaties gevonden tussen gewichtsstatus en consulten voor respiratoire klachten. Kinderen van 12-18 jaar met overgewicht consulteren de huisarts dus vaker voor respiratoire, astma-achtige, en respiratoire allergie gerelateerde klachten dan kinderen van 12-18 jaar met een normaal gewicht.

DEEL 3:

Hoofdstuk 6 presenteert de uitkomsten van een studie naar de effecten van een multidisciplinair interventie programma voor kinderen met obesitas in achterstandswijken op bloeddruk en cardiorespiratoire fitheid. Kinderen met obesitas die zich aanmeldden voor het 12-weken durende interventieprogramma ‘Kids4Fit’ konden worden geïncludeerd in deze studie. Bij het aanmelden van de kinderen voor Kids4Fit werden de kinderen op een wachtlijst geplaatst, welke werd gebruikt als controle periode, totdat er een groep van 8-12 kinderen beschikbaar was om de interventie te starten. Cardiorespiratoire fitheid werd gemeten door middel van de shuttle-run-test (SRT). De bloeddruk en de SRT werden afgenomen bij aanmelden voor Kids4Fit, bij het starten van de interventie, aan het einde van de interventie, en op 52 weken na de start van de interventie. Het effect van Kids4Fit op de bloeddruk en op de SRT scores werd geanalyseerd door middel van mixed models en effectplots. In het totaal deden 154 kinderen mee aan de studie met een gemiddelde leeftijd van 8.5 jaar (standaard deviatie 1.8). Effectplots laten een initiële significante stijging van de SRT scores zien, maar dit effect is 52 weken na de interventie niet meer aanwezig. Er was geen significante verandering in systolisch bloeddruk percentielen op 52 weken na start van de Kids4Fit interventie (β 0.08; 95%BI -0.06, 0.22). Diastolische bloeddruk percentielen waren significant hoger op 52 weken na start van de interventie, vergeleken met baseline (β 0.20; 95%BI 0.08, 0.31). Concluderend verbetert een lokaal multidisciplinair interventie programma cardiorespiratoire fitheid, maar de positieve gezondheidseffecten zijn na beëindigen van de interventie niet meer aanwezig.

In **hoofdstuk 7** zijn de verschillen in niveau van fysieke activiteit tussen kinderen met- en zonder overgewicht beschreven, en is de nauwkeurigheid van zelf-gerapporteerde fysieke activiteit vergeleken met objectief gemeten fysieke activiteit voor kinderen met- en zonder overgewicht gepresenteerd. Er werd gebruik gemaakt van de DOERAK database, waarvan een subgroep (n=65) van de deelnemers gedurende een week een

ActiGraph hebben gedragen om fysieke activiteit objectief te meten. Tevens vulden de deelnemers gedurende dezelfde week een dagboek in over hun fysieke activiteit. Linear mixed models en generalized estimating equestions (GEE) werden toegepast om het verschil in objectief gemeten fysieke activiteit tussen kinderen met- en zonder overgewicht te testen. GEE werd toegepast om het verschil in tijd besteed aan televisie kijken, computeren, buiten spelen en sporten tussen kinderen met- en zonder overgewicht te testen. Kinderen met overgewicht besteedden significant minder tijd in sedentaire activiteit (β -1.65; 95%BI -3.12, -0.18), significant meer tijd in lichte tot matige fysieke activiteit (β 1.48; 95%BI 0.07, 2.89), en significant meer tijd in matige tot hevige fysieke activiteit (β 0.45; 95%BI 0.02, 0.87) dan kinderen met normaal gewicht. Er werden geen significante verschillen gevonden tussen kinderen met normaal gewicht en met overgewicht voor gerapporteerde TV-tijd, computer tijd, tijd besteed aan buiten spelen en tijd besteed aan sporten. Zelf-gerapporteerde waardes van fysieke activiteit correleerden niet goed met objectief gemeten waarden. Concluderend lijken kinderen met overgewicht niet minder actief dan kinderen met normaal gewicht. Daarnaast moeten zelf-gerapporteerde waarden van fysieke activiteit van kinderen met- en zonder overgewicht met enige voorzichtigheid geïnterpreteerd worden.

In **hoofdstuk 8** werden de belangrijkste resultaten van dit proefschrift in een breder perspectief besproken, en werden implicaties voor de huisarts en suggesties voor toekomstig wetenschappelijk onderzoek gegeven.

Dankwoord

Vanaf september 2015 ben ik bezig geweest met het schrijven van dit proefschrift, en hier heb ik de nodige hulp bij gekregen waarvoor ik een aantal mensen wil bedanken.

Mijn copromotor en promotoren

Marienke, bedankt voor de intensieve begeleiding en steun tijdens mijn gehele promotie traject. Ik vond het erg fijn om met je samen te werken en je directe manier van communiceren stel ik erg op prijs. Je was altijd kritisch op mijn stukken en stelde de juiste vragen waardoor ik getriggerd werd om na te denken hoe het stuk beter kon worden. De afgelopen jaren is mijn wetenschappelijk schrijven enorm verbeterd door jouw tips: je moet mensen meenemen in je verhaal, geen gedachtestappen overslaan, wel 'to the point', elke alinea moet een boodschap hebben, etc. Dank hiervoor! Ook heb je het voor elkaar gekregen om mijn creatieve kant naar boven te krijgen, met name bij het maken van posters en presentaties. Het gebruik van infographics heb ik nu helemaal onder de knie!

Jouw 'open-door policy' heb ik erg gewaardeerd en hier heb ik dan ook optimaal gebruik van gemaakt. Hoe vaak ik bij jou in de deuropening stond met: "mag ik even een korte vraag stellen?" en niet één keer zei je dat het even niet uit kwam…oké, misschien 1 keer, maar die is je vergeven ;).

Gelukkig was er ook altijd even tijd om het over dingen buiten werk te hebben, zoals verhuizen, hockey, wintersport etc. Jouw oprechte interesse hierin heb ik erg op prijs gesteld en heeft ook bijgedragen aan onze fijne samenwerking. In het laatste jaargesprek gaf je me een compliment over dat het een mooi proefschrift is geworden en dat het mooi binnen de tijd afgerond zou zijn. Ik bedankte jou toen voor je hulp, waarop jij zei: "je hebt het zelf gedaan". Maar zonder jouw input, kritische blik en aanmoediging was dit zeker niet gelukt. Dus bij deze nogmaals, heel erg bedankt!

Bart, jij was vanaf het begin bij mijn promotie betrokken als mijn promotor. Bij onze meetings wist jij vaak net wat andere vragen te stellen waardoor mijn artikelen inhoudelijk nog beter werden. Als ik mijn stukken naar jou toe stuurde was je altijd positief en enthousiast. Daarnaast gaf je altijd heel snel feedback waardoor ik direct verder kon. Ook jij had een open-door policy waardoor ik makkelijk bij je naar binnen kon lopen met mijn vragen. Bedankt voor je positiviteit, vertrouwen en je fijne begeleiding waarbij ik jouw humor ook zeker heb gewaardeerd.

Patrick, jij bent pas later als promotor toegevoegd aan mijn projectgroep, maar vanaf het begin was je al erg betrokken. Ondanks je drukke agenda wist jij altijd op zeer korte termijn mijn artikelen te voorzien van opbouwende kritiek. Met name jouw huisartsenview gaf extra dimensies aan mijn stukken. "Wat merkt de huisarts hiervan?" of "wat kan de huisarts hiermee?". Bedankt voor deze waardevolle feedback. Gelukkig heb ik ook de kans gekregen om naar de NAPCRG te gaan met jou en een aantal collega's. Het congres was wellicht niet het beste congres waar we zijn geweest, maar de Chicago Bulls, Chicago verkennen, en het dansen in de jazz-club was waanzinnig. Dank voor deze leuke ervaring.

Opzetten en uitvoeren van DOERAK

Winifred, ik heb van meerdere kanten gehoord dat jij een hele belangrijke rol hebt gespeeld in het opzetten en uitvoeren van DOERAK, en hiervoor wil ik je bedanken. Door jouw inzet kon ik direct aan de slag met een prachtige, complete, en overzichtelijke dataset. Daarnaast ben je na jouw eigen promotie betrokken gebleven bij mijn promotietraject, ondanks dat je inmiddels ergens anders aan het werk was. Bedankt voor alle input die je hebt gegeven en voor je kritische en enthousiaste feedback om mijn stukken.

Naast Winifred waren er nog velen andere betrokken bij het opzetten van DOERAK en het verzamelen van de data. Alle HAIO's, huisartsen en onderzoeksmedewerkers bedankt voor jullie inspanningen! Toke, voor jou nog een extra bedankje, aangezien ik tijdens mijn promotietraject bij jou terecht kon met alle vragen over de dataset; jij had alle ins en outs direct paraat, zodat ik weer snel verder kon.

Natuurlijk gaat ook mijn grote dank uit aan alle kinderen en ouders die hebben deelgenomen aan de DOERAK studie!

Co-auteurs

Alle co-auteurs, bedankt voor de samenwerking en jullie bijdrage aan de verschillende artikelen in dit proefschrift.

Huisartsopleider

Dick, tijdens mijn 1e opleidingsjaar bij jou in de praktijk heb je me alle ruimte gegeven voor mijn promotie traject. Ik werkte part-time in de praktijk en besteedde elke week 1 dag aan mijn onderzoek. Daarnaast was ik ook af en toe weg naar een congres. Jij hebt hier nooit een probleem van gemaakt en had altijd interesse in hoe het met mijn onderzoek ging. Hartelijk dank hiervoor!

Collega's

Zonder leuke collega's gaat werken ook een stuk minder makkelijk. Alle collega's van de 19e, bedankt voor de gezelligheid, het lachen, de leuke discussies, de 1e-donderdag-van-de-maand-borrels, etc.

Ik kwam vanaf dag 1 terecht in het Kippenhok, eerst nog even wennen, maar ik had me geen betere plek kunnen bedenken. Collega's uit kippenhoek: het was heerlijk om met jullie op een kamer te zitten en zo nu en dan afgeleid te worden met stomme grappen, youtube fimpjes (Oh my god, hij heeft ….), muziekjes, chocola, koekjes, koffie drinken en spelletjes. En natuurlijk werd er ook hard gewerkt op zijn tijd. Ik heb van jullie genoten en jullie hebben het werken hier absoluut een gouden randje gegeven, dank voor de leuke tijd!

Vrienden

Naast werk besteed ik ook nog steeds veel tijd op de hockeyclub. Alle coaches, managers, supporters, en natuurlijk mijn (oud-)teamgenootjes: bedankt voor de gezelligheid, de biertjes, en de afleiding van het werk.

Mijn grote dank gaat ook uit naar al mijn vrienden en vriendinnetjes die op zijn of haar manier iets hebben bijgedragen. Ieders interesse in hoe het met mijn promotie ging, de discussies over overgewicht bij kinderen, de ontspanning door etentjes en drankjes en de weekendjes weg, heb ik allemaal zeer op prijs gesteld.

Familie

Lieve Rietje en Loes, mijn grote zussen, wat ben ik blij met jullie. Ik vind het zo fijn om twee zussen te hebben die me door en door kennen en waarmee ik alles kan bespreken. Jullie enthousiasme en trotsheid als ik een artikel af had werkten stimulerend. En ja, kleine zusjes worden groot, zo klein ben ik niet meer ;). En Rietje, onwijs bedankt voor het tekenen van mijn cover, hij is echt heel gaaf geworden!

Lieve mama en Rob; mama jij wist al wat eerder dat onderzoek doen iets voor mij was. Jij zei: “is het niet wat voor jou om promotieonderzoek te doen”, ik: “nee, niks voor mij”. Maar je had gelijk! Ik vond het super leuk om tijdens mijn promotietraject mijn verschillende bevindingen met je te bespreken en jouw oprechte interesse vond ik heel fijn. Wellicht heb ik dat analytische vermogen van jou geërfd Als ik jullie belde of appte om te delen dat er een stuk was gepubliceerd waren jullie altijd lovend en trots! Bedankt voor jullie steun.

En last but not least: Lieve Jacob, de afgelopen 3 jaar waren niet altijd even makkelijk, maar gelukkig zijn we er nu eindelijk over uit: we zijn voor elkaar gemaakt. Ik bof met iemand als jij die al mijn verhalen van werk aanhoort (lange of korte versie?), mijn presentaties aanhoort, eten kookt, de was doet, schoonmaakt, champagne met me drinkt om publicaties te vieren, trots aan vrienden vertelt dat ik de huisartsopleiding EN promotieonderzoek doe, en zo kan ik nog wel even door gaan... Wat zou ik zonder jou moeten... Dankjewel voor al je steun en liefde de afgelopen jaren.

Curriculum Vitae

Janneke van Leeuwen was born on October 23rd, 1986, in Hilversum, the Netherlands. She attended secondary school at 'the Alberdink Thijm College' in Hilversum and graduated in 2004. She then received a full scholarship to play field hockey at the University of Maryland, College Park, The United States from which she graduated with a Bachelor of Science Degree in Economics in 2008.

In September 2008 Janneke moved to Rotterdam and started studying medicine at the Erasmus MC. She completed her 21-week master research project at the Department of Health and Rehabilitation Sciences, at the University of Queensland in Brisbane, Australia. Her master research topic was: knee osteoarthritis 1 year after ACL reconstruction, using the MOAKS. She graduated in January 2015 with a Master of Science in medicine. Hereafter Janneke gained medical experience by working in an elderly home for 6 months, and in September 2015 she started her general practice vocational training in combination with her PhD-project (AIOTHO). In September 2016 she graduated from the Netherlands Institute of Health Sciences (NIHES) with a Master of Science in Clinical Epidemiology. Janneke will continue to finish her general practice vocational training in the upcoming year(s).

PhD Portfolio

Erasmus MC Department: General Practice
PhD Period: September 2015 – March 2019
Promotors: Prof. dr. B.W. Koes and Prof. dr. P.J.E. Bindels
Co-promotor: Dr. M. van Middelkoop

	Year	Workload (ECTS)
Courses/training		
Master of Science in Clinical Epidemiology, NIHES, Rotterdam	2015-2016	70
Research Integrity	2017	0.7
EndNote, Erasmus MC, Rotterdam	2015	0.3
Systematic literature search, Erasmus MC, Rotterdam	2015	0.3
BKO (Basiskwalificatie Onderwijs) – Ontwikkelen onderwijs	2016	0.5
BKO (Basiskwalificatie Onderwijs) – Blended learning	2017	0.5
BKO (Basiskwalificatie Onderwijs) – Teach the Teacher	2016	1
Professional education		
Vocational training for general practitioner, Erasmus MC, Rotterdam	2015 – present	
Oral presentations		
NASO meeting, Utrecht, 1 presentation	2017	1
NHG Wetenschapsdag, Zeist, 2 presentations	2017	2
BJGP conference, London, England, 2 presentations	2018	2
NHG Wetenschapsdag, Amsterdam, 1 presentation	2018	1
Primeuravond, Rotterdam, 1 presentation	2018	1
Poster presentations		
ECO, Porto, Portugal, 2 posters	2017	2
NAPCRG, Chicago, United states, 1 poster	2018	1
Participation (inter)national conferences		
LOVAH wetenschapsdag, Utrecht	2015	0.3
NHG wetenschapsdag, Amsterdam	2016	0.3
ECO, Gothenburg, Sweden	2016	1
Wetenschapsbijeenkomst Centrum Gezond Gewicht	2017	0.3
LOVAH Wetenschapsdag, Utrecht	2017	0.3
Nationaal Obesitas Symposium, Rotterdam	2018	0.3
Teaching		
Supervision of research projects by medical students (2x)	2016-2018	4.0
Clinical reasoning for bachelor and master students	2016-2019	3.0
Coaching bachelor medical students	2016-2018	1.6
Lecturing GP assistants	2016-2019	1
Total		**95.4**

List of publications

THIS THESIS

van Leeuwen J, Koes BW, Paulis WD, van Middelkoop M. Differences in bone mineral density between normal-weight children and children with overweight and obesity: a systematic review and meta-analysis. *Obes Rev* 2017;**18**:526-546

van Leeuwen J, van Middelkoop M, Paulis WD, Bueving HJ, Bindels PJE, Koes BW. Overweight and obese children do not consult their general practitioner more often than normal weight children for musculoskeletal complaints during a 2-year follow-up. *Arch Dis Child* 2018;**103**:149-154

van Leeuwen J, Andrinopoulou E, Hamoen M, Paulis WD, van Teeffelen J, Kornelisse K, van der Wijst-Ligthart K, Koes BW, van Middelkoop M. The effect of a multidisciplinary intervention program for overweight and obese children on cardiorespiratory fitness and blood pressure. *Fam Prac* 2018;1-7

van Leeuwen J, van Middelkoop M, Paulis WD, Bindels PJE, Koes BW. General practitioners cannot rely on reported weight and height of children*. Prim Health Care Res Dev* 2018;1-6

van Leeuwen J, van Middelkoop M, Paulis WD, Bindels PJE, Koes BW. Differences in respiratory consultations in primary care between underweight, normal-weight and overweight children. *NPJ Prim Care Respir Med.* 2019; **29**:15

OTHER PUBLICATIONS

Culvenor AG, Collins NJ, Guermazi A, Cook JL, Vicenzino B, Khan KM, Beck N, **van Leeuwen J**, Crossley KM. Early knee osteoarthritis is evident one year following anterior cruciate ligament reconstruction: a magnetic resonance imaging evaluation. *Arthritis Rheumatol* 2015;**67**:946-55

Van Helden H, van Seters CM, **van Leeuwen J**, Bohnen AM. Can portion-controlled prepackaged foods promote weight loss?. *Obesity* 2016;**24**:2259