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A WEB- AND MOBILE PHONE-BASED OBESITY PREVENTION INTERVENTION IN 4-YEAR-OLDS: A POPULATION-BASED RANDOMIZED CONTROLLED TRIAL

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A Web- and Mobile Phone-Based Obesity Prevention
Intervention in 4-Year-Olds: A Population-Based
Randomized Controlled Trial
THESIS FOR DOCTORAL DEGREE (Ph.D.)

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To my amazing husband Jocke

ABSTRACT

Background: Childhood overweight and obesity has increased significantly over the past two decades. Many well-conducted obesity prevention trials have been conducted in pre-school aged children but the majority have not been able to show changes in obesity related markers. These trials have used traditional face-to-face methods to conduct the interventions, which are expensive and difficult to scale up. Therefore, new dissemination methods for intervention studies such as mobile health (mHealth) should be explored.

Aims: The overall aim of this thesis was to determine whether a mHealth intervention targeted towards parents could improve obesity markers in pre-school aged children.

Paper I: To outline the study design and methodologies utilized in the MINISTOP trial.

Paper II: To evaluate the validity of reported energy and food intake assessed using the mobile based Tool for Energy Balance in Children (TECH) against total energy expenditure (TEE) and 24hr dietary recalls, respectively.

Paper III: To evaluate the capacity of the wrist-worn ActiGraph wGT3x-BT accelerometer to capture variations in free-living activity energy expenditure (AEE) and to assess wear compliance of the ActiGraph using a seven day 24hr protocol.

Paper IV: To assess the effectiveness of the MINISTOP intervention on body composition, intakes of fruits, vegetables, candy, and sweetened beverages, as well as the amount of time spent sedentary and in moderate-to-vigorous physical activity after the 6-month intervention.

Paper V: To investigate if the MINISTOP intervention 12-months after baseline improved fat mass index (FMI) and had a maintained effect on a composite score (made up of FMI as well as dietary and physical activity variables).

Methods

Paper II: A nested validation study including 39 children aged 5.5 years. Energy and food intakes were measured using TECH and compared to TEE assessed using the doubly labelled water method and 24hr dietary recalls, respectively.

Paper III: A nested validation study including 40 children aged 5.5 years. TEE was assessed using the doubly labelled water method and AEE was calculated as TEE minus a predicted basal metabolic rate. The ActiGraph was worn on the non-dominant wrist and the utilized outputs were mean of daily filtered vector magnitudes (mean VM total) and mean of awake filtered vector magnitudes (mean VM waking).

Papers IV and V: A randomized controlled trial including 315 children aged 4.5 years. After baseline assessments, the children were randomly allocated into the intervention or control group for six months. The intervention group and control group received the MINISTOP app or a pamphlet on dietary and physical activity behaviors for pre-school children, respectively.

The outcome measures were FMI (primary) and intakes of fruits, vegetables, candy, and sweetened beverages, as well as time spent sedentary and in moderate-to-vigorous physical activity (secondary). Two composite scores, a seven component (including all primary and secondary outcomes) and a six component (including only secondary outcomes) were computed.

Results

Paper II: No significant difference between mean energy intake and TEE was found ($P = 0.064$). For all eight food groups assessed no significant differences in the mean intakes were observed when using TECH and 24hr dietary recalls and all intakes were correlated when using both methods (range for rho: 0.665 to 0.896, all $P < 0.001$).

Paper III: Mean VM total and mean VM waking alone were able to explain 14% ($P = 0.009$) and 24% ($P = 0.001$) of the variation in AEE. When adding fat and fat free mass to the models 58% and 62% ($P < 0.001$) of the variation in AEE was explained, using mean VM total and mean VM waking, respectively.

Paper IV: No intervention effect for the primary outcome FMI was observed between the intervention and control group ($P = 0.922$). At the 6-month follow-up, for the seven component composite score the intervention group significantly increased their score compared to the control group ($+0.36 \pm 1.47$ units vs. -0.06 ± 1.33 units, respectively, $P = 0.021$ between groups), with the difference being more evident in children with a higher FMI. For the six component composite score the children in the intervention group had a higher odds of increasing their score in comparison to the control group (odds ratio: 1.99; 95% confidence interval: 1.20, 3.30, $P = 0.008$).

Paper V: For FMI there was no significant difference observed between the intervention and control group ($P = 0.566$) between the 12-month follow-up and baseline. Furthermore, there was no maintained effect observed in the change in the difference in the seven component composite score between the intervention and control group ($P = 0.248$).

Conclusions: The results from this thesis suggest that both TECH and the wrist-worn ActiGraph have the potential to provide useful information in studies where diet and physical activity in young children are assessed. Furthermore, this thesis presents results from the first mHealth obesity prevention study in pre-school aged children. Although no difference between the intervention and control group for FMI was observed, the intervention group showed a significantly higher seven component composite score difference than the control group at the 6-month follow-up, especially in children with a higher FMI. Topics for future research include modifications of the MINISTOP app to more specifically target high risk children as well as further studies on to how maintain behavior changes in mHealth interventions.

LIST OF SCIENTIFIC PAPERS

- I. **Delisle C**, Sandin S, Forsum E, Henriksson H, Trolle-Lagerros Y, Larsson C, Maddison R, Ortega FB, Ruiz JR, Silfvernagel K, Timpka T, Löf M. A web- and mobile phone-based intervention to prevent obesity in 4-year-olds (MINISTOP): A population-based randomized controlled trial. *BMC Public Health*. 2015;15:95
- II. **Delisle Nyström C**, Forsum E, Henriksson H, Trolle-Lagerros Y, Larsson C, Maddison R, Timpka T, Löf M. A mobile phone based method to assess energy and food intake in young children: A validation study against the doubly labelled water method and 24 h dietary recalls. *Nutrients*. 2016;8(1)
- III. **Delisle Nyström C**, Pomeroy J, Henriksson P, Forsum E, Ortega FB, Maddison R, Migueles JH, Löf M. Evaluation of the wrist-worn ActiGraph wGT3x-BT for estimating activity energy expenditure in preschool children. *Eur J Clin Nutr*. 2017;71(10):1212-1217.
- IV. **Delisle Nyström C**, Sandin S, Henriksson P, Henriksson H, Trolle-Lagerros Y, Larsson C, Maddison R, Ortega FB, Pomeroy J, Ruiz JR, Silfvernagel K, Timpka T, Löf M. Mobile-based intervention intended to stop obesity in preschool-aged children: The MINISTOP randomized controlled trial. *Am J Clin Nutr*. 2017;105(6):1327-1335.
- V. **Delisle Nyström C**, Sandin S, Henriksson P, Henriksson H, Maddison R, Ortega FB, Ruiz JR, Löf M. A 12-month follow-up of a mobile-based (mHealth) obesity prevention intervention in pre-school children: The MINISTOP randomized controlled trial. *Manuscript*

RELATED PUBLICATIONS

(Not included in the thesis)

- I. Henriksson H, Bonn SE, Bergstrom A, Balter K, Balter O, **Delisle C**, Forsum E, Lof M. A new mobile phone-based tool for assessing energy and certain food intakes in young children: A validation study. *JMIR Mhealth Uhealth*. 2015;3:e38.
- II. Cadenas-Sanchez C, **Nystrom CD**, Sanchez-Delgado G, Martinez-Tellez B, Mora-Gonzalez J, Risinger AS, Ruiz JR, Ortega FB, Lof M. Prevalence of overweight/obesity and fitness level in preschool children from the north compared with the south of europe: An exploration with two countries. *Pediatr Obes*. 2016;11(5): 403-10.
- III. Leppanen MH*, **Nystrom CD***, Henriksson P, Pomeroy J, Ruiz JR, Ortega FB, Cadenas-Sanchez C, Lof M. Physical activity intensity, sedentary behavior, body composition and physical fitness in 4-year-old children: Results from the ministop trial. *Int J Obes*. 2016;40(7): 1126-33.
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- IV. **Delisle Nystrom C**, Henriksson P, Alexandrou C, Lof M. The tanita sc-240 to assess body composition in pre-school children: An evaluation against the three component model. *Nutrients*. 2016;8(6).
- V. Henriksson P, Cadenas-Sanchez C, Leppanen MH, **Delisle Nystrom C**, Ortega FB, Pomeroy J, Ruiz JR, Lof M. Associations of fat mass and fat-free mass with physical fitness in 4-year-old children: Results from the ministop trial. *Nutrients*. 2016;8(8).
- VI. **Nystrom CD**, Larsson C, Ehrenblad B, Eneroth H, Eriksson U, Friberg M, Hagstromer M, Lindroos AK, Reilly JJ, Lof M. Results from Sweden's 2016 report card on physical activity for children and youth. *J Phys Act Health*. 2016;13: S284-90.
- VII. **Delisle Nystrom C**, Henriksson H, Alexandrou C, Bergstrom A, Bonn S, Balter K, Lof M. Validation of an online food frequency questionnaire against doubly labelled water and 24 h dietary recalls in pre-school children. *Nutrients*. 2017;9(1).
- VIII. Migueles JH, Cadenas-Sanchez C, Ekelund U, **Delisle Nystrom C**, Mora-Gonzalez J, Lof M, Labayen I, Ruiz JR, Ortega FB. Accelerometer data collection and processing criteria to assess physical activity and other outcomes: A systematic review and practical considerations. *Sports Med*. 2017; 47(9): 1821-45.
- IX. Cadenas-Sanchez C, Henriksson P, Henriksson H, **Delisle Nystrom C**, Pomeroy J, Ruiz JR, Ortega FB, Lof M. Parental body mass index and its association with body composition, physical fitness and lifestyle factors in their 4-year-old children: Results from the ministop trial. *Eur J Clin Nutr*. 2017;71(10): 1200-05.
- X. Parekh N, Henriksson P, **Delisle Nystrom C**, Silfvernagel K, Ruiz JR, Ortega FB, Pomeroy J, Lof M. Associations of parental self-efficacy with diet, physical activity, body composition, and cardiorespiratory fitness in swedish preschoolers: Results from the ministop trial. *Health Educ Behav*. 2017. doi: 10.1177/1090198117714019 [Epub ahead of print].
- XI. Leppanen MH, Henriksson P, **Delisle Nystrom C**, Henriksson H, Ortega FB, Pomeroy J, Ruiz JR, Cadenas-Sanchez C, Lof M. Longitudinal physical activity, body composition, and physical fitness in preschoolers. *Med Sci Sports Exerc*. 2017; 49(10): 2078-85.

- XII. **Delisle Nyström C**, Henriksson P, Martínez-Vizcaíno V, Medrano M, Cadenas-Sánchez C, Arias-Palencia N, Löf M, Ruiz JR, Labayen I, Sánchez-López M, Ortega FB. Does cardiorespiratory fitness attenuate the adverse effects of severe/morbid obesity on cardiometabolic risk and insulin resistance in children? A pooled analysis. 2017. doi: 10.2337/dc17-1334 [Epub ahead of print].
- XIII. **Delisle Nyström C**, Henriksson P, Ek A, Henriksson H, Ortega FB, Ruiz JR, Löf M. Is BMI a relevant marker of fat mass in 4 year old children? Results from the MINISTOP trial. *Submitted manuscript*.

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LIST OF ABBREVIATIONS

ADP	Air displacement plethysmography
AEE	Activity energy expenditure
App	Application
BMI	Body mass index
BMR	Basal metabolic rate
CI	Confidence interval
CPM	Counts per minute
DLW	Doubly labelled water
EI	Energy intake
ENMO	Euclidean norm minus one
FFM	Fat free mass
FFM _{ADP}	Fat free mass measured using air displacement plethysmography
FFM _{ISO}	Fat free mass measured using isotope dilution
FFMI	Fat free mass index
FFMI _{ADP}	Fat free mass index measured using air displacement plethysmography
FM	Fat mass
FM _{ADP}	Fat mass measured using air displacement plethysmography
FM _{ISO}	Fat mass measured using isotope dilution
FM%	Fat mass percentage (fat mass in proportion to body weight)
FMI	Fat mass index
FMI _{ADP}	Fat mass index measured using air displacement plethysmography
HFEN	Euclidean norm of the high-pass filtered signs
HFEN+	Euclidean norm of the high-pass filtered signs plus Euclidean norm of low-pass filtered signals minus 1g
MAD	Mean amplitude deviation
Mean VM total	Mean per minute filtered vector magnitude for all worn time
Mean VM waking	Mean per minute filtered vector magnitude for time classified as awake worn time

mHealth	Mobile health
MINISTOP	Mobile-based intervention intended to stop obesity in preschoolers
MVPA	Moderate-to-vigorous physical activity
N _D	Deuterium dilution space
N _O	Oxygen-18 dilution space
OR	Odds ratio
PAL	Physical activity level
RCT	Randomized controlled trial
SD	Standard deviation
TBW	Total body water
TECH	Tool for energy balance in children
TEE	Total energy expenditure
VM	Vector magnitude
² H	Deuterium
¹⁸ O	Oxygen-18

1 INTRODUCTION

1.1 CHILDHOOD OVERWEIGHT AND OBESITY

1.1.1 Prevalence

Childhood overweight and obesity is a global and serious public health issue affecting low, middle, and high income countries (1). In 2015, it was approximated that 107.7 million children aged 2 to 19 years were obese, which represents an overall prevalence rate of 5% worldwide (2). In children under five years of age the increase in childhood overweight and obesity has been rapid. For example, between 1990 and 2013 childhood overweight and obesity increased from 32 to 42 million and if these global trends persist approximately 70 million children will be overweight or obese by 2025 (3).

In Stockholm and surrounding suburbs in 2012, 9.4% of four year old children were overweight and 1.8% were obese, with higher rates being observed in girls than in boys (4). In 2010, in the Uppsala-Örebro region overweight and obesity rates for girls were approximately 14% and 3% with corresponding figures in boys being approximately 10% and 2.5% (5). Although, reports are showing that the prevalence of childhood overweight and obesity has stabilized (5-8), the levels of overweight and obesity are between two and four times as high as a few decades before, depending on the age group (9, 10). Additionally in Sweden, a socioeconomic gradient for overweight and obesity is evident with a higher prevalence being observed among socioeconomically disadvantaged groups (11, 12). For instance, for four year old children the prevalence rates in Stockholm and surrounding suburbs differed by 11.5% with the lowest rates being observed in the more affluent city center (Norrmalm) and the highest rates being observed in the less affluent suburb (Salem) (4).

In addition to looking at the prevalence of childhood obesity by body mass index (BMI) it is also important to look at body composition. A recent study investigated the longitudinal development of adiposity in 26 healthy, Swedish children from 1 week to 4.5 years of age (13). Body composition was measured at 1 and 12 weeks as well as at 1.5, 3, and 4.5 years of age and results showed that in comparison to reference data by Fomon et al. (14), starting at 1.5 years, these children had a higher fat mass percentage (FM%); however, their BMI was similar. The largest difference in FM% was found at 4.5 years of age where boys and girls had on average 68% and 52% higher values than the reference children (13). This data demonstrates that childhood overweight and obesity is still an issue in Swedish society and that it is important to measure body composition along with BMI.

1.1.2 Determinants

The etiology of overweight and obesity is multi-factorial and is influenced by a multitude of determinants ranging from the individual to the societal level. For instance, from early childhood, genetics have been found to be an important determinant in explaining the variation in height, weight, and BMI (15, 16). There are also numerous environmental or

modifiable lifestyle determinants that influence childhood obesity. These include and are not limited to: eating behaviors, physical activity, sedentary behavior or screen time, sleep, as well as early-life factors (e.g. maternal gestational weight gain or breastfeeding) (17).

Overweight and obesity occurs when there is an energy imbalance, i.e. energy intake (EI) exceeds energy expenditure (18). For example, in young children EI has been positively related to BMI z-scores in both cross-sectional and longitudinal studies (19, 20). Furthermore, low energy expenditure depicted by low levels of physical activity and high levels of sedentary behavior/screen time has been associated with a positive energy balance (21). In pre-school aged children significant inverse correlations have been found between objectively measured moderate-to-vigorous physical activity (MVPA) and FM% (22-24) as well as fat mass index (FMI) (23, 24). In regards to objectively measured sedentary behavior no significant associations have been observed for FM% or FMI (22-24). Even though null associations were found between sedentary behavior and FM% as well as FMI it may have an indirect influence on body composition indices. For instance, in pre-school children it has been found that sedentary behavior, especially in the form of television viewing has been associated with the intake of energy dense food (25). Further research is needed on body movements, especially how sedentary behavior and screen time influence childhood overweight and obesity.

1.1.3 Consequences

Childhood overweight and obesity is of serious concern as it can persist throughout adolescence and adulthood causing an array of physical and psychological consequences (26). Nader et al. (27) found that children who were overweight at four years of age had a 60% risk of being overweight at age 12. Similarly, another study stated that 34% of children who were overweight at seven years of age were classified as obese at age 13 (28). This is very concerning from a health perspective as it is well established that childhood obesity is associated with cardio-metabolic risk factors such as hypertension, insulin resistance, and dyslipidemia (29). Many studies e.g. (30, 31) have examined the prevalence of cardio-metabolic risk factors in relation to weight status in children and found that as BMI increased the risk factors followed concurrently. Furthermore, a study in 8 to 11 year old Spanish children found that children who were overweight, mildly obese, severely obese, or morbidly obese had 0.4, 0.8, 1.3, and 1.6 standard deviation (SD) higher cardio-metabolic risk score, respectively than their normal weight counterparts (32). Due to the fact that in 2015 a high BMI was related to approximately 4 million deaths and 120 million disability adjusted life years in adults worldwide (2), intervention in the early years is highly motivated.

1.2 OBESITY PREVENTION INTERVENTIONS IN PRE-SCHOOL CHILDREN

During the recent years there has been a pique in interest in obesity prevention interventions targeting pre-school aged children (33-36) due to the increased prevalence of overweight and obesity in this age group. Primary prevention is being brought to the forefront due to the fact that once obesity is established reversal through interventions is challenging (37).

Furthermore, due to the fact that it has been observed that obesity, as well as obesogenic behaviors, can track from early childhood onward, intervention at the younger years is highly warranted (38). It has also been found that treatment started at a younger age is more effective than at older ages because parents or caregivers have the ability to exert greater control over their child's environment (39).

The setting of the intervention also has to be considered with interventions being able to be conducted in one or a combination of settings (e.g. school/childcare, home, primary care, or community). A systematic review conducted in 2016 found that the majority of overweight and obesity prevention interventions in pre-school aged children have been conducted in a school-based environment (16 of 23), followed by the community setting (5 of 23), and then the home environment (2 of 23) (40). Only 8 of the 23 (35%) prevention interventions included in this review (with five, two, and one being conducted in the school, community, and home environment, respectively) found a significant effect on at least one anthropometric variable (BMI, BMI percentile, or BMI z-scores) (40).

Furthermore, in Europe there has been several well-conducted obesity prevention trials in young children; however, the majority have failed to demonstrate significant changes in obesity markers (41-46). The TOYBOX study was a school-based intervention with parental involvement which comprised of six countries (Belgium, Bulgaria, Germany, Greece, Poland, and Spain) and included 4964 pre-school children aged 3.5 to 5.5 years. To date, they have found limited effects of the intervention regarding beverage consumption (41) and in the Belgian sample the intervention had no effects on sedentary time measured either objectively or subjectively (42). The IDEFICS study was a large-scale community oriented intervention which included 16 228 children aged 2 to 9.9 years from eight European countries (Belgium, Cyprus, Estonia, Germany, Hungary, Italy, Spain, and Sweden). IDEFICS found no significant differences between the intervention and control groups in regards to the prevalence of overweight and obesity or measures of body fatness (43). Furthermore, no significant effects were found on parental reported diet, physical activity or sedentary behaviors (44). The Ballabeina study was a lifestyle intervention implemented in the pre-school setting in Switzerland and included 652 children with a mean age of 5.1 years. Significant intervention effects were found for aerobic fitness, FM% (measured by bioelectrical impedance), as well as parental reported diet (food frequency questionnaire), physical activity and media use; however, no significant difference was observed for objectively measured physical activity (45). Finally, the PRIMROSE study was a population-based randomized controlled trial (RCT) delivered through child healthcare centers in Sweden (n = 1053). When the children were four years of age no significant intervention effects were observed for BMI, MVPA, or sedentary behaviors; however, children in the intervention group had a higher consumption of vegetables and lower intake of sweetened beverages (46).

It is evident that the prevention interventions that have been implemented to date have had limited effectiveness in reducing overweight and obesity as well as other obesity markers. As

the home-based environment has not been largely investigated in this age group, possibly future trials should focus there, as pre-school children consume approximately 75% of their food at home (47). Furthermore, the first years of life are considered the formative years where the child's family, especially the parents are the principal social influence shaping their child's development (48, 49). Therefore, it is believed that modifiable obesity markers such as diet and physical activity are ingrained in the family environment (48). However, we cannot dismiss the fact that the family environment is changing and time constraints for parents are increasing, which will probably affect participation rates in traditional face-to-face interventions (50). Therefore, obesity prevention interventions need to be developed using different methods to disseminate information to parents of pre-school aged children.

1.3 MOBILE HEALTH (MHEALTH)

The use of mobile phones and applications (apps) to disseminate information or interventions has exploded in recent years. Mobile health (mHealth) refers to the usage of wireless and mobile technologies to achieve health related objectives (51). Mobile phone subscriptions have increased by 97% between 2000 and 2015 (52), with approximately 95% of the global population (7 billion people) residing in an area with a mobile-cellular network (53). In Sweden 78% of the population access the internet via their phone, with approximately 65% doing it every day. On average, Swedish men and women aged 16 to 45 years spend between 8.4 and 15.9 hours per week using the internet on their mobile phone (54).

Due to the wide availability and use of mobile phones in Sweden the use of mHealth to deliver interventions has great potential. mHealth has been used in many trials to promote behavior change in various areas. For example, it has been used with the aim to increase smoking cessation, physical activity, safer sexual behavior, and to decrease caloric intake and alcohol consumption (55). mHealth has also been used for disease management for both acute and chronic conditions for a variety of diseases and disorders (55). The benefits of using mHealth instead of more traditional face-to-face interventions are: that the interventions can be delivered at any time or place, participants are not required to attend a clinic, they are interactive, and they can be tailored towards specific groups.

A recent meta-analysis in adults investigating the use of mobile phone delivered weight loss interventions found significant decreases in body weight in the intervention group compared to the control group (56). Flores Mateo et al. (57) conducted a systematic review/meta-analysis on the use of mobile apps to promote weight loss and increase physical activity in adults. They found that the use of mobile app interventions significantly decreased body weight and BMI (pooled estimate: -1.04 kg and -0.43 kg/m², respectively). In regards to physical activity an increase was observed in the intervention compared to the control group, but the results for the pooled estimate did not reach statistical significance (57). According to two systematic reviews few interventions have used apps to target dietary (58, 59) and sedentary (59) behaviors in adults. For those that have investigated such outcomes 6 out of 11 studies found improvements in diet (various markers) and 1 of 2 studies found an improvement in sedentary behavior (59).

Very few studies have been conducted using apps to prevent or treat obesity or related behaviors in children and adolescents (59). Quelly et al. (60) conducted a systematic review in this area and found that apps did not lead to changes in anthropometric outcomes (waist circumference, BMI, or FM%) in older children and adolescents. In regards to physical activity for older children and adolescents the results were varied with some studies finding positive outcomes and others not. Changes in nutritional behavior were promising with some studies showing increases in fruit and/or vegetable intake and decreases in sugar sweetened beverages and/or unhealthy snack consumption (60). There has been no studies conducted using apps to prevent or treat obesity in pre-school aged children. As mHealth weight loss interventions have been effective in adults it would be interesting to investigate if mHealth has the ability to promote behavior change that would aid in preventing overweight and obesity in young children.

1.4 CLASSIFICATION & DEFINITION OF OVERWEIGHT AND OBESITY

Classification of children and adults into weight status categories (i.e. underweight, normal weight, overweight, and obese) is commonly done using BMI. In adults there is only one cut-off for overweight ($\text{BMI} \geq 25 \text{ kg/m}^2$) and obesity ($\geq 30 \text{ kg/m}^2$), whereas children are classified into weight status categories using age- and sex-specific cut-points (61, 62). However, BMI is a crude measure of overweight and obesity, as it is an estimate of weight in relation to height and it cannot differentiate between fat mass (FM) and fat free mass (FFM) (63). A few studies (64-67) have investigated the validity of BMI in pre-school aged children; however, they have compared BMI to FM% which comes with limitations. For instance, FM% is influenced by the proportion of both FM and FFM in the body and it is not completely independent of body size (63). Therefore, in order to overcome this problem, body composition indices such as FMI and fat free mass index (FFMI) should be used instead of FM%, as both FMI and FFMI represent height adjusted measures of FM and FFM, respectively (63, 68).

To date, no studies in the pre-school age group have compared BMI to the FMI or FFMI. Unpublished data, from 303 4.5 year old children found that BMI was as strongly correlated with the FMI and FFMI in both boys and girls (e.g. for boys $r^2 = 0.468$ and 0.621 , both P -values < 0.001 for BMI vs. FMI and BMI vs. FFMI, respectively) (Delisle Nyström et al., manuscript under review, 2017 Oct 1). These results indicate that caution is needed when interpreting body composition from BMI in pre-school aged children.

1.5 ASSESSMENT OF BODY COMPOSITION USING AIR DISPLACEMENT PLETHYSMOGRAPHY

There are numerous methods to measure body composition such as: skinfolds, bioelectrical impedance, dual energy x-ray absorptiometry, underwater weighing, isotope dilution, and air displacement plethysmography (ADP). However, not all of these methods are accurate or possible to use in young children and they all come with their own unique advantages and disadvantages. In the middle of the 1990's the first feasible system to measure body

composition via ADP was made available in adults (BodPod, Cosmed USA, Concord, USA) (69, 70). It was not until 2012 that children between the ages of two and six could be measured using ADP when the Pediatric Option for BodPod was created (71). Advantages of ADP over other methods include that it is: fast and non-invasive; safe (i.e. no radiation); and it allows for the measurement of all types of subjects (e.g. children, disabled, elderly, and obese) (70).

The Pediatric Option for BodPod includes the test chamber (i.e. BodPod plethysmograph), a pediatric seat, and an electronic weighing scale. Body volume is assessed using ADP, by measuring how much air the subject displaces when sitting inside the chamber; which is based upon the relationship between pressure and volume as described by Boyle's Law and Poisson's Law (69-71). Body volume is then adjusted for the surface area artifact as well as the thoracic gas volume (71). Body density can then be calculated by dividing the subject's weight by their body volume. FM% can then be computed assuming that the density of FM is 0.9007 kg/L (72) and a sex- and age-specific density value of FFM (73). The Pediatric Option for BodPod, which is a two-component model has been validated against the four-component model and has been found to be an accurate and reliable method for assessing body composition in young children (71).



Measuring a child in the Pediatric Option for BodPod

1.6 THE DOUBLY LABELLED WATER METHOD

The doubly labelled water method (DLW) was introduced in humans in the 1980's and this method is considered the gold standard to assess total energy expenditure (TEE) in free living conditions (74, 75). TEE in combination with basal metabolic rate (BMR) can be used to calculate activity energy expenditure (AEE) and physical activity level (PAL). Additionally, TEE can also be used to validate EI, as EI and TEE should be equal as long as the person is in energy balance (i.e. remains weight stable). Finally, isotope dilution can be used to estimate body composition. As this technique is non-invasive and safe it allows it to be easily applied in all types of populations, such as young children for a variety of purposes. When the DLW method is appropriately applied it is possible to acquire TEE estimates with an accuracy and precision between 1-3% and 2-8%, respectively (76).

1.6.1 Total energy expenditure

The DLW method involves the subject consuming a carefully measured dose of deuterium (^2H) and oxygen-18 (^{18}O), which are stable isotopes (74, 75). For young children DLW is often mixed with fruit juice and consumed with a straw in order to avoid spillage and ensure that the water is consumed in entirety. Urine samples are collected prior to dosing and for up to two weeks after dosing. The urine samples are then analyzed using isotope ratio mass spectrometry to determine the isotope enrichments throughout the period. The DLW method is built upon the assumptions that ^2H incorporates with body water and ^{18}O combines with both body water and carbon dioxide. Therefore, ^2H is lost only via water, whereas ^{18}O is lost as both water and carbon dioxide. Carbon dioxide production can then be calculated as the elimination rate of ^{18}O minus the elimination rate of ^2H (77). Using the Weir equation (78) and a food quotient (usually 0.85) (79) the carbon dioxide elimination rate can be used to calculate TEE.

1.6.2 Energy expenditure in response to physical activity

AEE and PAL can be calculated as TEE minus BMR (corrected for dietary induced thermogenesis) and TEE divided by BMR, respectively. Measures of BMR can be acquired via indirect calorimetry; however, due to the fact that BMR needs to be measured when a subject is lying still and fasting it is not able to be done in young children. Instead, prediction equations based on age and sex can be used to estimate BMR (80). AEE and PAL provide estimates of the energy utilized for physical activity (81) under free-living conditions. Energy expenditure estimates assessed using the DLW method are considered the reference standard for physical activity assessment methods (77).

1.6.3 Body composition

Isotope dilution can be used to assess body composition through using a carefully measured dose of either ^2H or ^{18}O (or a combination of both isotopes) corresponding to the subject's weight. The amount(s) of the stable isotope(s) present in the urine samples collected before and after dosing is determined using isotope ratio mass spectrometry and total body water

(TBW) can then be calculated. FFM can then be computed using the hydration coefficient, which is the portion of FFM that consists of water by dividing TBW by the hydration coefficient. It is important to note that the hydration coefficient varies throughout the life course with infants having the highest hydration coefficient (14, 72). For instance, at birth, 5 years of age, and in adulthood hydration values are approximately 81% (14), 77% (14, 72), and 73% (72), respectively.

1.7 DIETARY ASSESSMENT

Methods for assessing dietary intake have remained relatively constant over the years. Prospective methods for assessing diet and EI include both the weighed and estimated food records; whereas 24hr dietary recalls and food frequency questionnaires are considered retrospective methods. All of these methods come with their own set of limitations and are all time-consuming and burdensome on the participant or proxy (if the participant is a young child). Burrows et al. (82) conducted a systematic review investigating the accuracy of traditional dietary assessment methods against TEE assessed using the DLW method in children and found that EI was misreported in all studies. Both significant under- and over-reporting have been found in children and adolescents (82, 83), whereas usually only under-reporting was found in adults (83). Specifically in pre-school children differences in EI and TEE has varied between -14% and +59% (84).

New dietary methods that reduce participant burden, are easily administered, and can be scaled up are needed. The use of mobile phones to assess dietary intake has piqued interest in recent years. These methods usually involve participants taking pictures of the foods and beverages they consume throughout the day and sending them via SMS or email to the research team. Two reviews have reported that participants favored mobile phone based dietary assessment methods over traditional ones (85, 86). Thus far, the majority of these new assessment methods have only been tested in pilot and feasibility studies (86). Tool for energy balance in children (TECH) is a mobile phone based dietary assessment method to assess energy and food intake in young children, which was developed by our research group. In a pilot study, one day of food recordings assessed using TECH were compared to TEE measured via the DLW method. Some promising results were obtained as mean EI assessed using TECH was not statistically different from the mean TEE (87). Dietary assessment methods such as TECH need to be further tested to see whether these methods can begin to replace the traditional assessment methods.



1.8 PHYSICAL ACTIVITY ASSESSMENT

Physical activity can be measured subjectively or objectively. Subjective measures include physical activity questionnaires and activity diaries; whereas objective measures include pedometers and accelerometers.

Accelerometers are devices that capture the body's accelerations and are commonly used to measure physical activity, sedentary time, energy expenditure, and sleep related behaviors (88). Accelerometers have a distinct advantage over pedometers as they have the ability to obtain information on the intensity and duration of the physical activity performed (89). However, accelerometers as with pedometers have a limited ability to capture energy expenditure when skating, cycling, and performing load-bearing activities. Furthermore, the majority of accelerometers are not waterproof and thus miss all activities performed during water-based activities (90). There are two main types of accelerometers, uniaxial and triaxial. Uniaxial accelerometers measure acceleration in one plane (horizontal), whereas the triaxial accelerometer measures in three planes (horizontal, vertical, and diagonal) (91). As the technology for accelerometers developed it has allowed the sampling intervals (epochs) to become shorter, from one minute down to one second. The shorter epochs are recommended for young children due to the random nature of their activity patterns (90, 92).

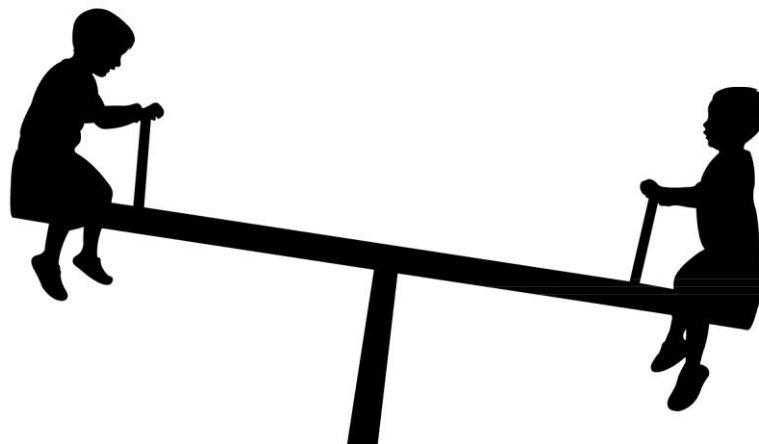
There are numerous brands of accelerometers, with the ActiGraph being the most commonly used in research (88) and each can be worn on a different part of the body (e.g. wrist, waist, hip etc.). Prediction equations to determine energy expenditure and cut-points to define physical activity intensities must be determined for each type of accelerometer, placement site, and population it is to be used in (88). In the past few years there has been an increase in the number of studies using wrist-worn monitors as it was believed they would increase compliance (93). For instance, large-scale studies such as NHANES have switched from the traditional waist-worn accelerometers to the wrist-worn ones (94). This allows the accelerometers to be worn for 24 hours per day which has significantly increased compliance rates (94-96). One study has compared physical activity intensities using the hip- and wrist-worn placement using the ActiGraph GT3X+ in pre-school children and found that the mean vector magnitude (VM) counts per minute as well as the total VM counts differed significantly between placement sites. More specifically they found greater sedentary time in the hip-worn monitor and higher MVPA in the wrist-worn monitor (97). However, due to the change in placement site of the accelerometers new validation studies are needed to evaluate the ability of the monitors to predict energy expenditure in various populations. Waist-worn accelerometers have been validated to predict AEE under free-living conditions in pre-school aged children (81); however, there is also a need for wrist-worn accelerometers to be validated in this population as well.

2 AIMS

The overall aims of this thesis were: (i) to evaluate the validity of a new dietary assessment tool (TECH) as well as the ActiGraph wGT3x-BT accelerometer and (ii) to determine whether a mHealth intervention (MINISTOP) targeted towards parents could improve body composition, dietary habits, physical activity, and sedentary behavior in their 4.5 year old children. The study protocol (Paper I) is included in this thesis to provide an overview for Papers II through V.

The specific aims were:

1. To evaluate the validity of reported energy and food intake assessed using TECH against TEE measured via the DLW method and 24 hour dietary recalls, respectively (Paper II).
2. To evaluate the capacity of the wrist-worn ActiGraph wGT3x-BT triaxial accelerometer to capture variations in free living AEE and to assess wear compliance of the accelerometers (Paper III).
3. To assess the effectiveness of the MINISTOP intervention on body composition, intakes of fruits, vegetables, candy, and sweetened beverages, as well as the amount of time spent sedentary and in MVPA after the intervention, i.e. 6-months after baseline (Paper IV).
4. To investigate if the MINISTOP intervention 12-months after baseline improved FMI and had a maintained effect on a composite score (made up of FMI as well as dietary and physical activity variables) (Paper V).



3 MATERIALS AND METHODS

3.1 STUDY DESIGN AND POPULATION

3.1.1.1 *The MINISTOP trial*

The MINISTOP trial was a population based, two-arm parallel RCT, conducted in Östergötland Sweden. For each assessment period (baseline, 6-month follow-up, and 12-month follow-up) the children came to Linköping University Hospital to assess body composition and physical fitness. In the two week period after the assessment at the hospital, diet and physical activity were assessed. The parents in the intervention group received the MINISTOP app for their smartphones and the parents in the control group were given a handout which provided information on physical activity and a healthy diet for pre-school aged children. A protocol for the MINISTOP trial was published in 2015 (Paper I) and the trial was registered at ClinicalTrials.gov (NCT02021786; 20 December 2013). The reporting of this trial followed the Consolidated Standards of Reporting Trials statement (98) and the EHEALTH checklist version 1.6.1 (99).

Within the MINISTOP trial a nested validation study was conducted in order to validate the methods used to assess diet (Paper II) (100), physical activity (Paper III), as well as body composition (not included in this thesis) (101).

3.1.1.2 *Participants and recruitment*

Figure 1 presents an overview of the MINISTOP trial from recruitment to the 12-month follow-up and **Table 1** describes each of the five studies included in this thesis. Using Statistics Sweden, letters were sent out to all parents and caregivers of all four year old children born between July 2009 and February 2010 living in the county of Östergötland in Sweden. A total of 3368 letters were sent out and 593 parents or caregivers responded to the letter. Two hundred and thirty-six children were excluded ($n = 36$ for not meeting the inclusion criteria and $n = 200$ declined to participate).

Inclusion criteria consisted of:

- Parent(s) having a four year old child and living in the county of Östergötland.
- Having the ability to have their child come to the baseline assessment at 4.5 years \pm 2 months of age.
- Having one parent that could speak and read Swedish sufficiently well.

Exclusion criteria consisted of:

- If the child had a neurological or endocrine disorder which could possibly affect body composition or size.
- If one of the parents had been diagnosed with a psychological or physical disease which would make the study too demanding for them.

A total of 357 children came to the baseline assessment at Linköping University Hospital. Forty-two children did not complete the baseline assessments leaving 315 children to be randomized. These children were randomized into the intervention or control group in a 1:1 ratio using a random allocation sequence in blocks of ten, leading to 156 children in the intervention group and 159 children in the control group. Participants were unable to be blinded to their group allocation owing to the nature of the intervention; however, outcome assessors were blinded to the group allocation. At the end of intervention follow-up (i.e. 6-months after baseline) and at the 12-month follow-up 281 children (89.2%) and 263 children (83.5%) had complete outcome measures.

Recruitment for Papers II and III (the validation studies) occurred when the child and parent(s) were returning for the 12-month follow-up visit. The parents were asked sequentially in the order of their appointments if they would like to participate in a study to validate the methodologies being used in the MINISTOP trial. Recruitment ended when 40 parents agreed for their child to participate, with a total of 45 families being asked to partake. Due to one child having missing data, only 39 children were included in Paper II.

3.1.1.3 Ethics

The MINISTOP trial was conducted in accordance with the guidelines of the Declaration of Helsinki. The Research and Ethics Committee, Stockholm, Sweden approved this study on the 10th of October 2013 (2013/1607-31/5) and the 19th of December 2013 (2013/2250-32). Informed consent was collected from both parents before the first measurement.

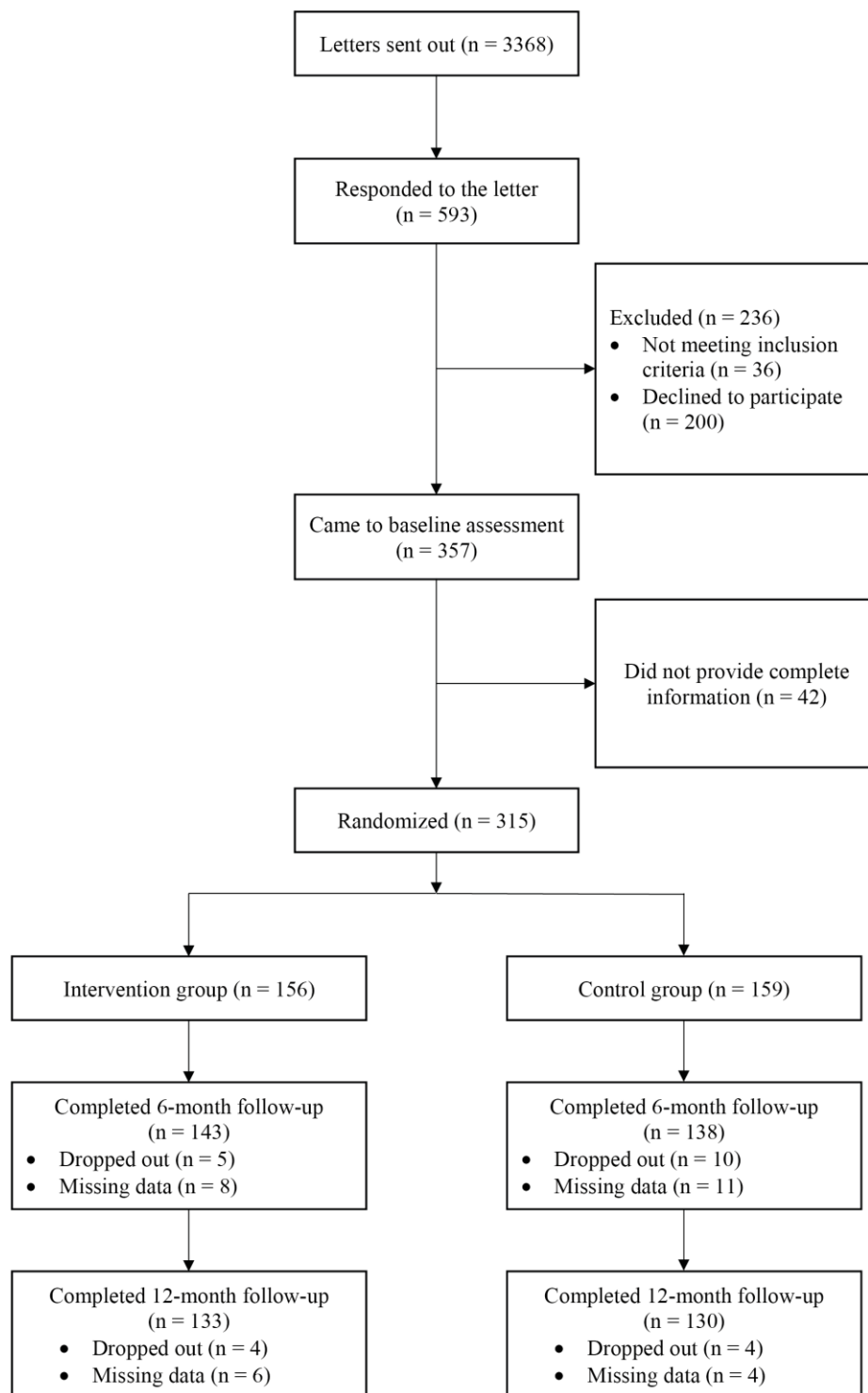


Figure 1. Flowchart from recruitment to the 12-month follow-up for the MINISTOP trial.

Table. 1 Overview of the studies included in this thesis.

	Paper I	Paper II	Paper III	Paper IV	Paper V
Aim(s)	To outline the study design and methodology used in the MINISTOP trial.	To compare energy intake (TECH) with total energy expenditure (doubly labelled To compare the intakes of certain foods acquired using TECH with those measured using 24hr dietary recalls.	To evaluate the capacity of the wrist-worn ActiGraph wGT3x-BT accelerometer to predict free-living activity energy expenditure. To assess wear compliance of the ActiGraph using a 7-day, 24hr protocol.	To assess the effectiveness of a mHealth obesity prevention program (MINISTOP) on body composition, dietary habits, as well as physical activity and sedentary behaviors.	To investigate if the MINISTOP intervention improved body composition and had a maintained effect on a composite score 12-months after baseline.
Design	Study protocol	Cross-sectional	Cross-sectional	Randomized controlled trial	Randomized controlled trial
Participants	-	39 children at 5.5 years of age	40 children at 5.5 years of age	281 children at 4.5 and 5 years of age	263 children at 4.5 and 5.5 years of age
Methods & Variables	-	Energy metabolism, energy and food intake (TECH and 24hr dietary recalls)	Energy metabolism, body composition (isotope dilution), and physical activity (ActiGraph)	Body composition (ADP), food intake (TECH), and physical activity (ActiGraph)	Body composition (ADP), food intake (TECH), physical activity (ActiGraph)

TECH, Tool for Energy Balance in Children; mHealth, Mobile health; ADP, Air displacement plethysmography

3.2 INTERVENTION

The MINISTOP intervention (i.e. MINISTOP app) was created by a team of researchers with expertise in the fields of nutrition, physical activity, medicine, behavioral science, psychology, engineering, and statistics. The content provided in the app was based upon the Social Cognitive Theory (102), behavior change techniques known to influence lifestyle change (103), and evidence based recommendations for obesity interventions in young children (104).

The intervention was composed of comprehensive information as well as push notifications utilizing the existing guidelines for a healthy diet and physical activity in pre-school aged children (105). The MINISTOP app comprised of 12 themes that changed bi-weekly. The 12

themes included were: healthy foods in general; breakfast; healthy small meals; physical activity and sedentary behavior; candy and sweets; fruits and vegetables; drinks; eating between meals; fast food; sleep; food outside the home; and food at special occasions. For every theme, general information, advice, and strategies were provided to aid the parents in changing unwanted behaviors. Parents also had the possibility to record their child's daily intake of fruits and vegetables, sweetened beverages, candy and salty snacks, as well as physical activity and sedentary behavior. At the end of each week the parents received feedback by means of bar graphs as well as by colors via "stop-light" indicators (i.e. green meant the child was meeting the recommendations; yellow meant the child was close to meeting the recommendations; red meant the child was far from meeting the recommendations; and gray meant they have not registered any parameters). This was a voluntary function within the app; however, it was highly recommended that the parent's register the parameters at least twice a week. These parameters were not being used as outcome measures and this feature was built into the app to promote motivation and compliance. Furthermore, within the app the parents had access to four weeks of dinner recipes with grocery lists which were created for kids by a dietician. Finally, the parents also had the ability to contact a dietician and/or psychologist through the app and ask questions pertaining specifically to their child. **Figures 2 and 3** are screenshots from the MINISTOP app demonstrating some of the functions.



Figure 2. The screen shot to the left is the main screen in the MINISTOP app and the image to the right is an example of a push notification the parents would receive.

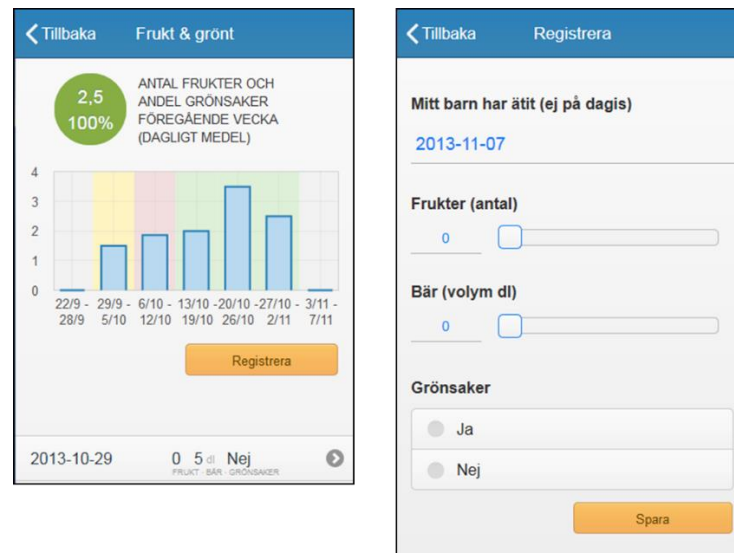


Figure 3. The screen shot to the right is how the parents register the amount of fruits, berries, and vegetables their child has consumed and the image to the left is an example of the type of feedback the parents would receive at the end of each week.

3.3 CONTROL

The parents of the children in the control group each received a hand-out on healthy eating, physical activity, and sedentary behavior for four to five year old children. The information included in the hand-outs were based on existing guidelines from the National Food Agency of Sweden (105).

3.4 MEASURES

3.4.1 Anthropometric variables (Papers II, III, IV, and V)

At baseline, the 6-month follow-up, and the 12-month follow-up weight, to the nearest gram, was measured when the children were wearing underwear using the electronic scale from the BodPod (COSMED USA, Inc., Concord, CA, USA). Height was then measured using a wall stadiometer to the nearest 0.1cm. BMI was calculated as:

$$\text{BMI (kg/m}^2\text{)} = \text{weight (kg)} / \text{height (m)}^2$$

The cut-points by Cole et al. (62) were utilized to classify the children into weight status categories. Weight-for-age and height-for-age z-scores were also computed using Swedish reference data (106).

3.4.2 Doubly labelled water method (Papers II and III)

Before the final assessment, parents of the children participating in the nested validation study ($n = 40$) were instructed to take two urine samples from their child and bring them with them to the Linköping University Hospital. Each child was then given an accurately weighed dose of stable isotopes ($0.14\text{g } ^2\text{H}_2\text{O}$ and $0.35\text{g H}_2^{18}\text{O}$ per kilogram of body weight) mixed with fruit juice as described in detail in Papers II and III. During the following two week

period parents took five urine samples (days 1, 5, 7, 10, and 14). The samples were kept in glass vials with an aluminum-lined screw cap and were stored at four degrees Celsius until all samples were collected and thereafter they were stored at -20 degrees Celsius until they were analyzed. The Finnigan MAT Delta Plus Isotope-Ratio Mass Spectrometer (ThermoFinnigan, Gothenburg, Sweden) (107) was used to analyze both the pre and post urine samples as well as the dose for ^2H and ^{18}O enrichments. The ^2H and ^{18}O dilution spaces (N_D and N_O , respectively) were calculated using zero time enrichments obtained from the exponential isotope disappearance curves that provided the ^2H and ^{18}O elimination rates, respectively. The method by Davies et al. (108) was used to calculate carbon dioxide production, using the assumption that 27.1% of the water losses were fractionated. The quotient between the N_D and the N_O was 1.039 ± 0.008 for both the 39 children in Paper II and the 40 children in Paper III.

3.4.2.1 Total energy expenditure

TEE was computed from carbon dioxide production using the Weir equation (78) assuming a food quotient of 0.85 (79).

3.4.2.2 Activity energy expenditure

A predicted BMR using the equations provided in the Nordic Nutrient Recommendations, which were based on weight (80) were used to compute AEE and PAL. The following equation was used to compute AEE and PAL:

$$\text{AEE (kJ/24hr)} = (\text{TEE (kJ/24hr)} \times 0.9) - \text{BMR (kJ/24hr)}$$

The above equation assumed that dietary induced thermogenesis corresponded to 10% of TEE.

$$\text{PAL} = \text{TEE (kJ/24hr)} / \text{BMR (kJ/24hr)}$$

3.4.3 Body composition (Papers III, IV, and V)

3.4.3.1 Isotope dilution

In Paper III body composition was assessed using isotope dilution as described in the section above. TBW and body composition were computed using the following equations:

$$\text{TBW} = [(N_D / 1.041) + (N_O / 1.007)] / 2 \quad (74)$$

$$\text{FFM}_{\text{ISO}} (\text{kg}) = \text{TBW} / 0.764 \quad (72)$$

$$\text{FM}_{\text{ISO}} (\text{kg}) = \text{weight (kg)} - \text{FFM}_{\text{ISO}} (\text{kg})$$

3.4.3.2 Air displacement plethysmography

In the MINISTOP trial body composition was assessed by means of ADP using the Pediatric Option for BodPod (COSMED USA, Inc., Concord, CA, USA). Body volume was measured

using the BodPod and adjusted for surface area artifact and thoracic gas volume. Body density was then calculated as:

$$\text{Body density} = \text{body weight (kg)} / \text{body volume}$$

Using Lohman's FFM density values (73) and assuming the density of FM is 0.9007 kg/L (72) FM% was calculated. FM_{ADP} and FFM_{ADP} were then calculated using the following equations:

$$\text{FM}_{\text{ADP}} (\text{kg}) = (\text{FM}\% / 100) \times \text{weight (kg)}$$

$$\text{FFM}_{\text{ADP}} (\text{kg}) = \text{weight (kg)} - \text{FM}_{\text{ADP}} (\text{kg})$$

3.4.3.3 Bioelectrical impedance

Even though previous data has shown good compliance for pre-school children sitting in the BodPod (64), when the MINISTOP trial was planned body composition was also assessed using the Tanita SC-240 foot-to-foot body composition analyzer (Tanita Cooperation, Tokyo, Japan) as a back-up measure. All measurements were collected at 50 Hz and the child's FM% was collected using the standard setting after imputing the child's sex, age, and height. FM% was then predicted from the Tanita for the children that refused to be measured in the BodPod by using prediction equations derived from the children who had body composition assessed using both methodologies. FM and FFM were then calculated using the aforementioned equations. Even though results from the nested validation study within MINISTOP confirmed that bioelectrical impedance is relatively inaccurate in pre-school children (101), this was not a major issue as only 12 (4%) children refused to be measured in the BodPod. As reported in Paper IV the main findings were not affected by the inclusion of these children.

3.4.3.4 Fat mass index and fat free mass index

The FMI_{ADP} and FFMI_{ADP} were calculated as:

$$\text{FMI}_{\text{ADP}} (\text{kg/m}^2) = \text{FM}_{\text{ADP}} (\text{kg}) / \text{height (m)}^2$$

$$\text{FFMI}_{\text{ADP}} (\text{kg/m}^2) = \text{FFM}_{\text{ADP}} (\text{kg}) / \text{height (m)}^2$$

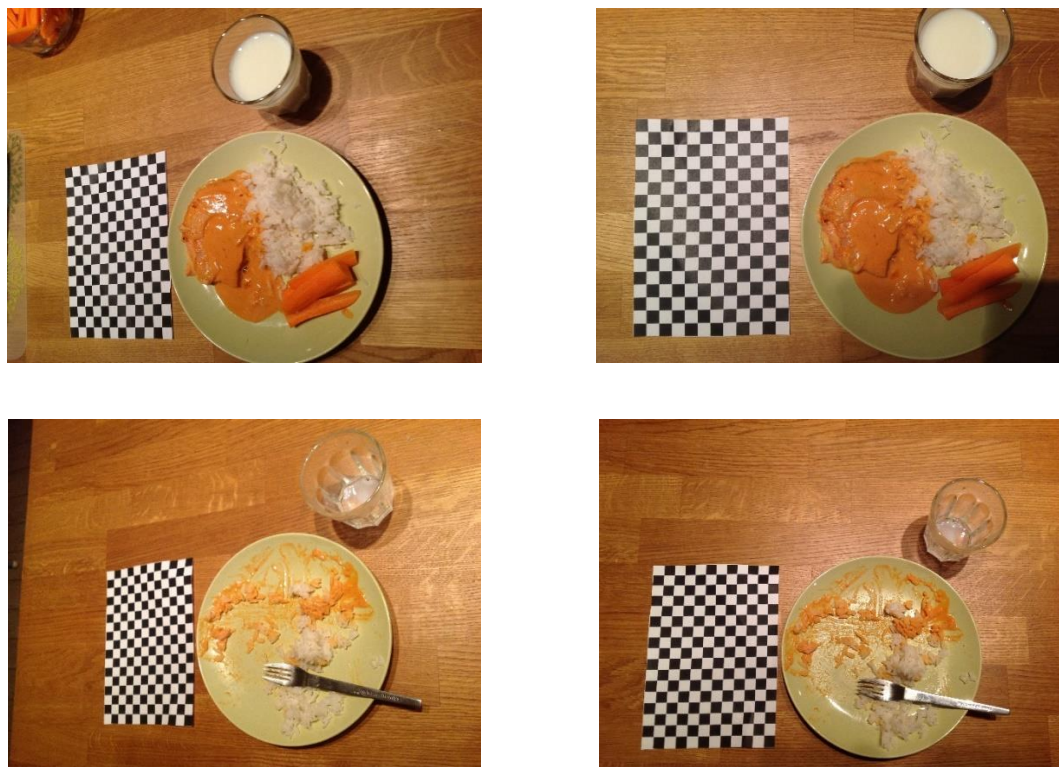
3.4.4 Dietary assessment (Papers II, IV, and V)

3.4.4.1 Tool for Energy Balance in Children (TECH)

The method for assessing diet in the MINISTOP trial was TECH. For this method parents chose four days when they were home with their child, in the following two-week period after they were at the Linköping University Hospital. Parents were informed via oral and written instructions that they were to take two pictures before and after every food or beverage their child consumed using their smartphone. If a child had a second or third serving parents were also instructed to take pictures in the same manner. All pictures were then sent to us via SMS or email along with some basic information regarding the food items or beverages (e.g. fat percentage in milk or yogurt, butter or margarine, or real or diet soda).

Figure 4 displays an example of what the parents would send us. A trained nutritionist went through the pictures as soon as possible to ensure they were complete and all information was provided. If vital pictures or descriptions were missing the parents, were contacted for complimentary information. At the baseline assessment all families were provided with a plate, bowl, and cup and instructed to use these during the measurement period. They were also given a fiducial marker and asked to include this in all pictures. The china as well as the fiducial marker were to aid the nutritionists in estimating the amount of foods and beverages consumed.

Two trained nutritionists reviewed all of the food pictures and calculated EI (only for Paper II) as well as the amount of fruits, vegetables, candy, bakery products, ice cream, fruit juice, and sweetened beverages consumed per day (Papers II, IV, and V). In order to accurately estimate portion sizes a compendium of pictures, of foods commonly consumed by Swedish pre-school children in varying amounts was created using the standardized china. For bakery products and fruit, standardized weights, which were provided from the Swedish Food Agency were utilized (109). The amount of food (in grams) and beverages (in milliliters) were estimated as the difference between the before and after pictures, including all servings. For Paper II, EI per day was calculated from the intakes of all foods and beverages via linkage to the Swedish Food Database (110) and the intakes of the eight food and beverage groups stated above were computed. High inter- and intra-rater reliability was observed between the nutritionists (111).



1.5% milk, sausage, sauce made with full fat crème fraiche and 3% milk

Figure 4. The top two and bottom two pictures are the before and after pictures, respectively and the text is the information the parents provided about the meal.

3.4.4.2 24hr dietary recalls

The 24hr dietary recalls were used in Paper II to compare intakes of foods and beverages as no gold standard exists. For each of the 40 families participating in the nested validation study four scheduled telephone dietary recalls (112) were performed using the same days as the parents took the food pictures. At the beginning of each interview the parents were told not to look at any of the food pictures they had taken. Parents were then asked about their child's food and beverage consumption from the previous day and asked to use household measures (e.g. deciliters or tablespoons) or descriptive words such as slice (for bread) or piece (for candy). Information regarding the types of foods as well as the cooking methods were also collected. EI and the grams for each of the food groups were then calculated using the same methods as TECH.

3.4.5 Physical activity and sedentary behavior assessment (Papers III, IV, and V)

The ActiGraph wGT3x-BT accelerometer (ActiGraph Corporation, Pensacola, FL, USA) was used to assess physical activity and sedentary behavior. Starting the day after the measurement at the hospital the children wore the monitor on their non-dominant wrist for seven consecutive days (24hrs per day). The parents were given a log book and they were asked to record when and why they removed the monitor. The only time they were supposed to remove the ActiGraph was for any water based activities (e.g. going to the pool/beach or showering/bathing). The ActiGraph was set to collect data at 50Hz and a valid day was when the child had greater or equal to 600 minutes of awake wear time (23). Non-wear time was accessed using the raw accelerations in a process that was adapted from Van Hees et al. (24, 113). The Sadeh algorithm (114, 115) was used to classify the worn time into sleep and awake periods.

For Paper III, using the ActiLife software Version 6.13.0 (ActiGraph Corporation, Pensacola, FL, USA) the low frequency filter was used to process the raw data into filtered sum of VM in one second epochs. The mean per minute filtered VM for all worn time (mean VM total) and mean per minute filtered VM for time classified as awake worn time (mean VM waking) were then computed and expressed as counts per minute (cpm).

For Paper IV and V, again using the ActiLife software (version 6.13.0) the low frequency filter was used to process the raw data into the filtered sum of VM in ten second epochs. We then used the cut-points created by Chandler et al. (116) to classify the children into activity levels (sedentary VM < 305 and MVPA VM \geq 818).

3.4.6 Demographic measures (Papers II, III, IV, and V)

At the baseline measurement, all parents were asked to fill in a demographic questionnaire as well as report their own weight and height.

3.5 STATISTICAL ANALYSES

3.5.1 Statistical methods

Table 2 provides an overview of the statistical analyses used in Papers II through V (Paper I is not included as it is the study protocol). In all of the studies SPSS version 22 or 23 (IBM, Armonk, NY, USA) were used to analyze the data. All statistical tests were two-sided using a 5% level of significance.

Table 2. Statistical methods utilized in each study.

	Paper II	Paper III	Paper IV	Paper V
Descriptive statistics	x	x	x	x
Paired samples t-test	x			
Wilcoxon signed rank test	x			
Pearson correlation	x			
Spearman rank order correlation	x			
Bland and Altman procedure	x			
Linear regression	x	x		
Wilcoxon's rank-sum test			x	x
Exact logistic regression			x	x

3.5.2 Main analyses

3.5.2.1 Paper II

Using paired samples t-tests and the Wilcoxon signed rank test mean differences between EI and TEE and differences in the mean intakes in the eight food groups were assessed, respectively. The Bland and Altman procedure (117) was used to assess the agreement between EI and TEE by plotting the differences between the two methods on the y-axis and the average of the two methods on the x-axis. Linear regression was then used to test for a trend between the x and y axis. For normally distributed and non-normally distributed data Pearson or Spearman correlations, respectively were used to assess the relationship between variables.

3.5.2.2 Paper III

Multiple linear regression analyses were used to determine the amount of variation in AEE and PAL that could be explained by the ActiGraph outputs alone (mean VM total or mean VM waking) and in combination with sex, age, and weight or with sex, age, FFM_{ISO}, and FFM_{ISO}.

3.5.2.3 *Papers IV and V*

In a completer's only analysis, the Wilcoxon's rank-sum test was used to test for differences between the intervention group and the control group for the primary outcome (FMI_{ADP}) and the secondary outcomes (intakes of fruits, vegetables, candy, and sweetened beverages as well as time spent sedentary and in MVPA). In secondary analyses two composite scores were created, a seven component and a six component composite score which included all primary and secondary outcomes and only the secondary outcomes, respectively. For each component the child received either 1 or 0 (i.e. meeting or not meeting a pre-defined goal based on relevant guidelines, respectively). At all three measurement points, scores were the sum of the individual components with a range from 0 to 7 or 0 to 6. The difference in the composite scores (follow-up - baseline) were calculated. If a child scored zero or had a negative score difference, this meant the child did not respond to the intervention, whereas a positive score difference indicated they responded to the intervention. Exact logistic regression was used to compute the success rates between the intervention and control groups and were expressed as odds ratios (OR).

In complementary analyses we also investigated whether the intervention was more successful in the children with a higher FMI_{ADP} by dividing the children into two groups using the median at baseline (4.11 kg/m²). Furthermore, potential confounding by parental socioeconomic position was tested for using a stratified Wilcoxon's rank-sum test using parental education (only in Paper IV). Lastly, all analyses were re-ran excluding the 12 children who were not measured in the BodPod (only in Paper IV).

In Paper IV, in sensitivity analyses we tested the robustness of our data using a series of analyses (118). Firstly, the group specific first and third quartiles were used to replace missing data. Secondly, to find the tipping point (i.e. the reversal of the study conclusion for the seven component composite score) we imputed favorable values for the control group (i.e. one, meeting the pre-defined goal) until the intervention effect disappeared. Lastly, an extreme approach was used in which drop-outs in the control group were considered an intervention success and drop-outs in the intervention group an intervention failure.

4 RESULTS

4.1 MINISTOP STUDY POPULATIONS

Table 3 presents the baseline characteristics of the parents and **Table 4** displays the baseline characteristics of the children participating in the MINISTOP trial (Papers IV and V). Two children had corrupt ActiGraph files and were therefore excluded so the total study sample of the MINISTOP trial was 313. There were no differences observed for the baseline characteristics between the intervention and control group. At both the 6-month and 12-month follow-ups there were no differences in the baseline characteristics between the children that provided complete data and those that did not.

Characteristics of the MINISTOP trial sample in comparison to the whole study sample (i.e. all families that were invited to participate in MINISTOP) are provided in **Table 5**. There were no major differences observed between the families that participated and all of the invited families in regards to the children's sex, birth country, or residence. There was however, somewhat lower participation rates observed in parents with lower incomes and those in the lowest age group (20-29 years). Due to one of the parents needing to be able to speak or read Swedish sufficiently well in order to participate there was a greater number of parents born in Sweden (91%) compared to the whole study sample (75%) participating in the MINISTOP trial.

Table 3. Baseline characteristics of the 313 parents participating in the MINISTOP trial.

	Intervention (n = 155)	Control (n = 158)
<i>Mothers</i>		
Age (years)	36.0 ± 4.1	35.2 ± 4.4
BMI (kg/m ²) ¹	24.8 ± 4.5	23.9 ± 4.2
Education status ≥ university degree, % (n)	74 (114)	68 (107)
<i>Fathers</i>		
Age (years) ²	38.1 ± 5.1	38.1 ± 5.3
BMI (kg/m ²) ¹	25.3 ± 3.4	25.6 ± 3.6
Education status ≥ university degree, % (n) ³	59 (92)	55 (87)

BMI, Body mass index.¹ BMI was missing for two mothers and three fathers in the control group. ² Age was missing for two fathers in the control group. ³ Education status was missing for one father in the intervention group and four fathers in the control group.

Table 4. Baseline characteristics of the 313 children participating in the MINISTOP trial, given as mean \pm standard deviation or percent (n).

	Intervention (n = 155)	Control (n = 158)
Sex (female)	45% (69)	47% (74)
Age (years)	4.5 \pm 0.1	4.5 \pm 0.1
Weight (kg)	18.5 \pm 2.6	18.2 \pm 2.4
Weight-for-age z-score ¹	0.00 \pm 1.16	-0.13 \pm 1.04
Height (cm)	107.6 \pm 4.2	107.6 \pm 4.3
Height-for-age z-score ¹	-0.03 \pm 0.97	-0.03 \pm 0.97
BMI (kg/m ²) ²	15.9 \pm 1.5	15.6 \pm 1.2
Waist circumference (cm) ³	53.7 \pm 3.9	53.3 \pm 3.4
Fat mass (%)	26.4 \pm 4.4	25.7 \pm 4.3
FMI _{ADP} (kg/m ²)	4.23 \pm 0.97	4.04 \pm 0.84
FFMI _{ADP} (kg/m ²)	11.69 \pm 0.98	11.60 \pm 0.94
Fruit intake (grams/day) ⁴	107 \pm 72	103 \pm 81
Vegetable intake (grams/day) ⁴	64 \pm 46	55 \pm 41
Candy intake (grams/day) ⁴	14 \pm 18	12 \pm 16
Sweetened beverage intake (ml/day) ⁴	69 \pm 72	54 \pm 69
Sedentary time (minutes/day) ⁵	477 \pm 49	479 \pm 55
MVPA (minutes/day) ⁵	101 \pm 26	100 \pm 25

BMI, Body mass index; FMI_{ADP}, Fat mass index measured using air displacement plethysmography; FFMI_{ADP}, Fat free mass index measured using air displacement plethysmography; MVPA, Moderate-to-vigorous physical activity. ¹ Calculated using Swedish reference data (106). ² Overweight and obese in the intervention group (n = 14, 9%; n = 3, 2%, respectively) and control group (n = 10, 6%; n = 1, 0.6%, respectively) (62). ³ The number of children in the intervention and control group with waist circumference was 154 and 156, respectively. ⁴ The number of recording days for the dietary components was 3.8 \pm 0.5 (intervention) and 3.7 \pm 0.6 (control). ⁵ The number of recording days for physical activity were 6.7 \pm 0.8 (intervention) and 6.4 \pm 1.3 (control).

Table 5. Characteristics of the whole study sample (parent or guardians¹ that received the invitation letter) and the MINISTOP sample (parent or guardians that participate in the MINISTOP trial with their child).

		Whole study sample (n = 3368) % (95% CI)	MINISTOP sample (n = 315) % (95% CI)
Child sex			
	Male	51.4 (49.7, 53.1)	53.0 (47.5, 58.5)
	Female	48.6 (46.9, 50.3)	47.0 (41.5, 52.7)
Child country of birth			
	Sweden	95.3 (94.6, 96.0)	98.1 (96.6, 99.6)
	Other	4.7 (4.0, 5.4)	1.9 (0.4, 3.4)
Child residence			
	Main cities	68.5 (67.0, 70.1)	70.5 (65.4, 75.5)
	Suburbs	3.0 (2.4, 3.5)	2.9 (1.0, 4.7)
	Larger cities	7.4 (6.5, 8.2)	5.1 (2.7, 7.5)
	Smaller cities or countryside	21.1 (19.8, 22.5)	21.5 (17.0, 26.1)
Parent or guardian 1, age			
	20 – 29 years	8.7 (7.8, 9.7)	2.5 (0.8, 4.3)
	30 – 39 years	54.8 (53.1, 56.5)	59.7 (54.3, 65.1)
	40 – 49 years	32.7 (31.1, 34.2)	35.3 (30.0, 40.5)
	50 – 59 years	3.4 (2.8, 4.0)	2.2 (0.6, 3.9)
	60 – 69 years	0.4 (0.2, 0.6)	0.3 (0.0, 0.9)
Parent or guardian 1, country of birth			
	Sweden	76.7 (75.3, 78.1)	91.4 (88.3, 94.5)
	Other	23.3 (21.9, 24.7)	8.6 (5.5, 11.7)
Parent or guardian1, income ²			
	None	6.1 (5.3, 6.9)	0.6 (0.0, 1.5)

	Very low	12.4 (11.2, 13.5)	4.1 (1.9, 6.3)
	Low	8.7 (7.7, 9.7)	5.7 (3.2, 8.3)
	Middle	17.8 (16.5, 19.1)	11.2 (7.6, 14.6)
	Middle/High	24.9 (23.5, 26.4)	27.6 (22.7, 32.6)
	High	30.1 (28.5, 31.6)	50.8 (45.3, 56.3)
Parent or guardian 2, age			
	20 – 29 years	17.4 (16.1, 18.6)	7.9 (5.0, 10.9)
	30 – 39 years	63.3 (61.7, 65.0)	75.6 (70.8, 80.3)
	40 – 49 years	13.8 (12.6, 14.9)	14.9 (11.0, 18.9)
	50 – 59 years	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)
	Unknown ³	5.5 (4.7, 6.3)	1.6 (0.2, 3.0)
Parent or guardian 2, country of birth			
	Sweden	73.3 (71.8, 74.8)	91.1 (88.0, 94.3)
	Other	21.1 (19.7, 22.5)	7.3 (4.4, 10.2)
	Unknown ³	5.6 (4.8, 6.4)	1.6 (0.2, 3.0)
Parent or guardian 2, income ²			
	None	6.3 (5.5, 7.1)	1.3 (0.0, 2.5)
	Very low	16.8 (15.5, 18.0)	8.9 (5.7, 12.0)
	Low	14.8 (13.6, 16.0)	16.2 (12.1, 20.3)
	Middle	22.6 (21.2, 24.0)	26.0 (21.2, 30.9)
	Middle/High	18.1 (16.8, 19.4)	20.0 (15.6, 24.4)
	High	15.8 (14.6, 17.0)	26.0 (21.2, 30.9)
	Unknown ³	5.6 (4.8, 6.4)	1.6 (0.2, 3.0)

CI, Confidence interval. ¹ We also use the word guardian since this information was obtained from Statistics Sweden where guardians are formally registered. The guardian is a parent or other caretaker. Parent or guardian 2 is the oldest guardian as defined by Statistics Sweden. ² Income per year categorized as very low (1 - 124 999 Swedish crowns), low (125 000 - 199 999 Swedish crowns), middle (200 000 - 279 999 Swedish crowns), middle/high (280 000 - 369 999 Swedish crowns), high (>370 000 - Swedish crowns). ³ For 188 children in the whole study sample, only one guardian was registered at Statistics Sweden. This is the case if one parent has single custody or the father is unknown. Thus, we lack information on country of birth and income on 188 guardians. For 3 of these 188 children, Statistics Sweden had a personal number, and thus age is only lacking for 185 guardians.

The descriptive characteristics of the children and parents participating in the nested validation studies for TECH (Paper II) and the ActiGraph wGT3x-BT (Paper III) are displayed in **Table 6**.

Table 6. Descriptive statistics for the participating children and parents in Papers II and III (n = 40)¹.

Characteristics	Mean \pm SD
<i>Children</i>	
Sex (female) % (n)	45% (18)
Age (years)	5.5 \pm 0.2
Weight (kg)	20.5 \pm 4.2
Weight for age z-score ²	-0.05 \pm 1.55
Height (cm)	114.2 \pm 4.4
Height for age z-score ²	0.00 \pm 0.90
BMI (kg/m ²) ³	15.6 \pm 2.3
<i>Parent, mothers</i>	
Age (years)	36.3 \pm 4.2
BMI (kg/m ²)	24.3 \pm 4.0
Education status \geq university degree, % (n)	72.5% (29)
<i>Parent, fathers</i>	
Age (years)	38.2 \pm 4.9
BMI (kg/m ²)	25.3 \pm 3.6
Education status \geq university degree, % (n)	65.0% (26)

BMI, Body mass index; SD, Standard deviation.¹ One child did not provide all information in the TECH validation (Paper II), therefore, that study included only 39 children. ² Calculated using Swedish reference values (106). ³ One (2.5%) and two (5.0%) children were classified as overweight and obese, respectively (62).

4.2 TECH VALIDATION (PAPER II)

Mean EI assessed using TECH (5820 ± 820 kJ/24hr) was not statistically different from TEE assessed using the DLW method (6040 ± 680 kJ/24hr) ($P = 0.064$). The Bland and Altman plot for EI (TECH) and TEE (DLW) is shown in **Figure 5**. The limits of agreement (± 2 SDs) were wide demonstrating that TECH is not ideal for assessing EI in individuals. However, there was no association observed between the average and the difference of EI and TEE ($P = 0.189$), demonstrating there was no systematic bias (i.e. there was no trend that the difference between EI and TEE differed across the various EI levels).

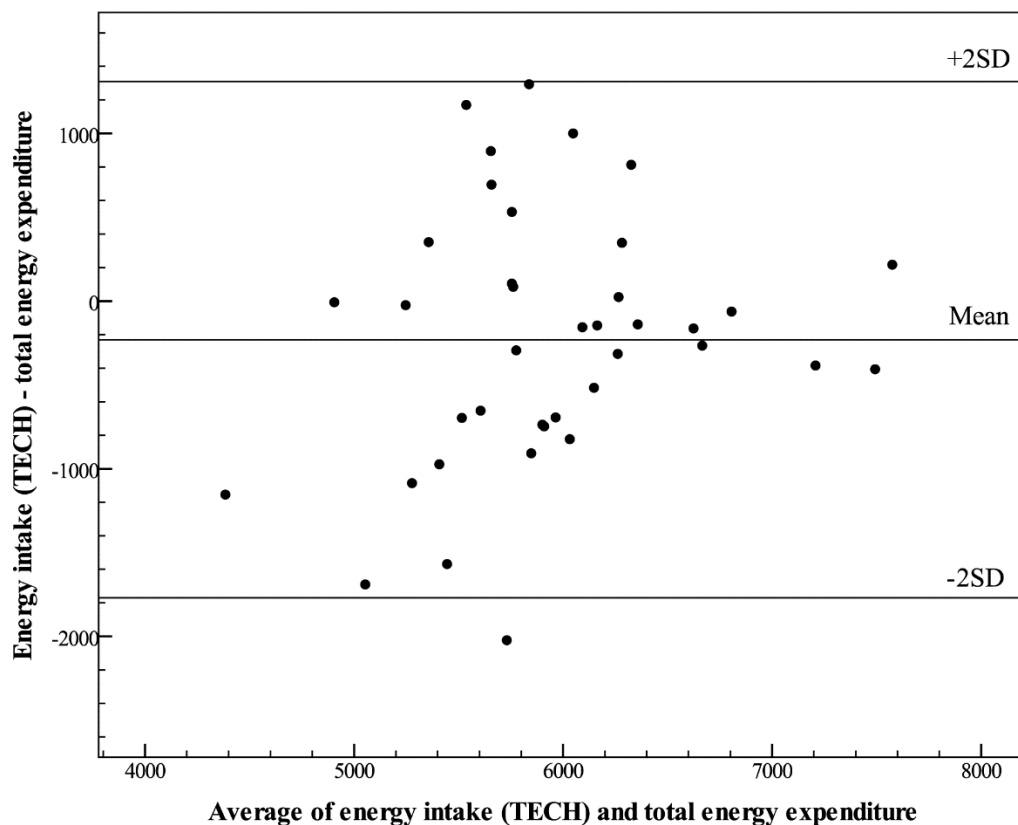


Figure 5. A Bland and Altman plot for 39 5.5 year old children showing energy intake (EI) (Tool for Energy Balance in Children, TECH) and total energy expenditure (TEE) (doubly labelled water, DLW). The average EI (TECH) minus the average TEE (DLW) was -220 kJ/24hr and the limits of agreement (2 standard deviations) was 1540 kJ/24hr. Regression equation: $y = 0.253x - 1733$ ($r = 0.215$, $P = 0.189$).

For the eight food categories assessed there were no significant differences observed between the mean values determined using TECH and 24hr dietary recalls (P -values: 0.087 – 0.728) and significant correlations ranging from 0.665 to 0.896 (all P -values < 0.001) were found.

Table 7 provides the average intakes of each of the eight food categories using TECH and 24hr dietary recalls. **Figure 6** presents the Bland and Altman plots for each of the categories and compares the intakes assessed using TECH and 24hr dietary recalls. For all plots there were wide limits of agreement. Only one trend was observed, for sweetened beverages between the average and difference of the two methods ($\rho = -0.333$, $P = 0.038$).

Table 7. Average intake of the eight food groups estimated using TECH and 24hr dietary recalls (n = 39).

<i>Food intakes (g/day)</i>	<i>TECH¹</i>	<i>24hr dietary recalls²</i>
Fruit	103 ± 65	110 ± 76
Vegetables	64 ± 49	67 ± 52
Fruits and vegetables ³	230 ± 138	227 ± 148
Fruit juice	56 ± 73	46 ± 89
Sweetened beverages	77 ± 93	90 ± 93
Candy	19 ± 22	15 ± 16
Ice cream	12 ± 19	11 ± 15
Bakery products	19 ± 14	18 ± 16

TECH, Tool for Energy Balance in Children. ¹ Number of recorded days using TECH: four days (n = 31, 79%); three days (n = 7, 18%); and two days (n = 1, 3%). ² Number of food days using 24hr dietary recalls: four days (n = 27, 70%); three days (n = 6, 15%); two days (n = 4, 10%); and one day (n = 2, 5%). ³ Fruits and vegetables is the sum of all the fruits, vegetables, and fruit juice consumed.

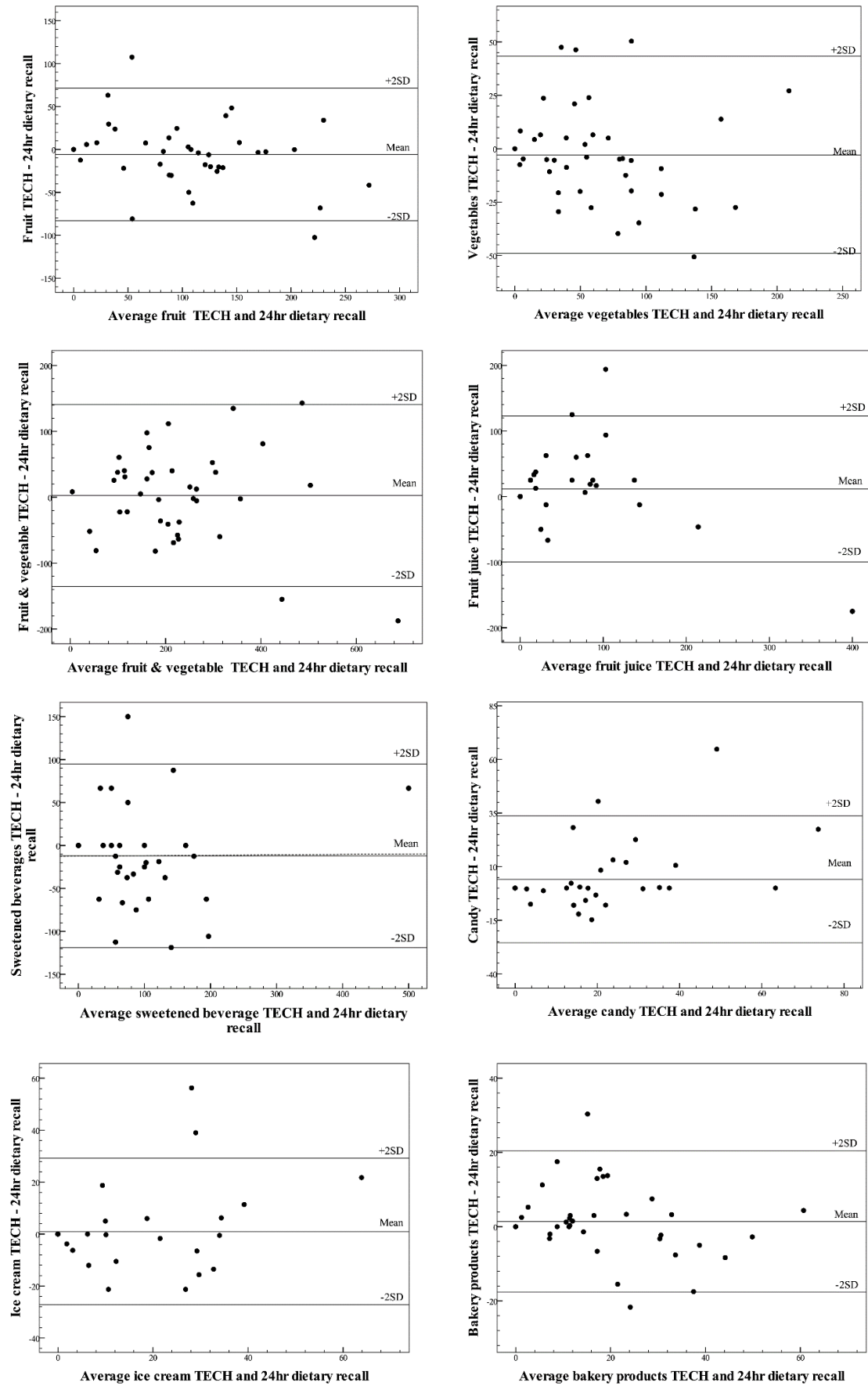


Figure 6. Bland and Altman plots for fruits, vegetables, fruits and vegetables, fruit juice, sweetened beverages, candy, ice cream, and bakery products.

4.3 ACTIGRAPH EVALUATION (PAPER III)

Table 8 presents the body composition, energy expenditure, and ActiGraph outputs for the 40 participating children. The results of the regression analyses when AEE is included as the dependent variable and mean VM total or mean VM waking as well as sex, age, weight, or FFM_{ISO} and FM_{ISO} are included as the independent variables are presented in **Table 9**. Alone mean VM total (model 1A) and mean VM waking (model 2A) were able to explain 14.3% ($P = 0.009$) and 23.5% ($P = 0.001$) of the variation in AEE, respectively. When sex, age, and weight were added into the models (models 1B and 2B) slightly more of the variation in AEE was explained for mean VM total (14.7%, $P = 0.048$) and mean VM waking (26.0%, $P = 0.005$). If weight was substituted for FFM_{ISO} and FM_{ISO} (models 1C and 2C) 57.6% ($P < 0.001$) and 62.4% ($P < 0.001$) of the variation in AEE was explained when using mean VM total and mean VM waking, respectively.

Table 8. Body composition, energy expenditure, and ActiGraph outputs of the children participating in Paper III (n = 40).

Characteristic	Mean \pm SD
FM _{ISO} (kg)	5.4 \pm 2.7
FFM _{ISO} (kg)	15.1 \pm 2.0
TEE (kJ/24hrs)	6040 \pm 680
AEE (kJ/24hrs)	1465 \pm 432
BMR (kJ/24hrs)	3970 \pm 400
Valid days ¹	6.8 \pm 0.6
Mean VM total (cpm)	3128 \pm 624
Mean VM waking (cpm)	4732 \pm 702
Awake worn time (min/day)	879 \pm 42
All non-wear time (min/day) ²	81 \pm 102

SD, Standard deviation; FM_{ISO}, Fat mass measured using isotope dilution; FFM_{ISO}, Fat free mass measured using isotope dilution; TEE, Total energy expenditure; AEE, Activity energy expenditure; BMR, Basal metabolic rate; Mean VM total, Daily mean of total filtered vector magnitude units during wear time; Mean VM waking, Daily mean of waking filtered vector magnitude units; cpm, Counts per minute. ¹ A valid day was defined as ≥ 600 minutes of awake wear time (23). ² Non-wear time was high as one male child did not wear the monitor at night. Analyses were run with and without this child and no differences were found.

Compliance to the ActiGraph protocol was good with:

- 85% (n = 34) wearing it for seven days.
- 10% (n = 4) wearing it for six days.
- 2.5% (n = 1) wearing it for five days.
- 2.5% (n = 1) wearing it for four days.

Table 9. Regression models for activity energy expenditure¹ and mean VM total and mean VM waking obtained using the ActiGraph (n = 40).

Model	Independent variables ²	Intercept	Unstandardized Beta	<i>P</i>	Adjusted R ²	SEE	<i>P</i> model
1A	Mean VM total	585.7	0.281	0.009	0.143	400	0.009
1B	Mean VM total	-1005.8	0.267	0.014	0.147	399	0.048
	Sex		-212.1	0.108			
	Age		333.0	0.457			
	Weight		5.59	0.717			
1C	Mean VM total	-1273.9	0.213	0.007	0.576	281	<0.001
	Sex		114.1	0.286			
	Age		-79.03	0.806			
	FFM _{ISO}		200.7	<0.001			
	FM _{ISO}		-125.5	<0.001			
2A	Mean VM waking	-5.84	0.311	0.001	0.235	378	0.001
2B	Mean VM waking	-1570.2	0.308	0.001	0.260	372	0.005
	Sex		-232.4	0.059			
	Age		328.7	0.430			
	Weight		5.43	0.705			
2C	Mean VM waking	-1655.8	0.230	0.001	0.624	265	<0.001
	Sex		76.18	0.450			
	Age		-49.17	0.871			
	FFM _{ISO}		187.7	<0.001			
	FM _{ISO}		-117.4	<0.001			

Mean VM total, Daily mean of total filtered vector magnitude units during wear time; Mean VM waking, Daily mean of waking filtered vector magnitude units; FFM_{ISO}, Fat free mass measured using isotope dilution; FM_{ISO}, Fat mass measured using isotope dilution; SEE, standard error of estimate for the model; cpm, Counts per minute. ¹Activity energy expenditure (kJ/24hr), dependent variable. ²Independent variable units: Mean VM total (cpm), Mean VM waking (cpm), Age (years), Weight (kg), FFM_{ISO} (kg), and FM_{ISO} (kg).

4.4 6-MONTH FOLLOW-UP INTERVENTION RESULTS (PAPER IV)

4.4.1 Efficacy of the intervention

Table 10 displays the differences between the 6-month follow-up and baseline for the primary and secondary outcomes for both the intervention and control groups. For FMI_{ADP}, the primary outcome, there was no difference observed between the values at the 6-month follow-up and baseline between the groups (mean difference: -0.03 kg/m^2 , $P = 0.922$). For the secondary outcomes, there was only one significant difference observed, which was for sweetened beverages, where the intervention group significantly decreased their intake in comparison to the control group ($P = 0.049$). A significant increase in FFMI_{ADP} was also observed in the intervention group compared to the control group between the 6-month follow-up and baseline (mean difference: $+0.14 \text{ kg/m}^2$, $P = 0.038$).

Table 10. Differences between 6-month follow-up and baseline in body composition, dietary, and physical activity variables for the intervention and control groups.

Characteristics	Intervention (n = 143) Mean \pm SD	Control (n = 138) Mean \pm SD	P-value ¹
Weight (kg)	$+1.42 \pm 0.81$	$+1.26 \pm 0.61$	0.432
Height (cm)	$+4.29 \pm 1.08$	$+4.32 \pm 1.16$	0.715
FMI _{ADP} (kg/m ²)	-0.23 ± 0.56	-0.20 ± 0.49	0.922
FFMI _{ADP} (kg/m ²)	$+0.15 \pm 0.55$	$+0.01 \pm 0.53$	0.038
Sedentary time (minutes/day) ²	$+3.6 \pm 48.0$	-1.6 ± 55.0	0.179
Sedentary time (% wear time) ²	-0.5 ± 4.9	-0.6 ± 5.0	0.385
MVPA (minutes/day) ²	$+9.3 \pm 24.2$	$+9.8 \pm 22.2$	0.589
MVPA (% wear time) ²	$+0.9 \pm 2.8$	$+1.1 \pm 2.5$	0.394
Fruit (grams/day) ³	$+2.9 \pm 78.9$	-12.1 ± 87.9	0.262
Vegetables (grams/day) ³	-6.7 ± 42.1	-3.6 ± 39.7	0.538
Candy (grams/day) ³	-0.7 ± 19.9	$+3.1 \pm 18.5$	0.106
Sweetened beverages (ml/day) ³	-12 ± 85	$+8 \pm 83$	0.049

SD, Standard deviation; FMI_{ADP}, Fat mass index measured using air displacement plethysmography; FFMI_{ADP}, Fat free mass index measured using air displacement plethysmography; MVPA, Moderate-to-vigorous physical activity.¹ Difference between intervention and control groups in the mean change from baseline assessed using the Wilcoxon rank-sum test. ² The number of recording days for physical activity at the 6-month follow-up were 6.4 ± 1.3 (intervention) and 6.6 ± 1.0 (control). ³ The number of recording days for food at the 6-month follow-up were 3.7 ± 0.6 (intervention) and 3.7 ± 0.6 (control).

The seven component composite scores (i.e. including primary and secondary outcomes) are displayed in **Table 11**. At the 6-month follow-up the intervention group significantly improved their seven component composite score difference in comparison to the control group ($P = 0.021$ between groups). The OR for increasing the seven component composite score for the intervention group compared to the control group was 1.49 (95% confidence interval (CI): 0.92, 2.42; $P = 0.11$). However, the OR for increasing the six component composite score (including only secondary outcomes, i.e. excluding FMI_{ADP}) for the intervention group compared to the control group was 1.99 (95% CI: 1.20, 3.30; $P = 0.008$). The main drivers for the significant changes in the composite score were the intakes of fruits and vegetables.

Table 11. Seven component composite score for the intervention (n = 143) and control (n = 138) groups at baseline and after the 6-month follow-up.

	Intervention		Control	
	Baseline	6-month follow-up	Baseline	6-month follow-up
Composite score ¹	3.52 ± 1.27	3.89 ± 1.37	3.65 ± 1.35	3.59 ± 1.49
Difference in composite score ²		+0.36 ± 1.47*		-0.06 ± 1.33
+1 or more in score difference (%) ³		42.7		33.3
0 in score difference (%) ⁴		32.2		32.6
-1 or less in score difference (%) ⁵		25.1		34.1

¹ Seven component composite score (i.e. includes the scores for: fat mass index measured by air displacement plethysmography, intake of fruits, vegetables, candy, and sweetened beverages, as well as moderate-to-vigorous physical activity and sedentary behavior). ² Difference in composite score was calculated as the difference between the composite score at the 6-month follow-up and at baseline. ³ The percentage of children that increased their composite score by one or more which is defined as a successful response to the intervention. ⁴ The percentage of children that had no change in their composite score which is defined as an unsuccessful response to the intervention. ⁵ The percentage of children that decreased their composite score by one or more which is defined as an unsuccessful response to the intervention. *Statistically significantly different than the corresponding value in the control group ($P = 0.021$), tested using the Wilcoxon rank-sum test.

4.4.2 Complementary analyses

The seven component composite scores for the children with a higher or lower FMI_{ADP} at baseline are presented in **Table 12**. For children with a higher FMI_{ADP} , those in the intervention group had a statistically significant improvement in their seven component composite score compared with their counterparts in the control group ($P = 0.019$). There were no significant differences in the seven component composite score observed for the children with a lower FMI_{ADP} between the intervention and control group ($P = 0.506$).

After adjustment for potential confounding by parental education the significant difference in the seven component composite score between the intervention and control group remained ($P = 0.019$). When excluding the 12 children who had their body composition assessed by bioelectrical impedance instead of the BodPod, all results remained unchanged.

Table 12. Seven component composite score¹ comparison for the children with higher and lower FMI_{ADP} for the intervention group (n = 143) and control group (n = 138) at baseline and at the 6-month follow-up.

	Intervention				Control			
	Baseline		6-month follow-up		Baseline		6-month follow-up	
	Lower FMI _{ADP} ⁶ (n=68)	Higher FMI _{ADP} ⁶ (n=75)	Lower FMI _{ADP} ⁶ (n=68)	Higher FMI _{ADP} ⁶ (n=75)	Lower FMI _{ADP} ⁶ (n=75)	Higher FMI _{ADP} ⁶ (n=63)	Lower FMI _{ADP} ⁶ (n=75)	Higher FMI _{ADP} ⁶ (n=63)
Composite score ¹	+3.97 ± 1.27	+3.12 ± 1.23	+4.01 ± 1.38	+3.77 ± 1.37	+3.89 ± 1.27	+3.37 ± 1.41	+3.76 ± 1.27	+3.40 ± 1.70
Difference in composite score ²			+0.04 ± 1.51	+0.65 ± 1.38*			-0.13 ± 1.34	+0.03 ± 1.33
+1 or more in score difference (%) ³			33.8	50.7			26.7	41.3
0 in score difference (%) ⁴			32.4	32.0			40.0	23.8
-1 or less in score difference (%) ⁵			33.8	17.3			33.3	34.9

FMI_{ADP}, Fat mass index measured using displacement plethysmography.¹ Seven component composite score (i.e. includes the scores for: FMI_{ADP}, intake of fruits, vegetables, candy, and sweetened beverages, as well as moderate-to-vigorous physical activity and sedentary behavior). ² Difference in composite score was calculated as the difference between the composite score at the 6-month follow-up and at baseline. ³ The percentage of children that increased their composite score by one or more which is defined as a successful response to the intervention. ⁴ The percentage of children that had no change in their composite score which is defined as an unsuccessful response to the intervention. ⁵ The percentage of children that decreased their composite score by one or more which is defined as an unsuccessful response to the intervention. ⁶ Lower is characterized by all of the children with a FMI_{ADP} equal or less than the median and higher is characterized by all of the children with a FMI_{ADP} greater than the median (median = 4.11 kg/m²) at baseline. *Statistically significantly different than the corresponding value in the control group ($P = 0.019$), tested using the Wilcoxon rank-sum test.

4.4.3 Sensitivity analyses

At the 6-month follow-up very few children had missing values or dropped-out. The reasons for missing values were: the child refusing to wear the ActiGraph ($n = 10$); parents not supplying complete food pictures because of time constraints ($n = 4$); the child missing both food pictures and the ActiGraph due to time constraints ($n = 2$); missing body composition ($n = 1$); and corrupt ActiGraph data ($n = 2$). The reasons cited for dropping out were: lack of time ($n = 12$); family issues ($n = 2$); and relocating to a new city ($n = 1$). Due to these reasons none of the missing values or drop-outs were considered to be connected to the intervention and thus would probably not bias the results. When we imputed the first and third quartile values the obtained results were similar. For example, when imputing the first quartile for missing values the intervention group in comparison to the control group significantly decreased their intake of sweetened beverages (-15 ± 83 ml/day vs. $+4 \pm 81$ ml/day, respectively, $P = 0.041$) and increased their seven component composite score ($+0.32 \pm 1.44$ units vs. -0.12 ± 1.29 units, respectively, $P = 0.008$). When imputing the third quartile for missing values the intervention group in comparison to the control group significantly decreased their intake of sweetened beverages (-10 ± 83 ml/day vs. $+12 \pm 81$ ml/day, respectively, $P = 0.016$); however, their increase in the seven component composite score was no longer significant ($+0.33 \pm 1.46$ units vs. $+0.02 \pm 1.30$ units, respectively, $P = 0.082$). **Table 13** presents the tip-over analysis for the seven component composite score.

Table 13. Sensitivity analysis using intention-to-treat to identify the tipping point that reverses our conclusions for the seven component composite score.

Scenario	Assumptions for handling missing values		Difference in composite score between 6-month follow-up and baseline		<i>P</i> -value ¹
	Intervention Group	Control Group	Intervention Group (n = 155)	Control Group (n = 158)	
1) Tipping point	All children (n = 12) with missing values treated as failures in response to the intervention	25% of children (n = 5) with missing values treated as failures and 75% of children treated as success (n = 15) in response to the intervention	+0.34 ± 1.42	-0.02 ± 1.26	0.042
2) Conservative	All children (n = 12) with missing values treated as failures in response to the intervention	50% of children (n = 10) with missing values treated as failures and 50% of children treated as success (n = 10) in response to the intervention	+0.34 ± 1.42	+0.02 ± 1.27	0.081
3) Extreme conservative	All children (n = 12) with missing values treated as failures in response to the intervention	All children (n = 20) with missing values treated as success in response to the intervention	+0.34 ± 1.42	+0.08 ± 1.30	0.238

¹ Difference between intervention and control groups in the mean change from baseline assessed using the Wilcoxon rank-sum test

4.4.4 Process evaluation

All parents (n = 156) in the intervention group were able to download the MINISTOP app and everyone except two read messages and registered parameters. Sixty percent of parents reported using an iOS operating system. Throughout the entire intervention period the parents reported no technical issues. **Table 14** presents the parents activity within the MINISTOP app with the activity within the app differing greatly between parents.

Table 14. Parents' use and recordings within the MINISTOP application (n = 155).

Variable	n ¹	Median	25 th percentile	75 th percentile	Range
Number of feedback messages read	153	87	18	116	0-140
Number of days candy registration	147	59	16	134	0-168
Number of days sweetened beverage registration	147	53	15	130	0-168
Number of days sedentary behavior registration	147	56	18	130	0-168
Number of days fruit registration	147	58	21	131	0-168

¹ Parents of two children only downloaded the application but did not use it at all and hence the maximum n is 155

4.5 12-MONTH FOLLOW-UP INTERVENTION RESULTS (PAPER V)

The differences between the 12-month follow-up and baseline measures for body composition as well as the dietary and physical activity variables are presented in **Table 15**. For the primary outcome, FMI_{ADP}, there was no significant difference in the change between the 12-month follow-up and baseline observed between the intervention and control groups (mean difference: +0.06 kg/m², $P = 0.566$). Furthermore, no other significant differences were observed between the intervention or control group for any of the secondary outcomes. However, the intervention group increased their FFMI_{ADP} in comparison to the control group between the 12-month follow-up and baseline (mean difference: 0.14 kg/m², $P = 0.050$).

Table 15. Differences between the 12-month follow-up and baseline for body composition dietary, and physical activity variables for the intervention and control groups.

	Difference between 12-month follow-up and baseline		P -value ¹
	Intervention (n = 133) Mean \pm SD	Control (n = 130) Mean \pm SD	
Weight (kg)	+2.61 \pm 1.22	+2.34 \pm 0.95	0.078
Height (cm)	+7.53 \pm 1.61	+7.60 \pm 1.41	0.251
FMI _{ADP} (kg/m ²)	-0.76 \pm 0.66	-0.82 \pm 0.57	0.566
FFMI _{ADP} (kg/m ²)	+0.70 \pm 0.67	+0.56 \pm 0.58	0.050
Sedentary (min/day) ²	+13.8 \pm 51.4	+7.9 \pm 58.4	0.218
Sedentary time (%/wear time) ²	-0.3 \pm 5.1	-0.5 \pm 5.6	0.434
MVPA (min/day) ²	+14.6 \pm 25.5	+15.8 \pm 24.9	0.434
MVPA (%/wear time) ²	+1.3 \pm 2.8	+1.6 \pm 2.8	0.383
Fruit (g/day) ³	+4.3 \pm 81.2	-10.0 \pm 84.5	0.172
Vegetables (g/day) ³	+59.5 \pm 42.8	+51.3 \pm 39.9	0.099
Candy (d/day) ³	+1.3 \pm 23.3	+3.9 \pm 18.2	0.234
Sweetened beverages (ml/day) ³	-4 \pm 100	+9 \pm 128	0.708
Composite Score ⁴	+0.53 \pm 1.49	+0.35 \pm 1.27	0.248

SD, Standard deviation; FMI_{ADP}, Fat mass index measured using air displacement plethysmography; FFMI_{ADP}, Fat free mass index measured using air displacement plethysmography; MVPA, Moderate-to-vigorous physical activity. ¹ Difference between intervention and control group assessed using Wilcoxon's rank-sum test. ² The number of recording days for physical activity at baseline and the 12-month follow-up were: 6.8 \pm 0.8 and 6.5 \pm 1.1 (intervention) and 6.4 \pm 1.2 and 6.5 \pm 1.1 (control), respectively. ³ The number of recording days for food at baseline and the 12-month follow-up were 3.9 \pm 0.5 and 3.6 \pm 0.8 (intervention) and 3.8 \pm 0.5 and 3.7 \pm 0.6 (control), respectively. ⁴ Includes the scores for FMI_{ADP}, the intakes of fruits, vegetables, candy, and sweetened beverages, as well as MVPA, and sedentary time.

There was no significant difference found for the seven component composite score between the intervention and the control group (3.53 ± 1.27 units vs. 3.61 ± 1.26 units, $P = 0.479$ between groups, respectively) at baseline. At the 12-month follow-up the intervention group and control group increased their seven component composite score by $+0.53 \pm 1.49$ units and $+0.35 \pm 1.27$ units, respectively (i.e. difference in change from 12-month follow-up and baseline); however, they were not significantly different ($P = 0.248$). The OR for increasing the seven and six component composite score for the intervention group compared to the control group was 1.26 (95% CI: 0.77, 2.04; $P = 0.357$) and 1.38 (95% CI: 0.84, 2.28; $P = 0.210$), respectively. When splitting the children into those with a higher and lower FMI_{ADP} (based on the baseline median), no significant differences in the changes in the seven component composite scores were found (P -value between groups for a higher $FMI_{ADP} = 0.264$ and P -value between groups for a lower $FMI_{ADP} = 0.616$).

5 DISCUSSION

This thesis incorporates two validation studies for diet and physical activity as well as three articles describing the methods and results (6- and 12-month follow-ups) of a unique mHealth obesity prevention program in four year old children.

5.1 VALIDATION STUDIES

Even though a leveling off in the obesity epidemic has been observed for children and adolescents in many countries around the globe, the levels are still the highest they have ever been (8). Therefore, there has been a major push for research in childhood overweight and obesity investigating causality, prevention, and treatment (8), with the last two being highlighted in the World Health Organization's *Commission for Ending Childhood Obesity* (1). In order for obesity prevention and treatment interventions to work effectively, valid instruments are needed in order to accurately measure obesity related behaviors such as diet and physical activity.

5.1.1 Validation of TECH

Dietary assessment methods utilizing images taken by the subject can be divided into two classes, image-assisted and image-based methods. Image-assisted methods are those that use images to aid conventional dietary assessment methods in regards to serving size estimations or in the recollection of foods/beverages consumed but not reported. Image-based methods are those that use images as the main approach to collect data on dietary intake and can be either active (i.e. the subject taking the picture) or passive (i.e. a wearable device is taking pictures automatically) (119). In regards to this classification system TECH would be considered an active image-based method as pictures taken by the parents were the main approach to collect dietary data with supplemental information being provided in writing (e.g. the fat percentage in milk or yogurt).

5.1.1.1 Main findings and interpretation

EI measured using TECH and TEE assessed using the DLW method did not differ significantly and the mean difference was minimal at -4% (-220 kJ/24hr). Furthermore, no systematic error was observed for EI (TECH) across EI levels in the Bland and Altman plot; however, wide limits of agreement were observed. To date, the only other study that has validated a mobile phone based dietary assessment method against the DLW method in pre-school aged children is Henriksson et al. (87). In that study TECH was used to assess EI under one day in 30 three year old children and they found a higher mean difference (+7%, +330 kJ/24hr), larger limits of agreement (2990 kJ/24hr vs. 1540 kJ/24hr in the present study), as well as systematic bias showing that TECH overestimated and underestimated high and low EIs, respectively. The authors attributed the observed bias to be due to only having one day of food recordings (87), which is sensible as TECH showed no bias when multiple days of recordings were obtained in the present study. Compared to other studies that have evaluated EI using traditional dietary assessment methods the mean difference observed in

our study was similar or lower than the majority of studies that have been conducted in young children (range: -6 to 59%) (108, 120-126). Furthermore, the wide limits of agreement found in this study, which demonstrate that TECH should not be used in individuals is common and has been found in both young children (108, 120-124) and adults (83). The wide limits of agreement are expected as there is greater variation in EI from day to day than for TEE (127).

Compared to EI where TEE assessed using the DLW method is the gold standard, no such standard exists when validating groups of foods. In regards to the eight food groups assessed there were no differences in mean values between TECH and the 24hr dietary recalls and only one trend was found in the Bland and Altman plots, which was for sweetened beverages. Only one other study has used the Bland and Altman method to analyze food groups and they also observed wide limits of agreement in pre-school children (128). Together, these results indicate that TECH has the ability to determine mean EI as well as mean intakes for almost all of the food groups in an unbiased manner.

5.1.1.2 Movement within the field

As two reviews have found that the majority of participants prefer mobile dietary assessment methods over traditional methods (85, 86) further research within this area is highly warranted. The majority of studies to date have used a trained analyst, usually a nutritionist or dietician to estimate the amount of food and beverages consumed (119). From our experience within the MINISTOP trial this can be a very time consuming process with a four day analysis taking between four to six hours per child depending on the complexity and the amount of food pictures, which highlights the need for automated analysis systems. Therefore, a multi-disciplinary team of researchers in the United States created the mobile device food record, which is a dietary assessment method that uses an automated system to identify foods and estimate portion sizes (119, 129). The application works by subjects taking pre and post meal pictures within the app and sending them to the processing server for analysis. The automated analysis is then performed (130) and the analyzed images are then sent back to the subject, where they are supposed to confirm or change the identification of the food products (119). As technology continues to develop automated analysis of food pictures will hopefully aid in more accurately assessing dietary intake as well as reducing the burden on researchers.

It is relevant to note that our research group began working with engineers in 2011 to develop an automated image analysis system for the MINISTOP trial. This work resulted in a prototype for a software called FoodIQ presented in a master thesis (131); however, as experienced from other research groups in this field such as Professor Carol Boushey (<http://www.uhcancercenter.org/about-us/2-directory/62-carol-jo-boushey-phd>), developing a software with sufficient accuracy and precision for all possible foods and dishes is very complex, time-consuming, and associated with high costs. Therefore, unfortunately we were not able to finalize the software in time for use within the MINISTOP trial. However, this previous work may be built upon for future trials.

Active image-based methods such as TECH require participants to actively remember to take pictures and send them to the research team. New passive based methods such as wearable cameras are beginning to be developed and tested. Two studies have investigated the use of wearable monitors for image-assisted dietary assessment, one which was worn on a lanyard around the neck (132) and the other which was worn above the ear (133). Gemming et al. (132) found that EI measured only with multiple pass 24hr dietary recalls was 17% and 13% lower than TEE assessed using the DLW method, for men and women respectively; however, when multiple pass 24hr dietary recalls were combined with the wearable camera corresponding figures were 9% and 7%. Pettitt et al. (133) found an under-reporting rate of 34% when EI assessed using a two day weighed food record was compared to TEE (DLW); however, when the food record was combined with the wearable monitor the under-reporting rate reduced to 30%. The initial results for wearable cameras are promising and hopefully in the future wearable monitors will be able to lighten the burden for participants partaking in dietary assessment studies.

5.1.2 Evaluation of the ActiGraph wGT3x-BT

The gold standard to assess energy expenditure is the DLW method. However, the DLW method is expensive and is more than often not able to be used in large-scale studies. Therefore, new methods for predicting AEE are needed. Accelerometry provides a promising alternative; however, there are many brands of accelerometers (e.g. ActiGraph, Tracmor, GENEActive etc.) and placement sites (e.g. wrist, waist, thigh etc.) that all need to be evaluated and validated in the population of use before prediction equations for AEE can be created.

5.1.2.1 Main findings and interpretation

The wrist-worn ActiGraph wGT3x-BT accelerometer alone was able to explain 14% (mean VM total) and 24% (mean VM waking) of the variation in AEE. When FM_{ISO} and FFM_{ISO} were added to the models 58% (mean VM total) and 62% (mean VM waking) of the variation in AEE was explained. Comparisons to other studies are difficult due to the use of different monitors and placement sites. Three studies in three to seven year old children using the Actiheart accelerometer (chest attached), ActiTrainer accelerometer (attached to the right hip), and Tracmor accelerometer (attached to the middle of the lower back) were able to explain 6% (134), 22% (135), and 31% (81) of the variation in AEE. The study by Sijtsma et al. (81) was able to explain 7% more in the variation of AEE than the present study. This difference could be attributed to the fact that they measured sleeping metabolic rate in their study whereas we used a predicted BMR. Also, one study hypothesized that accelerometers placed centrally on the body are superior at capturing movements from the larger muscle groups than the wrist-worn monitor (136).

The ability of the wrist-worn ActiGraph combined with FM_{ISO} and FFM_{ISO} to explain up to 62% of the variation in AEE is encouraging. However, it is important to note that to date

there is no general agreement on how much variation an accelerometer should be able to explain to be considered meaningful for practical purposes.

5.1.2.2 Movement within the field

There are numerous considerations that need to be made when using accelerometry in any population, which include: placement, sampling frequency, filter, epoch, non-wear time definition, what constitutes a valid day/week, registration protocol (24hr or awake wearing), cut-points for sedentary time and physical activity intensities, and how to classify sleep. Due to all of these considerations it makes comparisons between studies within this field very difficult as every study does it differently. Therefore, Migueles et al. (88) decided to conduct a systematic review in order to provide practical considerations separated by age group for the ActiGraph accelerometer (GT3X, GT3X+, and wGT3x-BT) for the aforementioned considerations.

Currently, there is much discussion regarding the placement of the monitors, i.e. hip/lower back or the wrist. According to the recent systematic review only a small number of studies have compared the wrist- and waist-worn placement sites for ActiGraph with the majority of studies finding greater accuracy for predicting AEE as well as classifying sedentary and physical activity intensities with the waist-worn monitors (88). However, wear compliance seems to be improved when accelerometers are worn on the wrist instead of the hip/lower back (94-96). The results obtained in our evaluation study correspond well as we found that 85% (n = 34 of 40) followed the seven day 24hr protocol with an additional 10% (n = 4) wearing the monitor for six days. As it is very important in research to have complete data from as many of the participants as possible researchers should highly consider using wrist-worn monitors in future studies.

New ways to process accelerometry data are starting to be developed using raw data features instead of the traditionally used counts. Utilization of raw acceleration signals have resulted in new summary metrics which include: Euclidean norm minus one (ENMO), Euclidean norm of the high-pass filtered signs (HFEN), HFEN plus Euclidean norm of low-pass filtered signals minus 1g (HFEN+), and mean amplitude deviation (MAD) (137, 138). In pre-school aged children it was found that ENMO, HFEN+, and MAD were able to explain 36%, 32%, and 33% of the variation in AEE, respectively. When weight was added to the model up to 56% (ENMO) of the variation in AEE was explained (139). Thus, possibly indicating that raw data metrics are superior to counts when predicting AEE in young children.

5.1.3 Methodological considerations

Both validation studies in this thesis were nested within the MINISTOP trial, utilized the same study population, and the recruitment for the studies occurred at the 12-month follow-up. As these were validation studies, ideally they should have been conducted at the first time of measurement. This was the original plan within the study; however, due to the heavy burden already placed on the families who agreed to partake in the MINISTOP trial we made a judgement call to move the validation to the 12-month follow-up to avoid families from

dropping out. One could argue that the strong results obtained within the TECH validation could be due to the fact that the parents had already learned the method. We do not believe this was the case as there was six months between every measurement as well as it was not always the same parent or caregiver (e.g. grandparent or aunt/uncle) taking the food pictures.

The recruitment of the participants also needs to be addressed. We asked the parents in the order they came back to the follow-up measurement until 40 parents and their child agreed to do so. Therefore, it could be argued that the “best” 40 families were included in this study as they were the first to come to follow-up measurements. Again, we do not think this was an issue in our study because of the low amount of drop-outs and missing data observed at both the 6- and 12-month follow-ups, which demonstrates that the majority of families would have been capable of participating. Additionally, it can also be disputed that the difference in the measurement durations between EI (four days), AEE (7 days) and the reference the DLW method (14 days) could have influenced the results. We find this very improbable as the day to day variation in TEE is low (75, 140). Furthermore, for the ActiGraph evaluation we re-ran all the analyses using AEE calculated with only seven days and comparable results were obtained.

The major strength of these validation studies is the use of DLW as the reference method, as it is considered the gold standard for validating both dietary and physical activity assessment methods (77).

5.1.4 Future research

- Research needs to focus on the creation of automated image analysis systems to process food pictures. This will hopefully lead to more accurate analysis of food pictures by reducing human errors. Additionally, wearable cameras require further exploration as they have the potential to reduce participant bias by capturing food images throughout the day. Hopefully, they will be able to increase the completeness of food records as well as ease the burden on the participants.
- More research needs to focus on improving accelerometer’s abilities to predict AEE through investigating the use of raw data metrics (e.g. ENMO, HFEN+, MAD etc.).

5.2 INTERVENTION STUDIES 6- AND 12-MONTH FOLLOW-UPS

5.2.1 Main findings and interpretation

After the intervention, for the primary outcome, FMI_{ADP} no significant intervention effect was found. For the secondary outcomes (intakes of fruits, vegetables, candy, and sweetened beverages as well as time spent sedentary and in MVPA) the only observed intervention effect was a significant reduction in sweetened beverage consumption in the intervention group compared to the control group. However, there was a significant improvement in the seven component composite score in the intervention group compared to the control group, with this difference being more evident in the children with a FMI_{ADP} above the median. As stated in the introduction many obesity prevention studies in young children have failed to

demonstrate changes in obesity markers (41-44, 46). However, similar to MINISTOP both the Ballabeina (141) and IDEFICS (142) trials found evidence that the interventions were more effective in children that were overweight or obese.

At the 12-month follow-up no significant differences were observed between the intervention and control group for either the primary or secondary outcomes. Furthermore, the significant effect on the seven component composite score was not sustained, nor was the stronger effect which was observed in the children with a FMI_{ADP} above the median at the 6-month follow-up. To date, there are few obesity intervention trials that have had follow-up measurements in the pre-school age group. The High Five for Kids Study was a primary care based trial which aimed to prevent obesity in two to six year old American children. Similar to MINISTOP they observed no effect on the primary outcome, BMI z-scores after the one year intervention. However, a significant reduction in television viewing was observed in the intervention group compared to the control group (143). At their two year follow-up they also observed no effect on any of their outcome measures (144).

5.2.1.1 Why was MINISTOP not entirely effective?

One explanation for the lack of intervention results observed could be due to the fact that the parents did not participate enough in the intervention (i.e. reading the information provided in the intervention material). After the intervention period, parents who were in the intervention group were asked to complete a questionnaire pertaining to the MINISTOP app. When asked how many themes they have read, 51% of parents reported reading all 12 themes, 27% read six to ten themes, 20% read two to four themes, and 2% read no themes. Having 78% of parents stating they partook in greater than 50% of the themes is promising. However, this was self-reported data which needs to be interpreted cautiously as the parents might have wanted to please our research team by showing they participated. Even though a high rate of compliance was observed from the data within the app, we cannot rule out that the parents just opened the messages or themes and did not read them. Furthermore, parents also had the ability within the app to contact a dietician or psychologist to ask specific questions pertaining to their child. To our surprise the majority of parents did not take advantage of this function. By not using this function parents could have missed out on how to implement a behavior change more effectively within their own home environment, therefore contributing to the lack of intervention effect.

Another reason why the intervention was not entirely effective may have been that the majority of families in the intervention group (70%) reported that only the mother read the intervention material. Even though this is very common (145), it is problematic as the MINISTOP trial was a home based prevention program. If only one parent is acquiring the knowledge for creating a healthier diet and improving movement behaviors in the home environment than these habits will not be consistently shown to the child. Therefore, the child will be less likely to develop these healthier behaviors. This is especially important as role modeling has been found to influence children's eating (48).

The lack of intervention effect could also be due to the app itself. The MINISTOP app was designed in 2013 and at that time it was not possible to personalize messages to families (i.e. using the parents' or child's name in the messages) or to give specific feedback messages to each family based on the parameters they registered within the app. Furthermore, within the app the parents did not have the ability to set their own goals for the registration parameters. A systematic review of online trials in adults found that both tailored feedback as well as goal setting are promising components which have led to behavior changes (146). Finally, the MINISTOP app only targeted the parents and did not include the child which could have limited its effectiveness. A recent systematic review found that targeting both the child and the parents may aid in obesity prevention behavior in the early years (40). One possible way to engage children in mHealth interventions is through gamification. Gamification refers to "applying game mechanics to non-game contexts in order to engage audiences" (147). A recent pilot study conducted in 9 to 13 old children using this technique found that a modified version of Mario Brothers led to greater knowledge regarding a healthy diet and lifestyle (148). Therefore, creating age appropriate games within the app may aid young children in learning key behaviors for a healthier lifestyle.

5.2.2 Modifications to the MINISTOP app: what changes should be considered

The acceptability of the MINISTOP app by parents coupled with the positive intervention effects on the composite score could allow it to be a useful tool in healthcare. Today, the only children that receive help are those that are overweight or obese as measured by BMI. However, as stated in the introduction, BMI is surrogate marker of adiposity as it cannot differentiate between FM and FFM. Unpublished data from the MINISTOP trial at baseline has shown a large range in FM%, FMI, and FFMI in children who are considered normal weight by BMI (Delisle Nyström et al., manuscript under review, 2017 Oct 1). Therefore, some children with excess FM and a normal BMI are not being identified at a critical time point in life, and thus not receiving the help they need. A mHealth program such as MINISTOP could provide parents of these pre-school aged children with the needed help without putting excess strain on the healthcare system.

However, as with every program or intervention, adjustments need to be made in order to maximize optimization. Suggestions for improvements within the MINISTOP app are provided below.

- Diet was the key driver behind the significant differences observed in the composite scores in the MINISTOP trial. No differences in MVPA or sedentary behavior were observed at either follow-up in comparison to baseline. A reasonable explanation for this is that only one of the twelve themes was focused on physical activity and sedentary behaviors. A suggestion could be to combine one or two of the dietary themes in order to create room for more physical activity focused themes.
- Additional features should be added within the app which allow parents to create their own goals for the dietary and physical activity parameters. Furthermore, tailored

feedback that provides personalized messages to the families would be very beneficial.

- Creating a game within the app tailored towards increasing the child's knowledge of healthy eating and physical activity, would engage the child in the intervention. This could be as simple as a memory game with fruits and vegetables or asking the child to find all the fruits and vegetables in the picture. Hopefully, with more exposure to these products they will ask for them over other food items.

5.2.3 Methodological considerations

As in all research that is conducted it is vital that the right steps are taken from the beginning until the end, in order to increase the likelihood of success. The MINISTOP trial was a carefully planned study that included a multitude of steps before the final product, the MINISTOP app was ready and the trial initiated which has been described in detail in the study protocol (Paper I). The strengths and limitations of the intervention have been discussed in Paper IV. However, it is essential to highlight a few. For instance, the MINISTOP intervention content was based upon the Social Cognitive Theory (102), well established strategies for promoting behavior change (103), as well as evidence based recommendations for obesity interventions in young children (104). This is important as Kohl et al. (146) highlighted that the use of theory is a promising building block when creating online lifestyle interventions in adults. Furthermore, a recent systematic review on interventions to prevent and manage overweight and obesity in pre-school children found that almost 50% of the included interventions that were based upon the Social Cognitive Theory observed significant effects (40).

It is also important to note that all statistical analyses were planned a priori with Dr. Sven Sandin, a biostatistician who has great expertise in clinical trials. Dr. Sandin has been involved in the MINISTOP trial from the very beginning, starting with providing a detailed statistical plan for how to process the intervention data. Having an a priori statistical plan is important in interventional research in order to prevent researchers from optimizing their results by analyzing the data multiple ways and choosing the method that best portrays the results.

RCTs are regarded to be the gold standard for intervention research (149); however, how that data is treated and analyzed can influence the results. To date there is no consensus on which method should be used to analyze data from RCTs. However, as common with all interventions there is missing data, and it is important to understand the reasons why the data is missing to ensure that it will not bias the results (150). Missing data can be characterized into three types: missing completely at random, missing at random, and missing not at random (118). For instance, in the MINISTOP trial the majority of missing values were due to the fact that the child refused to wear the ActiGraph and the parents not having time to take food pictures. Therefore, these reasons would be classified as data which is missing completely at random as they were representative of all the families in the MINISTOP trial (118). Furthermore, the aforementioned reasons for missing values are unlikely to be linked

to the intervention, and therefore, it is unlikely to influence the results. In the MINISTOP trial we utilized a completers-only analysis, which is considered a suitable analysis method when the missing values are considered missing completely at random (150). A limitation of using this method is the loss of power due to running the analyses in a smaller sample (150); however, this was not a problem in MINISTOP as we had very few drop-outs and missing data. We needed 200 children (100 in each group) to complete all measurements in order to have greater than 80% power to detect differences between groups and at both follow-ups each group had at least 130 children. Finally, in order to assess the robustness of our results a series of sensitivity analyses were performed. As the results in the sensitivity analyses were similar to the completers-only analysis we can be fairly confident that MINISTOP's findings were robust (118).

Finally, questions may also be raised why the MINISTOP trial utilized the cut-points by Chandler et al. (116) as those cut-points were created for 8 to 12 year old children. The explanation for this is when baseline data analyzation began for cross-sectional studies the cut-points by Johansson et al. (151) were not published yet. By the time Paper IV was published, MINISTOP had already published papers using Chandler et al.'s (116) cut-points and decided to continue using them for consistency. The use of these cut-points was not deemed to be an issue, because in a cross-sectional study investigating the associations between body composition and physical fitness with physical activity and sedentary behavior both the cut-points by Chandler et al. (116) as well as VM percentiles were used to analyze the data with similar results being obtained using both methods (24).

5.2.4 Future research involving the MINISTOP app

- As the MINISTOP app was more successful among the children with a FMI above the median future studies should investigate whether the MINISTOP app can be converted into a treatment trial (i.e. focusing on children who are already overweight or obese).
- Investigation into interventions beginning earlier in the pre-school years is also warranted as an early adiposity rebound, which can occur as early as three years of age has been found to increase the risk of obesity in adulthood (152). Therefore, possibly prevention interventions such as MINISTOP may be more beneficial to be implemented at around three years of age instead of 4.5 years of age.
- Further research is warranted to investigate whether MINISTOP can be used to prevent and treat obesity in socially disadvantaged groups such as migrant populations who have a higher risk of becoming overweight in comparison to children born to parents of Swedish descent (153). This can be done by translating the app into other languages that are commonly spoken in Sweden so that we do not exclude any population due to language barriers.

5.3 STUDY POPULATION

The participating parents in the MINISTOP trial had higher educational attainment than the general Swedish population with 71% and 57% of MINISTOP mothers and fathers, respectively having a university degree compared to the corresponding figures in the general Swedish population, of 52% and 39% (154). A higher participation rate among parents with higher educational background is common in research (155), which could possibly limit the generalizability of the results in Paper IV. However, we do not believe this is a major issue in our study because similar results were obtained in Paper IV when the analyses were further adjusted for parental education. Additionally, the proportion of mothers and fathers in the MINISTOP trial that were overweight or obese were similar to the proportions found in the general population (156). In regards to the participating children their weight and height (106), prevalence of overweight and obesity (157), and dietary intake (158) were similar to Swedish four year olds in general.

The participating parents in the validations studies were representative of the parents in the MINISTOP trial in regards to prevalence of overweight and obesity, age, as well as educational attainment. Furthermore, there were no differences regarding age, weight, and BMI in the children in the validation studies and those in the MINISTOP trial. It is also important to note that the 40 participating children's TEE was similar to other previously collected data in European children (123, 159). The fairly small sample size of the validation studies may limit the generalizability of the results. Additionally, we cannot eliminate the fact that the higher educational attainment of the parents led to greater diligence when taking the food pictures as well as strong compliance with the ActiGraph protocol. However, without such parents, validation studies like these would not be possible. With this being said further studies should be conducted in parents with lower educational attainment to confirm the obtained results.

5.4 ETHICAL CONSIDERATIONS

As stated previously the MINISTOP trial was conducted according to the guidelines in the Declaration of Helsinki and all procedures were approved by the Research and Ethics Committee in Stockholm, Sweden. Furthermore, informed consent was provided by both parents before participation.

Young children such as those that participated in MINISTOP cannot consent to participate in research themselves, due to the fact that they cannot sufficiently understand the research that will be performed as well as any implications involved (160). In this case a proxy, usually a parent needs to provide consent for their child to participate in research. It is therefore important to discuss at what age a child should assent to participate in research. Assent refers to "affirmative agreement of a minor who is to take part in the informed consent procedure in a way adapted to his or her capabilities, while their legal representative has the formal role of consenting" (161). However, it is important to determine at what age a child can be competent enough to assent to participate. A recent study by Hein et al. (162) concluded that

children under 9.6 years of age did not have sufficient competence to assent to participate in research. Due to these reasons in the MINISTOP trial only parental consent was obtained.

It is also very important to discuss dissent in pediatric research, which “implies that children should not be required to participate in non-beneficial research that is more than minimally distressing” (163). Children at any age have the ability to show when they are in distress which usually comes in the form of verbal cues or body movements (163) and researchers need to be aware of this and stop measurements when distress is recognized. Throughout all of the measurements conducted in the MINISTOP trial distress such as fussiness or crying was not observed. We found that children in our study used verbal cues by outright refusing to participate in a certain measurement such as the BodPod or wearing the ActiGraph accelerometer. In these cases the children’s decisions were respected and they did not participate in those measurements at that time period. Therefore, dissent was not deemed to be an issue in the MINISTOP trial.

6 CONCLUSIONS

- TECH has the ability to accurately measure mean EI as well as the intakes of certain food groups (fruits, vegetables, fruit juice, ice cream, candy, and bakery products) in groups of pre-school aged children.
- Alone, the outputs from the wrist-worn ActiGraph wGT3x-BT accelerometer were able to explain up to 24% of the variation in AEE.
- A high wear compliance was observed for the wrist-worn ActiGraph with 85% of children completing the seven day, 24hr protocol and another 10% wearing the monitor for six out of seven days.
- A 6-month mHealth obesity prevention program targeting parents of pre-school aged children found no effect on the primary outcome FMI_{ADP} ; however, a significant decrease in the intake of sweetened beverages was found in the intervention compared to the control group.
- After the 6-month intervention significant differences were observed between the intervention and control group for the seven component composite score (comprising both primary and secondary outcomes), with these differences being more pronounced in the children with a FMI_{ADP} above the median. Children in the intervention group had a 99% higher odds of increasing the six component composite score (just diet and physical activity variables) compared to those in the control group.
- At the 12-month follow-up, no differences were observed between the intervention and control groups for any of the primary or secondary outcomes. Furthermore, the significant results for the seven component composite score found at the 6-month follow-up was not sustained at the 12-month follow-up.

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Arvid Elvis Christer Furemo Nyström

6.5 years



Tanner CJ Leclerc

2.5 years



Zachary Donald Leclerc

5 months



To my Mom always with me and always thinking of you.

In memory of Karen Susan Delisle

December 23, 1957 to May 25, 2015

8 REFERENCES

1. World Health Organization. The commission on ending childhood obesity. Geneva: World Health Organization; 2016.
2. Afshin A, Forouzanfar MH, Reitsma MB, Sur P, Estep K, Lee A, et al. Health effects of overweight and obesity in 195 countries over 25 years. *N Engl J Med*. 2017;377(1):13-27.
3. World Health Organization. Facts and figures on childhood obesity. [Internet]. Geneva: World Health Organization; 2014. [cited 2017 Aug 28] Available from: <http://www.who.int/end-childhood-obesity/facts/en/>.
4. Stockholm County Council. Child healthcare yearly report. Stockholm: Stockholm County Council; 2013.
5. Uppsala-Örebro Region Healthcare Program. Overweight and obesity in children and adolescents - Prevention and treatment. Uppsala and Örebro: Uppsala-Örebro Region Healthcare Program; 2015.
6. Bergstrom E, Blomquist HK. Is the prevalence of overweight and obesity declining among 4-year-old Swedish children? *Acta Paediatr*. 2009;98(12):1956-8.
7. de Munter J, Friedl A, Lind S, Kark M, Carlberg M, Andersson N, et al. Stability in the prevalence of Swedish children who were overweight or obese in 2003 and 2011. *Acta Paediatr*. 2016;105(10):1173-80.
8. Rokholm B, Baker JL, Sorensen TI. The levelling off of the obesity epidemic since the year 1999--A review of evidence and perspectives. *Obesity Rev*. 2010;11(12):835-46.
9. Marild S, Bondestam M, Bergstrom R, Ehnberg S, Hollsing A, Albertsson-Wikland K. Prevalence trends of obesity and overweight among 10-year-old children in western Sweden and relationship with parental body mass index. *Acta Paediatr*. 2004;93(12):1588-95.
10. Braback L, Gunnell B, Ekholm L. No further increase of obesity among Swedish 4-year old children. Large regional differences indicate the significance of socioeconomic factors. *Lakartidningen*. 2009;106(43):2758-61.
11. Bammann K, Gwozdz W, Lanfer A, Barba G, De Henauw S, Eiben G, et al. Socioeconomic factors and childhood overweight in Europe: Results from the multi-centre IDEFICS study. *Pediatr Obes*. 2013;8(1):1-12.
12. Moraes L, Lissner L, Yngve A, Poortvliet E, Al-Ansari U, Sjoberg A. Multi-level influences on childhood obesity in Sweden: Societal factors, parental determinants and child's lifestyle. *Int J Obes*. 2012;36(7):969-76.
13. Henriksson H, Eriksson B, Forsum E, Flincke E, Henriksson P, Lof M. Longitudinal assessment of body composition in healthy Swedish children from 1 week until 4 years of age. *Eur J Clin Nutr*. 2017 Aug 23. doi: 10.1038/ejcn.2017.125.
14. Fomon SJ, Haschke F, Ziegler EE, Nelson SE. Body composition of reference children from birth to age 10 years. *Am J Clin Nutr*. 1982;35(5 Suppl):1169-75.
15. Silventoinen K, Rokholm B, Kaprio J, Sorensen TI. The genetic and environmental influences on childhood obesity: A systematic review of twin and adoption studies. *Int J Obes*. 2010;34(1):29-40.

16. Dubois L, Ohm Kyvik K, Girard M, Tatone-Tokuda F, Perusse D, Hjelmberg J, et al. Genetic and environmental contributions to weight, height, and BMI from birth to 19 years of age: An international study of over 12,000 twin pairs. *PLoS One*. 2012;7(2):e30153.
17. Rao DP, Kropac E, Do MT, Roberts KC, Jayaraman GC. Status report -- Childhood overweight and obesity in Canada: An integrative assessment. *Health Promot Chronic Dis Prev Can*. 2017;37(3):87-93.
18. Hill JO, Melanson EL. Overview of the determinants of overweight and obesity: Current evidence and research issues. *Med Sci Sports Exerc*. 1999;31(11 Suppl):S515-21.
19. Hebestreit A, Bornhorst C, Barba G, Siani A, Huybrechts I, Tognon G, et al. Associations between energy intake, daily food intake and energy density of foods and BMI z-score in 2-9-year-old European children. *Eur J Nutr*. 2014;53(2):673-81.
20. Hebestreit A, Barba G, De Henauw S, Eiben G, Hadjigeorgiou C, Kovacs E, et al. Cross-sectional and longitudinal associations between energy intake and BMI z-score in European children. *Int J Behav Nutr Phys Act*. 2016;13:23.
21. Reilly JJ. Physical activity, sedentary behaviour and energy balance in the preschool child: opportunities for early obesity prevention. *Proc Nutr Soc*. 2008;67(3):317-25.
22. Butte NF, Puyau MR, Wilson TA, Liu Y, Wong WW, Adolph AL, et al. Role of physical activity and sleep duration in growth and body composition of preschool-aged children. *Obesity*. 2016;24(6):1328-35.
23. Collings PJ, Brage S, Ridgway CL, Harvey NC, Godfrey KM, Inskip HM, et al. Physical activity intensity, sedentary time, and body composition in preschoolers. *Am J Clin Nutr*. 2013;97(5):1020-8.
24. Leppanen MH, Nystrom CD, Henriksson P, Pomeroy J, Ruiz JR, Ortega FB, et al. Physical activity intensity, sedentary behavior, body composition and physical fitness in 4-year-old children: Results from the MINISTOP trial. *Int J Obes*. 2016;40(7):1126-33.
25. Hobbs M, Pearson N, Foster PJ, Biddle SJ. Sedentary behaviour and diet across the lifespan: An updated systematic review. *Br J Sports Med*. 2015;49(18):1179-88.
26. Sanders RH, Han A, Baker JS, Cobley S. Childhood obesity and its physical and psychological co-morbidities: A systematic review of Australian children and adolescents. *Eur J Pediatr*. 2015;174(6):715-46.
27. Nader PR, O'Brien M, Houts R, Bradley R, Belsky J, Crosnoe R, et al. Identifying risk for obesity in early childhood. *Pediatrics*. 2006;118(3):e594-601.
28. Reilly JJ, Bonataki M, Leary SD, Wells JC, Davey-Smith G, Emmett P, et al. Progression from childhood overweight to adolescent obesity in a large contemporary cohort. *Int J Pediatr Obes*. 2011;6(2-2):e138-43.
29. Cali AM, Caprio S. Obesity in children and adolescents. *J Clin Endocrinol Metab*. 2008;93(11 Suppl 1):S31-6.
30. Skinner AC, Perrin EM, Moss LA, Skelton JA. Cardiometabolic risks and severity of obesity in children and young adults. *N Engl J Med*. 2015;373(14):1307-17.

31. Lambert M, Delvin EE, Levy E, O'Loughlin J, Paradis G, Barnett T, et al. Prevalence of cardiometabolic risk factors by weight status in a population-based sample of Quebec children and adolescents. *Can J Cardiol.* 2008;24(7):575-83.
32. Delisle Nystrom C, Henriksson P, Martínez-Vizcaíno V, Medrano M, Cadenas-Sánchez C, Arias-Palencia N et al. Does cardiorespiratory fitness attenuate the adverse effects of severe/morbid obesity on cardiometabolic risk and insulin resistance in children? A pooled analysis. 2017. doi: 10.2337/dc17-1334 [Epub ahead of print].
33. Manios Y. The 'ToyBox-study' obesity prevention programme in early childhood: An introduction. *Obesity Rev.* 2012;13 Suppl 1:1-2.
34. Onnerfalt J, Erlandsson LK, Orban K, Broberg M, Helgason C, Thorngren-Jerneck K. A family-based intervention targeting parents of preschool children with overweight and obesity: Conceptual framework and study design of LOOPS- Lund overweight and obesity preschool study. *BMC Public Health.* 2012;12:879.
35. Sobko T, Svensson V, Ek A, Ekstedt M, Karlsson H, Johansson E, et al. A randomised controlled trial for overweight and obese parents to prevent childhood obesity--Early STOPP (STockholm Obesity Prevention Program). *BMC Public Health.* 2011;11:336.
36. Doring N, Hansson LM, Andersson ES, Bohman B, Westin M, Magnusson M, et al. Primary prevention of childhood obesity through counselling sessions at Swedish child health centres: design, methods and baseline sample characteristics of the PRIMROSE cluster-randomised trial. *BMC Public Health.* 2014;14:335.
37. Waters E, de Silva-Sanigorski A, Hall BJ, Brown T, Campbell KJ, Gao Y, et al. Interventions for preventing obesity in children. *Cochrane Database Syst Rev.* 2011;12:CD001871.
38. Hesketh KD, Campbell KJ. Interventions to prevent obesity in 0-5 year olds: An updated systematic review of the literature. *Obesity.* 2010;18 Suppl 1:S27-35.
39. van Hoek E, Feskens EJ, Bouwman LI, Janse AJ. Effective interventions in overweight or obese young children: Systematic review and meta-analysis. *Child Obes.* 2014;10(6):448-60.
40. Ling J, Robbins LB, Wen F. Interventions to prevent and manage overweight or obesity in preschool children: A systematic review. *Int J Nurs Stud.* 2016;53:270-89.
41. Pinket AS, Van Lippevelde W, De Bourdeaudhuij I, Deforche B, Cardon G, Androutsos O, et al. Effect and process evaluation of a cluster randomized control trial on water intake and beverage consumption in preschoolers from six european countries: The ToyBox-study. *PLoS One.* 2016;11(4):e0152928.
42. De Craemer M, De Decker E, Verloigne M, De Bourdeaudhuij I, Manios Y, Cardon G. The effect of a cluster randomised control trial on objectively measured sedentary time and parental reports of time spent in sedentary activities in Belgian preschoolers: The ToyBox-study. *Int J Behav Nutr Phys Act.* 2016;13:1.
43. De Henauw S, Huybrechts I, De Bourdeaudhuij I, Bammann K, Barba G, Lissner L, et al. Effects of a community-oriented obesity prevention programme on indicators of body fatness in preschool and primary school children. Main results from the IDEFICS study. *Obesity Rev.* 2015;16 Suppl 2:16-29.

44. De Bourdeaudhuij I, Verbestel V, De Henauw S, Maes L, Huybrechts I, Marild S, et al. Behavioural effects of a community-oriented setting-based intervention for prevention of childhood obesity in eight European countries. Main results from the IDEFICS study. *Obesity Rev.* 2015;16 Suppl 2:30-40.
45. Puder JJ, Marques-Vidal P, Schindler C, Zahner L, Niederer I, Burgi F, et al. Effect of multidimensional lifestyle intervention on fitness and adiposity in predominantly migrant preschool children (Ballabeina): Cluster randomised controlled trial. *BMJ.* 2011;343:d6195.
46. Doring N, Ghaderi A, Bohman B, Heitman BL, Larsson C, Berglind D et al. Motivational interviewing to prevent childhood obesity: A cluster RCT. *Pediatrics.* 2016;137(5).
47. Adair LS, Popkin BM. Are child eating patterns being transformed globally? *Obes Res.* 2005;13(7):1281-99.
48. Ventura AK, Birch LL. Does parenting affect children's eating and weight status? *Int J Behav Nutr Phys Act.* 2008;5:15.
49. Skouteris H, McCabe M, Swinburn B, Newgreen V, Sacher P, Chadwick P. Parental influence and obesity prevention in pre-schoolers: A systematic review of interventions. *Obesity Rev.* 2011;12(5):315-28.
50. Knowlden AP, Sharma M. Systematic review of family and home-based interventions targeting paediatric overweight and obesity. *Obesity Rev.* 2012;13(6):499-508.
51. World Health Organization. mHealth new horizons for health through mobile technologies. Geneva: World Health Organization. 2011.
52. International Telecommunication Union. ICT facts & figures. Geneva: International Telecommunication Union. 2015.
53. International Telecommunication Union. ICT facts and figures. Geneva: International Telecommunication Union. 2016.
54. Internet Foundation in Sweden. Swedes and the Internet. A study of Swedes' internet habits. Stockholm: Internet Foundation in Sweden. 2016.
55. Free C, Phillips G, Galli L, Watson L, Felix L, Edwards P, et al. The effectiveness of mobile-health technology-based health behaviour change or disease management interventions for health care consumers: A systematic review. *PLoS Med.* 2013;10(1):e1001362.
56. Schippers M, Adam PC, Smolenski DJ, Wong HT, de Wit JB. A meta-analysis of overall effects of weight loss interventions delivered via mobile phones and effect size differences according to delivery mode, personal contact, and intervention intensity and duration. *Obesity Rev.* 2017;18(4):450-9.
57. Flores Mateo G, Granado-Font E, Ferre-Grau C, Montana-Carreras X. Mobile phone apps to promote weight loss and increase physical activity: A systematic review and meta-analysis. *J Med Internet Res.* 2015;17(11):e253.
58. DiFilippo KN, Huang WH, Andrade JE, Chapman-Novakofski KM. The use of mobile apps to improve nutrition outcomes: A systematic literature review. *J Telemed Telecare.* 2015;21(5):243-53.

59. Schoeppe S, Alley S, Van Lippevelde W, Bray NA, Williams SL, Duncan MJ, et al. Efficacy of interventions that use apps to improve diet, physical activity and sedentary behaviour: A systematic review. *Int J Behav Nutr Phys Act*. 2016;13(1):127.
60. Quelly SB, Norris AE, DiPietro JL. Impact of mobile apps to combat obesity in children and adolescents: A systematic literature review. *J Spec Pediatr Nurs*. 2015;21(1):5-17.
61. 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.
62. Cole TJ, Lobstein T. Extended international (IOTF) body mass index cut-offs for thinness, overweight and obesity. *Pediatr Obes*. 2012;7(4):284-94.
63. Wells JC. Toward body composition reference data for infants, children, and adolescents. *Adv Nutr*. 2014;5(3):320S-9S.
64. Forsum E, Flinck Carlsson E, Henriksson H, Henriksson P, Lof M. Total body fat content versus BMI in 4-year-old healthy Swedish children. *J Obes*. 2013;206715.
65. Sijtsma A, Bocca G, L'Abée C, Liem ET, Sauer PJ, Corpeleijn E. Waist-to-height ratio, waist circumference and BMI as indicators of percentage fat mass and cardiometabolic risk factors in children aged 3-7 years. *Clin Nutr*. 2014;33(2):311-5.
66. L'Abée C, Visser GH, Liem ET, Kok DE, Sauer PJ, Stolk RP. Comparison of methods to assess body fat in non-obese six to seven-year-old children. *Clin Nutr*. 2010;29(3):317-22.
67. Mei Z, Grummer-Strawn LM, Pietrobelli A, Goulding A, Goran MI, Dietz WH. Validity of body mass index compared with other body-composition screening indexes for the assessment of body fatness in children and adolescents. *Am J Clin Nutr*. 2002;75(6):978-85.
68. Cole TJ, Fewtrell MS, Prentice A. The fallacy of using percentage body fat as a measure of adiposity. *Am J Clin Nutr*. 2008;87(6):1959; author reply-60.
69. Dempster P, Aitkens S. A new air displacement method for the determination of human body composition. *Med Sci Sports Exerc*. 1995;27(12):1692-7.
70. Fields DA, Goran MI, McCrory MA. Body-composition assessment via air-displacement plethysmography in adults and children: A review. *Am J Clin Nutr*. 2002;75(3):453-67.
71. Fields DA, Allison DB. Air-displacement plethysmography pediatric option in 2-6 years old using the four-compartment model as a criterion method. *Obesity*. 2012;20(8):1732-7.
72. Wells JC, Williams JE, Chomtho S, Darch T, Grijalva-Eternod C, Kennedy K, et al. Pediatric reference data for lean tissue properties: Density and hydration from age 5 to 20 y. *Am J Clin Nutr*. 2010;91(3):610-8.
73. Lohman TG. Assessment of body composition in children. *Pediatr Exerc Sci*. 1989;1:19-30.
74. International Atomic Energy Agency. Assessment of body composition and total energy expenditure in humans using stable isotope techniques. Volume 3. Vienna: International Atomic Energy Agency. 2009.

75. Speakman J. Doubly labeled water. Theory and practice. 1 ed. London: Chapman and Hall; 1997.
76. Nagy K. The doubly-labelled water method for measuring energy expenditure. Technical recommendations for use in humans. Vienna: International Atomic Energy Agency; 1990.
77. Westerterp KR. Doubly labelled water assessment of energy expenditure: Principle, practice, and promise. *Eur J Appl Physiol.* 2017;117(7):1277-85.
78. Weir JB. New methods for calculating metabolic rate with special reference to protein metabolism. *J Physiol.* 1949;109(1-2):1-9.
79. Black AE, Prentice AM, Coward WA. Use of food quotients to predict respiratory quotients for the doubly-labelled water method of measuring energy expenditure. *Hum Nutr Clin Nutr.* 1986;40(5):381-91.
80. Nordic Council of Ministers. Nordic nutrient recommendations. Copenhagen: Nordic Council of Ministers; 2012.
81. Sijtsma A, Schierbeek H, Goris AH, Joosten KF, van Kessel I, Corpeleijn E, et al. Validation of the TracmorD triaxial accelerometer to assess physical activity in preschool children. *Obesity.* 2013;21(9):1877-83.
82. Burrows TL, Martin RJ, Collins CE. A systematic review of the validity of dietary assessment methods in children when compared with the method of doubly labeled water. *J Am Diet Assoc.* 2010;110(10):1501-10.
83. Hill RJ, Davies PS. The validity of self-reported energy intake as determined using the doubly labelled water technique. *Br J Nutr.* 2001;85(4):415-30.
84. Henriksson H. Development of body composition and its relationship with physical activity in healthy Swedish children - A longitudinal study until 4.5 years of age including evaluation of methods to assess physical activity and energy intake [dissertation on the internet]. Linköping: University of Linköping; 2015 [cited 2017 Aug 31]. Available from: <https://www.diva-portal.org/smash/get/diva2:808001/FULLTEXT01.pdf>.
85. Sharp DB, Allman-Farinelli M. Feasibility and validity of mobile phones to assess dietary intake. *Nutrition.* 2014;30(11-12):1257-66.
86. Gemming L, Utter J, Ni Mhurchu C. Image-assisted dietary assessment: A systematic review of the evidence. *J Acad Nutr Diet.* 2015;115(1):64-77.
87. Henriksson H, Bonn SE, Bergstrom A, Balter K, Balter O, Delisle C, et al. A new mobile phone-based tool for assessing energy and certain food intakes in young children: A validation study. *JMIR Mhealth Uhealth.* 2015;3(2):e38.
88. Migueles JH, Cadenas-Sanchez C, Ekelund U, Delisle Nystrom C, Mora-Gonzalez J, Lof M, et al. Accelerometer data collection and processing criteria to assess physical activity and other outcomes: A systematic review and practical considerations. *Sports Med.* 2017. doi: 10.1007/s40279-017-0716-0.
89. Hills AP, Mokhtar N, Byrne NM. Assessment of physical activity and energy expenditure: an overview of objective measures. *Front Nutr.* 2014;1:5.
90. Shephard RJ. The objective monitoring of physical activity. *Prog Prev Medi.* 2017;2(4):e0007.

91. Oliver M, Schofield GM, Kolt GS. Physical activity in preschoolers: Understanding prevalence and measurement issues. *Sports Med.* 2007;37(12):1045-70.
92. Cliff DP, Reilly JJ, Okely AD. Methodological considerations in using accelerometers to assess habitual physical activity in children aged 0-5 years. *J Sci Med Sport.* 2009;12(5):557-67.
93. Routen AC, Upton D, Edwards MG, Peters DM. Discrepancies in accelerometer-measured physical activity in children due to cut-point non-equivalence and placement site. *J Sports Sci.* 2012;30(12):1303-10.
94. Freedson PS, John D. Comment on "estimating activity and sedentary behavior from an accelerometer on the hip and wrist". *Med Sci Sports Exerc.* 2013;45(5):962-3.
95. Fairclough SJ, Noonan R, Rowlands AV, van Hees V, Knowles Z, Boddy LM. Wear compliance and activity in children wearing wrist and hip-mounted accelerometers. *Med Sci Sports Exerc.* 2016;48(2):245-53.
96. Scott JJ, Rowlands AV, Cliff DP, Morgan PJ, Plotnikoff RC, Lubans DR. Comparability and feasibility of wrist- and hip-worn accelerometers in free-living adolescents. *J Sci Med Sport.* 2017. doi: 10.1016/j.jsams.2017.04.017.
97. Hislop J, Palmer N, Anand P, Aldin T. Validity of wrist worn accelerometers and comparability between hip and wrist placement sites in estimating physical activity behaviour in preschool children. *Physiol Meas.* 2016;37(10):1701-14.
98. Schulz KF, Altman DG, Moher D. CONSORT 2010 statement: updated guidelines for reporting parallel group randomized trials. *Ann Intern Med.* 2010;152(11):726-32.
99. Eysenbach G. CONSORT-EHEALTH: improving and standardizing evaluation reports of web-based and mobile health interventions. *J Med Internet Res.* 2011;13(4):e126.
100. Delisle Nystrom C, Henriksson H, Alexandrou C, Bergstrom A, Bonn S, Balter K, et al. Validation of an online food frequency questionnaire against doubly labelled water and 24 h dietary recalls in pre-school children. *Nutrients.* 2017;9(1).
101. Delisle Nystrom C, Henriksson P, Alexandrou C, Lof M. The tanita SC-240 to assess body composition in pre-school children: an evaluation against the three component model. *Nutrients.* 2016;8(6).
102. Bandura A. Human agency in social cognitive theory. *Am Psychol.* 1989;44(9):1175-84.
103. Michie S, Ashford S, Sniehotta FF, Dombrowski SU, Bishop A, French DP. A refined taxonomy of behaviour change techniques to help people change their physical activity and healthy eating behaviours: The CALO-RE taxonomy. *Psychol Health.* 2011;26(11):1479-98.
104. Summerbell CD, Moore HJ, Voge C, Kreichauf S, Wildgruber A, Manios Y, et al. Evidence-based recommendations for the development of obesity prevention programs targeted at preschool children. *Obes Rev.* 2012;13 Suppl 1:129-32.
105. National Food Administration. Food habits, health, and environment: Advice and recommendations for children aged 2-17 [Internet]. Uppsala: National Food Administration Sweden; 2015. [cited 2017 Aug 29] Available from: <http://www.livsmedelsverket.se/>.

106. Wikland KA, Luo ZC, Niklasson A, Karlberg J. Swedish population-based longitudinal reference values from birth to 18 years of age for height, weight and head circumference. *Acta Paediatr.* 2002;91(7):739-54.
107. Slinde F, Ellegard L, Gronberg AM, Larsson S, Rossander-Hulthen L. Total energy expenditure in underweight patients with severe chronic obstructive pulmonary disease living at home. *Clin Nutr.* 2003;22(2):159-65.
108. Davies PS, Coward WA, Gregory J, White A, Mills A. Total energy expenditure and energy intake in the pre-school child: A comparison. *Br J Nutr.* 1994;72(1):13-20.
109. National Food Administration. Weights for foods and dishes. Uppsala: National Food Administration; 1992.
110. National Food Administration. Swedish food database [Internet]. Uppsala; 2014. [cited 2017 Aug 29] Available from: <http://www.slv.se/en-gb/>.
111. Delisle Nystrom C, Forsum E, Henriksson H, Trolle-Lagerros Y, Larsson C, Maddison R, et al. A mobile phone based method to assess energy and food intake in young children: A validation study against the doubly labelled water method and 24 h dietary recalls. *Nutrients.* 2016;8(1).
112. Gibson RS. Principles of Nutrition Assessment. 2 ed. New York, NY: Oxford University Press; 2005.
113. van Hees VT, Renstrom F, Wright A, Gradmark A, Catt M, Chen KY, et al. Estimation of daily energy expenditure in pregnant and non-pregnant women using a wrist-worn tri-axial accelerometer. *PLoS One.* 2011;6(7):e22922.
114. Sadeh A, Lavie P, Scher A, Tirosh E, Epstein R. Actigraphic home-monitoring sleep-disturbed and control infants and young children: A new method for pediatric assessment of sleep-wake patterns. *Pediatrics.* 1991;87(4):494-9.
115. Sadeh A, Sharkey KM, Carskadon MA. Activity-based sleep-wake identification: An empirical test of methodological issues. *Sleep.* 1994;17(3):201-7.
116. Chandler JL, Brazendale K, Beets MW, Mealing BA. Classification of physical activity intensities using a wrist-worn accelerometer in 8-12-year-old children. *Pediatr Obes.* 2016;11(2):120-7.
117. Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet.* 1986;1(8476):307-10.
118. de Souza RJ, Eisen RB, Perera S, Bantoto B, Bawor M, Dennis BB, et al. Best (but oft-forgotten) practices: Sensitivity analyses in randomized controlled trials. *Am J Clin Nutr.* 2016;103(1):5-17.
119. Boushey CJ, Spoden M, Zhu FM, Delp EJ, Kerr DA. New mobile methods for dietary assessment: Review of image-assisted and image-based dietary assessment methods. *Proc Nutr Soc.* 2016;1-12. doi:10.1017/S0029665116002913
120. Livingstone MB, Prentice AM, Coward WA, Strain JJ, Black AE, Davies PS, et al. Validation of estimates of energy intake by weighed dietary record and diet history in children and adolescents. *Am J Clin Nutr.* 1992;56(1):29-35.
121. Collins CE, Burrows TL, Truby H, Morgan PJ, Wright IM, Davies PS, et al. Comparison of energy intake in toddlers assessed by food frequency questionnaire

- and total energy expenditure measured by the doubly labeled water method. *J Acad Nutr Diet*. 2013;113(3):459-63.
122. Reilly JJ, Montgomery C, Jackson D, MacRitchie J, Armstrong J. Energy intake by multiple pass 24 h recall and total energy expenditure: A comparison in a representative sample of 3-4-year-olds. *Br J Nutr*. 2001;86(5):601-5.
 123. Bornhorst C, Bel-Serrat S, Pigeot I, Huybrechts I, Ottavaere C, Sioen I, et al. Validity of 24-h recalls in (pre-)school aged children: comparison of proxy-reported energy intakes with measured energy expenditure. *Clin Nutr*. 2014;33(1):79-84.
 124. O'Connor J, Ball EJ, Steinbeck KS, Davies PS, Wishart C, Gaskin KJ, et al. Comparison of total energy expenditure and energy intake in children aged 6-9 y. *Am J Clin Nutr*. 2001;74(5):643-9.
 125. Kaskoun MC, Johnson RK, Goran MI. Comparison of energy intake by semiquantitative food-frequency questionnaire with total energy expenditure by the doubly labeled water method in young children. *Am J Clin Nutr*. 1994;60(1):43-7.
 126. Salazar G, Vasquez F, Rodriguez MP, Andrade AM, Anziani MA, Vio F, et al. Energy expenditure and intake comparisons in Chilean children 4-5 years attending day-care centres. *Nutr Hosp*. 2015;32(n03):1067-74.
 127. Hall KD, Heymsfield SB, Kemnitz JW, Klein S, Schoeller DA, Speakman JR. Energy balance and its components: implications for body weight regulation. *Am J Clin Nutr*. 2012;95(4):989-94.
 128. Flood VM, Wen LM, Hardy LL, Rissel C, Simpson JM, Baur LA. Reliability and validity of a short FFQ for assessing the dietary habits of 2-5-year-old children, Sydney, Australia. *Public Health Nutr*. 2014;17(3):498-509.
 129. Ahmad Z, Kerr DA, Bosch M, Boushey CJ, Delp EJ, Khanna N, et al. A mobile food record for integrated dietary assessment. *MADiMa16*. 2016;2016:53-62.
 130. Zhu F, Bosch M, Woo I, Kim S, Boushey CJ, Ebert DS, et al. The use of mobile devices in aiding dietary assessment and evaluation. *IEEE J Sel Top Signal Process*. 2010;4(4):756-66.
 131. Mobasher Fard F. Quantitative image based modeling of food on a plate [master's thesis on the internet]. Linköping: Linköping University; 2012 [cited 2017 Sept 01] Available from: <http://liu.diva-portal.org/smash/get/diva2:548826/FULLTEXT02.pdf>.
 132. Gemming L, Rush E, Maddison R, Doherty A, Gant N, Utter J, et al. Wearable cameras can reduce dietary under-reporting: doubly labelled water validation of a camera-assisted 24 h recall. *Br J Nutr*. 2015;113(2):284-91.
 133. Pettitt C, Liu J, Kwasnicki RM, Yang GZ, Preston T, Frost G. A pilot study to determine whether using a lightweight, wearable micro-camera improves dietary assessment accuracy and offers information on macronutrients and eating rate. *Br J Nutr*. 2016;115(1):160-7.
 134. Henriksson H, Forsum E, Lof M. Evaluation of Actiheart and a 7 d activity diary for estimating free-living total and activity energy expenditure using criterion methods in 1.5- and 3-year-old children. *Br J Nutr*. 2014;111(10):1830-40.
 135. Ojiambo R, Konstabel K, Veidebaum T, Reilly J, Verbestel V, Huybrechts I, et al. Validity of hip-mounted uniaxial accelerometry with heart-rate monitoring vs. triaxial

- accelerometry in the assessment of free-living energy expenditure in young children: The IDEFICS validation study. *J Appl Physiol.* 2012;113(10):1530-6.
136. Rosenberger ME, Haskell WL, Albinali F, Mota S, Nawyn J, Intille S. Estimating activity and sedentary behavior from an accelerometer on the hip or wrist. *Med Sci Sports Exerc.* 2013;45(5):964-75.
 137. van Hees VT, Gorzelniak L, Dean Leon EC, Eder M, Pias M, Taherian S, et al. Separating movement and gravity components in an acceleration signal and implications for the assessment of human daily physical activity. *PLoS One.* 2013;8(4):e61691.
 138. Bakrania K, Yates T, Rowlands AV, Esliger DW, Bunnewell S, Sanders J, et al. Intensity thresholds on raw acceleration data: euclidean norm minus one (ENMO) and mean amplitude deviation (MAD) approaches. *PLoS One.* 2016;11(10):e0164045.
 139. Migueles JH, Delisle Nyström C, Cadenas-Sánchez, Henriksson P, Ortega FB, Löf M. Which is the best accelerometer-based metric to predict free-living activity energy expenditure? Abstract in: International Conference on Ambulatory Monitoring of Physical Activity and Movement. 2017; Bethesda, Maryland, USA.
 140. Coward WA, Cole TG . The double labeled water method for the measurement of energy expenditure in humans: risks and benefits. In: Whitehead RG, Prentice A, editors. *New techniques in nutritional research.* 9. ed. San Diego: Academic Press; 1991. p. 139-176.
 141. Niederer I, Burgi F, Ebenegger V, Marques-Vidal P, Schindler C, Nydegger A, et al. Effects of a lifestyle intervention on adiposity and fitness in overweight or low fit preschoolers (Ballabeina). *Obesity.* 2013;21(3):E287-93.
 142. Lissner L, De Bourdeaudhuij I, Konstabel K, Marild S, Mehlig K, Molnar D, et al. Differential outcome of the IDEFICS intervention in overweight versus non-overweight children: Did we achieve 'primary' or 'secondary' prevention? *Obesity Rev.* 2015;16 Suppl 2:119-26.
 143. Taveras EM, Gortmaker SL, Hohman KH, Horan CM, Kleinman KP, Mitchell K, et al. Randomized controlled trial to improve primary care to prevent and manage childhood obesity: The High Five for Kids study. *Arch Pediatr Adolesc Med.* 2011;165(8):714-22.
 144. Rifas-Shiman SL, Taveras EM, Gortmaker SL, Hohman KH, Horan CM, Kleinman KP, et al. Two-year follow-up of a primary care-based intervention to prevent and manage childhood obesity: The High Five for Kids study. *Pediatr Obes.* 2017;12(3):e24-e7.
 145. Morgan PJ, Young MD, Lloyd AB, Wang ML, Eather N, Miller A, et al. Involvement of fathers in pediatric obesity treatment and prevention trials: A systematic review. *Pediatrics.* 2017;139(2).
 146. Kohl LF, Crutzen R, de Vries NK. Online prevention aimed at lifestyle behaviors: a systematic review of reviews. *J Med Internet Res.* 2013;15(7):e146.
 147. Sardi L, Idri A, Fernandez-Aleman JL. A systematic review of gamification in e-Health. *J Biomed Inform.* 2017;71:31-48.
 148. Baghaei N, Nandigam D, Casey J, Direito A, Maddison R. Diabetic Mario: Designing and evaluating mobile games for diabetes education. *Games Health J.* 2016;5(4):270-8.

149. Bell ML, Fiero M, Horton NJ, Hsu CH. Handling missing data in RCTs; A review of the top medical journals. *BMC Med Res Methodol*. 2014;14:118.
150. Dziura JD, Post LA, Zhao Q, Fu Z, Peduzzi P. Strategies for dealing with missing data in clinical trials: From design to analysis. *Yale J Biol Med*. 2013;86(3):343-58.
151. Johansson E, Larisch LM, Marcus C, Hagstromer M. Calibration and validation of a wrist- and hip-worn actigraph accelerometer in 4-year-old children. *PLoS One*. 2016;11(9):e0162436.
152. Taylor RW, Grant AM, Goulding A, Williams SM. Early adiposity rebound: Review of papers linking this to subsequent obesity in children and adults. *Curr Opin Clin Nutr Metab Care*. 2005;8(6):607-12.
153. Besharat Pour M, Bergstrom A, Bottai M, Kull I, Wickman M, Hakansson N, et al. Effect of parental migration background on childhood nutrition, physical activity, and body mass index. *J Obes*. 2014;406529.
154. Statistics Sweden. Educational attainment of the population [Internet]. Örebro: Statistics Sweden; 2014. [cited 2017 Aug 29] Available from: <http://www.scb.se>.
155. Ulijaszek SJ, Pentecost M, Marcus C, Karpe F, Fruhbeck G, Nowicka P. Inequality and childhood overweight and obesity: a commentary. *Pediatr Obes*. 2017;12(3):195-202.
156. Public Health Agency of Sweden. Overweight and obesity national statistics [Internet]. Solna: Public Health Agency of Sweden; 2014. [cited 2017 Aug 29] Available from: www.folkhalsomyndigheten.se.
157. Public Health Agency of Sweden. Health in Sweden [Internet]. Solna: Public Health Agency of Sweden; 2014. [cited 2017 Aug 29] Available from: <http://www.folkhalsomyndigheten.se>.
158. National Food Administration. Riksmaten [Internet]. Uppsala: National Food Administration; 2003. [cited 2017 Aug 29] Available from: <http://www.slv.se>.
159. Reilly JJ, Kelly LA, Montgomery C, Jackson DM, Slater C, Grant S, et al. Validation of Actigraph accelerometer estimates of total energy expenditure in young children. *Int J Pediatr Obes*. 2006;1(3):161-7.
160. Davidson AJ, O'Brien M. Ethics and medical research in children. *Paediatr Anaesth*. 2009;19(10):994-1004.
161. Hein IM, De Vries MC, Troost PW, Meynen G, Van Goudoever JB, Lindauer RJ. Informed consent instead of assent is appropriate in children from the age of twelve: policy implications of new findings on children's competence to consent to clinical research. *BMC Med Ethics*. 2015;16(1):76.
162. Hein IM, Troost PW, Lindeboom R, Benninga MA, Zwaan CM, van Goudoever JB, et al. Accuracy of the MacArthur competence assessment tool for clinical research (MacCAT-CR) for measuring children's competence to consent to clinical research. *JAMA Pediatr*. 2014;168(12):1147-53.
163. Wendler DS. Assent in paediatric research: theoretical and practical considerations. *J Med Ethics*. 2006;32(4):229-34.