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Intervention Study Aiming at the Prevention of Excess Weight Gain in Childhood

Intensified dietary and physical activity counselling on mothers during pregnancy and child's first year at maternity or child health clinics

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ACADEMIC DISSERTATION
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Erratum:

last line on page 16 continuing to page 17, sentence starting: A prevalence report from Finland…,

must be replaced with the following sentence:

The prevalence reports by Vuorela et al. showed that nearly 9% of 2-year-old and 14% of 5-year-old children were overweight or obese in the 2000s; the corresponding prevalence was 21% among 12-year-old children in Finland (Vuorela et al. 2009 and 2011).

21.04.2013 Taina Mustila

Contents

LIST OF ORIGINAL PUBLICATIONS

This dissertation is based on the following original publications referred to in the text by their Roman numerals (I–IV).

I Mustila T, Raitanen J, Keskinen P, Saari A, Luoto R (2012): Lifestyle counselling during pregnancy and offspring weight development until four years of age: follow-up study of a controlled trial. J Negat Results Biomed 11:11.

II Mustila T, Raitanen J, Keskinen P, Saari A, Luoto R (2012): Lifestyle counselling targeting infant's mother during the child's first year and offspring weight development until 4 years of age: a follow-up study of a cluster RCT. BMJ Open 2:e000624.

III Mustila T, Keskinen P, Luoto R (2012): Behavioral counselling to prevent childhood obesity – study protocol of a pragmatic trial in maternity and child health care. BMC Pediatr 12:93.

IV Mustila T, Raitanen J, Keskinen P, Saari A, Luoto R (2013): Pragmatic controlled trial to prevent childhood obesity in maternity and child health care clinics: pregnancy and infant weight outcomes (The VACOPP Study). Manuscript submitted.

ABBREVIATIONS

BMI	Body mass index
BP	Blood pressure
CAD	Coronary artery disease
CCT	Controlled clinical trial
CHC	Child health care clinic
CI	Confidence interval
DM	Diabetes mellitus
GDM	Gestational diabetes mellitus
GWG	Gestational weight gain
HDL	High density lipoprotein
ICC	Intra-cluster correlation coefficient
IOM	Institute of Medicine of the National Academics
IOTF	International Obesity Task Force
MC4R	Melanocortin-4 receptor
MHC	Maternity health care clinic
NELLI	Neuvonta, ELintavat ja LIikunta neuvolassa – tutkimus (Counselling, lifestyle and physical activity in maternity or child health clinics study)
OGTT	Oral glucose tolerance test
PA	Physical activity
PHN	Public health nurse
P-ALAT	Plasma alanine aminotransferase
RCT	Randomised controlled trial
SD	Standard deviation
SDS	Standard deviation score
STRIP	Special Turku Coronary Risk Factor Intervention Project for Children
UK	United Kingdom
VACOPP	Vaasa Childhood Obesity Primary Prevention Study
WC	Waist circumference
WHO	World Health Organization

ABSTRACT

The prevalence of childhood obesity has more than doubled during the past three decades in Western countries and is rapidly increasing in developing countries. Some reports of abating prevalence numbers have started to emerge, but the prevalence is still high. Obesity results in many social and health-related disadvantages during childhood that often track to adulthood. Type 2 diabetes and cardiovascular diseases are the most serious complications of obesity. Overweight or obesity seems to frequently originate from preschool years. To prevent the continuum of obesity, preventive actions should start during this early period of life.

The aims of this dissertation were: 1) to evaluate the effect of lifestyle intervention targeting mothers in maternity or child health care clinics (The NELLI pilot study) regarding their offspring's weight development until four years of age; 2) to describe protocol of the pragmatic behavioural intervention trial (The VACOPP Study) aiming to prevent excess weight gain during preschool years; and 3) to report its first results on pregnancy and infant growth outcomes.

The participants in the two follow-up studies (I–II) were first-time pregnant mothers (N=109) or mothers with infants (N=89), who had participated in an intervention trial (The NELLI pilot study) with dietary and physical activity aims either during pregnancy or during their infant's first 2–10 months. The controlled trial was conducted in three intervention and control maternity or child health care clinics in the cities of Tampere and Hämeenlinna in Finland. The intervention consisted of intensified counselling on diet and physical activity at public health nurse (PHN) visits, with an option to participate in a weekly exercise group. The participant mothers received a follow-up questionnaire regarding their 4–5 years old child's growth measurements. The response rate in the gestational intervention (I) was 66.1%, and in the study concerning the infant age (II) that was 71.9%. The increase in z-scores for weight-for-height and BMI-for-age among the offspring of mothers, who received the lifestyle counselling when their infants were aged between 2 and 10 months, was significantly slower between 24 and 48 months compared to the control group (p-values 0.012 and 0.028). The weight gain of children whose mothers received the lifestyle intervention during pregnancy did not differ significantly from the control group's weight gain.

The third publication (III) is a report of the study protocol used in the pragmatic controlled intervention trial to prevent childhood obesity in preschool age children

(The VACOPP Study). The study was implemented in maternity and child health care clinics in the city of Vaasa. The participants were mothers (N=185) at risk of gestational diabetes mellitus (GDM) during the current pregnancy and their offspring up to six years of age. The offspring of these mothers are considered to be at risk for obesity. The intervention during pregnancy consisted of two group sessions given by a physiotherapist and a dietician. Information on healthy diet and suitable physical activity during pregnancy was also given in a written format. The PHNs in maternity clinics repeated the counselling briefly during routine visits. The behavioural counselling was to continue during visits to child health care clinics until the children reached the age of 5 years. The fourth study (IV) reports the results of the early part of the VACOPP Study, namely the results of the intervention implemented in the maternity health care clinics. The counselling had no significant effect on the mother's weight gain during pregnancy, the offspring's birth weight or the infant's weight gain until one year of age. A significantly lower proportion of mothers had impaired glucose tolerance in mid-pregnancy among the intervention group compared to the control group (14.6% vs. 29.2%; p-value 0.016).

In conclusion, lifestyle intervention targeting mothers during their offspring's first year seemed to slowdown the offspring's weight gain from 2 to 4 years of age, suggesting a possible effect towards a lower risk for obesity. Counselling on diet and physical activity, targeting mothers at risk of GDM during pregnancy, seemed to diminish the occurrence of GDM, which may lower the risk of obesity among offspring in later childhood. These findings need to be strengthened in future studies. To diminish the high prevalence of obesity beginning in childhood, preventive programs starting in early life and applicable to primary health care settings are needed.

TIIVISTELMÄ

Lihavien lasten määrä on yli kaksinkertaistunut viimeisten kolmen vuosikymmenen aikana länsimaissa, ja sen ilmaantuvuus on nopeasti lisääntymässä myös kehittyvissä maissa. Joidenkin tuoreiden tutkimusten mukaan lasten lihavuuden esiintyminen on vähentymässä, mutta esiintymisluvut ovat yhä korkeat. Lihavuus aiheuttaa monia sosiaalisia ja terveyshaittavaikutuksia jo lapsuudessa, ja lihavasta lapsesta tulee usein lihava aikuinen. Tyypin 2 diabetes sekä sydän- ja verisuonisairaudet ovat lihavuuden vakavimmat terveyshaitat. Ylipaino tai lihavuus ilmaantuu usein jo alle kouluiässä. Lihavuuden esiintymisen vähentämiseksi ehkäisevät toimet tulisi aloittaa jo tuossa varhaisessa elämänvaiheessa.

Tämän väitöskirjan tarkoituksena oli tutkia 1) äideille suunnatun joko äitiys- tai lastenneuvolassa toteutetun elintapaneuvonnan (NELLI-pilottitutkimus) vaikutusta heidän lastensa painonkehitykseen neljään ikävuoteen mennessä, 2) kuvata pragmaattisen kontrolloidun äitiys- ja lastenneuvoloissa toteutetun lasten liiallisen painonnousun ennaltaehkäisyyn tähtäävän, terveyskäyttäytymiseen vaikuttavan interventio-tutkimuksen (VACOPP-tutkimus) protokolla, sekä 3) raportoida sen ensimmäiset tulokset koskien raskausajan mittareita ja imeväisiän kasvua. Seurantatutkimusten (I–II) osallistujat olivat joko ensisynnyttäjä- (N=109) tai imeväisikäisten vauvojen äitejä (N=89), jotka olivat osallistuneet ravitsemus- ja liikuntaneuvontaa sisältäneeseen interventiotutkimukseen (NELLI-pilottitutkimus) joko raskausaikana tai heidän vauvojensa ollessa 2–10 kuukauden ikäisiä, ja heidän lapsensa. Kontrolloitu tutkimus oli toteutettu kolmessa koe- ja kontrolliäitiys- tai -lastenneuvolassa Tampereella ja Hämeenlinnassa. Interventio sisälsi tehostettua ravitsemus- ja liikuntaneuvontaa neuvolaterveydenhoitajakäyntien yhteydessä, minkä lisäksi oli tarjottu mahdollisuutta osallistua ryhmäliikuntatilaisuuteen kerran viikossa. Interventioon osallistuneille äideille lähetettiin heidän 4–5-vuotiaiden lastensa kasvutietoja koskeva seurantakysely. Vastausprosentti raskausajan (I) tutkimuksessa oli 66.1% ja 71.9% imeväisiän (II) tutkimuksessa. Tehostettuun neuvontaan lasten vauvaiän aikana osallistuneiden äitien lasten painonnousu mitattuna pituuteen suhteutetun painon tai painoindeksin (BMI) standardideviaationa (SD) oli merkitsevästi hitaampaa 24–48 kuukauden iässä verrattuna kontrolliryhmän lasten painnousuun (p-arvot 0.012 ja 0.028). Raskausaikana vastaavaan neuvontaan osallistuneiden äitien lasten painonnousuvauhdissa ei ollut merkitsevää eroa kontrolliryhmään verrattuna.

Kolmannessa osajulkaisussa (III) on raportoitu alle kouluikäisten lasten lihavuuden ennaltaehkäisyyn tähtäävän pragmaattisen kontrolloidun tutkimuksen (The VACOPP Study) protokolla. Tutkimus toteutetaan Vaasan kaupungin äitiys- ja lastenneuvoloissa. Osallistujat ovat äitejä (N=185), jotka kuuluivat raskausdiabeteksen riskiryhmään odotusaikana ja heidän lapsensa kuuteen ikävuoteen asti. Näiden äitien lapsilla oletetaan olevan suurentunut lihomisriski. Raskausajan neuvontaan sisältyi kaksi ryhmäneuvontatilaisuutta, joiden toteuttajat olivat ravitsemussuunnittelija ja fysioterapeutti. Äideille annettiin myös kirjallista materiaalia raskausajan terveellisestä ravitsemuksesta ja sopivasta liikunnasta. Äitiysneuvolan terveydenhoitajat kertasivat tätä tehostettua neuvontaa lyhyesti rutiinineuvolakäyntien yhteydessä. Tehostettu terveyskäyttäytymisneuvonta jatkuu lastenneuvolakäyntien yhteydessä lapsen viidenteen ikävuoteen asti.

Neljännessä osatyössä (IV) raportoidaan VACOPP-tutkimuksen äitiysneuvolaintervention tuloksia. Raskausajan interventiolla ei ollut merkittävää vaikutusta äidin raskausajan painonnousuun, vastasyntyneen painoon tai imeväisen painonnousuun yhteen ikävuoteen mennessä. Koeryhmän äideillä oli kuitenkin tilastollisesti merkitsevästi vähemmän poikkeavia glukoosiarvoja keskiraskauden glukoosirasitustestissä (14.6 % vs. 29.2 %, p-arvo 0.016).

Yhteenvetona voidaan todeta, että imeväisikäisten lasten äideille suunnattu ravitsemus- ja liikuntaneuvonta näytti hidastavan lasten painnousua 2 ja 4 ikävuoden välillä, mikä saattaa pienentää lasten myöhempää lihomisriskiä. Raskausdiabeteksen riskiryhmässä oleville äideille suunnattu ravitsemus- ja liikuntaneuvonta raskausaikana vähensivät raskausdiabeteksen ilmaantumista, mikä voi vähentää syntyneiden lasten liiallista painonnousua myöhemmin lapsuudessa. Nämä tutkimustulokset tulee varmistaa toisissa tutkimuksissa. Lihavuuden esiintymisen vähentämiseksi sen ennaltaehkäisyyn tähtäävät toimet tulisi käynnistää jo varhaisen elämän aikana, ja niiden tulisi olla sovellettavissa perusterveydenhuollon normaaliin toimintaan.

1 INTRODUCTION

Obesity is a worldwide costly health concern although the increase in the prevalence of childhood obesity seems to be abating, at least in some Western countries (Wang and Lobstein 2006, de Onis et al. 2010, Olds et al. 2011). Childhood obesity has many adverse influences during childhood, including psychosocial problems, in addition to adverse health consequences (Janssen et al. 2004, Daniels et al. 2005, Han et al. 2010). Childhood obesity often tracks to adulthood and thus increases the later risk of type 2 diabetes and cardiovascular diseases, as well as other health concerns in adult life (Freedman et al. 2005, Nader et al. 2006, Juonala et al. 2011).

Genetic susceptibility is a strong determinant for the risk of being an obese child, but the obesity epidemic is mainly attributable to societal, environmental and lifestyle changes that modern society has encountered (Han et al. 2010, Zhao and Grant 2011, Manco and Dallapiccola 2012). The environment starts to play a role in obesity risk early in life, even during foetal life, infancy and preschool years (Ong and Loos 2006, Dabalea and Crume 2011, Lawlor et al. 2011a). Reversing a child's obesity to a healthy weight with interventions is difficult (Oude et al. 2009). This reality supports the efforts to find obesity preventive interventions that are applicable in early life. Preventive actions should target modifiable elements that are known to increase the risk of obesity. There is evidence that mother's obesity, excessive weight gain and impaired glucose tolerance during pregnancy may induce such changes in foetal environment that offspring's risk for overweight or obesity increases (Dubois and Girard 2006, The HAPO Study Cooperative Research Group 2008, Wrotniak et al. 2008, Dabalea and Crume 2011). Also, rapid weight gain in infancy and during preschool years has been related to a later risk for obesity (Reilly et al. 2005, Ong and Loos 2006, Lagström et al. 2008). Breastfeeding may protect against obesity, especially if the mother is overweight (Buyken et al. 2008). Food preferences develop and are modifiable during preschool years, so parents play a critical role in introducing healthy dietary habits to their offspring (Lanigan and Singhal 2009, Jones et al. 2010, Singhal et al. 2010). Less physically active children are prone to excess weight gain, and reducing sedentary time has the potential to mitigate this risk (Reilly et al. 2005, Jiménez-Pavón et al. 2010, te Velde et al. 2012). Sleep duration shorter than the age appropriate recommendations has been associated with excess weight gain in children (Landhuis et al. 2008).

To date, the number of reported childhood obesity prevention studies starting during preschool years is sparse and the follow-up periods have been short (Ciampa et al. 2010, Hesketh and Campbell 2010, Waters et al. 2011). In these studies, some positive effects on children's weight development have been found, but evidence of effective preventive means to reduce childhood obesity is still insufficient. Childhood obesity is a common health problem concerning the whole community, which requires preventive interventions to be applicable in normal health care practice. Current evidence suggests that multifaceted intervention is more effective compared with targeting a single behaviour (Lindsay et al. 2006, Birch and Ventura 2009). By targeting preventive programs towards families at risk of having overweight or obese offspring, cost-effectiveness can be improved. Finding effective methods, which can combat the current obesity epidemic, calls for performing intervention studies aimed at healthy weight gain in infants and preschool age children.

2 REVIEW OF THE LITERATURE

2.1 Definition, classification and assessment of body composition in a child

Predicting health risks related to excessive weight during childhood requires methods to define obesity in a growing child. These methods should be easy to implement in a normal health care system, and should give a valid estimate of health-threatening excess weight. Childhood obesity is defined as a condition where a child has excess body fat in such a proportion that her/his wellbeing and health is at risk of being impaired (WHO 2000). Because body fat is difficult to measure directly in normal health care practice, it is estimated by assessing a child's weight and length/height, which are then converted into body mass index (BMI) or a weight-for-length/height value. BMI-for-age is considered the best estimate of adiposity in childhood in relation to later cardiovascular morbidity (Pietrobelli et al. 1998, Freedman et al. 2009). BMI is the ratio of weight in kilograms divided by the height in meters squared (kg/m^2). Diagnosing excess adiposity in a child requires the comparison of the BMI value with age- and gender-specific values in order to take into account changes in body composition with age (Ellis 2000). However, BMI-for-age can see major changes in children under two years of age, which is why it is not suggested for use in the evaluation of overweight in children in that age group (Saari et al. 2011, Childhood obesity: Current Care Guideline 2012).

There are several BMI references based on national or international growth data and there are currently no uniform internationally accepted cut-off-references for childhood overweight and obesity (Reilly et al. 2010, Rolland-Cachera 2011). The cut-off-values are based on different selected percentiles or standard deviation scores (SDS). Internationally, the most recommended definitions in assessing childhood overweight and obesity are WHO (World Health Organization) and IOTF (International Obesity Task Force) references (WHO 1995, Cole et al. 2000). IOTF established also age- and gender-specific cut-off-percentiles corresponding to adult cut-off-values for overweight (BMI ≥ 25 kg/m^2) and obesity (≥ 30 kg/m^2). These BMI cut-off-values called ISO-BMI -values have been recently established also in new Finnish growth data (Saari et al. 2011). Obesity in childhood has been also defined as weight-for-length/height. Children aged 7 years or older in Finland have been classified as overweight or obese if their weight-for-height is ≥ 20% or > 40% above the mean weight-for-height of

healthy Finnish children. Corresponding cut-offs for children younger than 7 years are ≥ 10% and > 20% above the mean. The disadvantage of weight-for-length/height-based definitions of child's weight status is that they do not take into account the age of the child. After establishing new Finnish growth references, using weight-for-length cut-offs in children under two years of age and ISO-BMI in children over two years of age are recommended when diagnosing overweight or obesity in Finnish children (Saari et al. 2011, Childhood obesity: Current Care Guideline 2012).

Another practical measure to assess obesity in children would be the measurement of waist circumference (WC). WC is known to correlate with adiposity and risk for cardiovascular diseases, but there are no Finnish or internationally accepted age- and gender-specific normal or cut-off values concerning children. Furthermore, a recent review has concluded that there is currently no evidence to prefer WC instead of age- and gender-specific BMI references in identifying excess adiposity in relation to adverse cardiometabolic risk profiles in children (Reilly et al. 2010).

The most accurate methods to assess excess adiposity in children are those which require special equipments or devices. For example, magnetic resonance imaging, dual-energy x-ray and computed tomography are reliable but costly and laborious methods and are therefore mainly used in research purposes and in the validation of other adiposity measurement methods (Ellis 2000). More easily accessed indirect methods to assess adiposity are skin-fold thickness measurements and bioelectrical impedance analysis, which lack reference values for children (Ellis 2001).

2.2 Prevalence of childhood obesity

During the last three decades, the prevalence of childhood obesity has increased to proportions earning the definition of an epidemic in most industrialised countries and is also increasing in the developing world, especially in urban areas (Lobstein et al. 2004, Wang and Lobstein 2006). From 1970 to 1990, the prevalence of overweight or obesity doubled or trebled in countries including Finland, the USA, Australia, Japan, Canada, Germany and the United Kingdom (UK) (Wang and Lobstein 2006). It is noticeable that the definitions of overweight and obesity used in these prevalence studies are based on several different growth references, as described in the previous section. The prevalence of overweight and obesity increases with age (Kautiainen et al. 2010). More than 40% of children in the North America and eastern Mediterranean WHO regions, 38% in Europe and 22% in Southeast Asia were predicted to be overweight or obese in year 2010. 11.7% of children aged 0–5 years in developed countries and 6.1% of children in developing countries were estimated to be overweight or obese in the year 2010 (de Onis et al. 2010), indicating that obesity is already prevalent in preschool years. In the UK, 23% of children between 4 and 5 years of age were overweight by 2010 (Department of Health 2010). A prevalence report from Finland in

2001 showed that nearly 18% of 2 year-old children are overweight or obese, 30% of 5 year-old children and that prevalence is 40% among 12 year-old children (Vuorela et al. 2010). According to this report of Vuorela et al., overweight and obesity among 2 year-old children had not increased, but had decreased in Finland between 1974 and 2001. The prevalence of overweight and obesity in 5–7 years of age children was quite stable from 1986 to 2006, but nearly doubled in boys aged 12 years, while the increase during this time period among girls was lower (Vuorela et al. 2009). Data from 2007–2009 in the report of National Institute of Health and Welfare shows that approximately 10% of three- to five-year-old boys and 15% of girls in the same age group are overweight or obese; the corresponding prevalence at school age is 20% for both genders (Kaikkonen et al. 2012). The most significant increases in overweight and obesity in Finland have occurred among adolescents: from the 1970s to the 2000s the prevalence increased 2- to 3-fold (Kautiainen 2008, Vuorela et al. 2011).

Some recent reports have shown a slightly decreasing prevalence of childhood overweight and obesity. In Massachusetts, USA, the prevalence of obesity slightly decreased among children less than 6 years of age between 2004 and 2008 (Wen et al. 2012). Olds et al. (2011) evaluated reports from nine countries (Australia, China, England, France, Netherlands, New Zealand, Sweden, Switzerland and USA) in a review article, and found that the prevalence of childhood excessive weight appeared to be levelling off more in girls than boys between 1995 and 2008, and the prevalence numbers were even slightly decreasing, especially in the preschool age group; the prevalence is still high. In Sweden, despite the stabilising rates of obesity and overweight in 10 year-olds, these conditions were more prevalent among the lower socioeconomic status population (Sundblom et al. 2008).

2.3 Health consequences of obesity in childhood

Childhood obesity has adverse effects on several organ systems (Daniels 2009). Psychosocial problems related to obesity in childhood are frequent. Obese children often have low self-esteem; they are easy targets for bullying and have been shown to have depression more often than their normal weight peers (Britz et al. 2000, Wardle and Cooke 2005, Lumeng et al. 2010). Obese children also seem to have a lower quality of life (Schwimmer et al. 2003); these psychosocial problems may have far-reaching consequences in life.

Obesity also commonly causes hypertension in childhood (Sorof and Daniels 2002) and is responsible for several metabolic abnormalities. Insulin resistance accompanying obesity during adolescence may lead to impaired glucose tolerance and ultimately to type 2 diabetes in case of persisting obesity (Pinhas-Hamiel et al. 1996). Dyslipidemia is commonly present in obese children (Cook and Kavey 2011); it usually presents as a low high-density lipoprotein concentration and increase in triglycerides,

a lipid profile known to accelerate the atherosclerotic process. A clustering of risk factors called metabolic syndrome can be diagnosed in paediatric patients aged at least 10 years (Zimmet et al. 2007). However, concerning children and adolescents from 10 to 16 years of age, no consistent definition of this syndrome exists.

An important adverse outcome of obesity is non-alcoholic fatty liver, which is usually asymptomatic in children, but may progress in time to hepatic fibrosis and cirrhosis (Schwimmer et al. 2003). Non-alcoholic fatty liver is also linked to an increased risk of type 2 diabetes (Nadeau et al. 2005). Mallory et al. (1989) found that about one third of severely obese children in their study had symptoms related to obstructive sleep apnoea and 5% had severe obstructive sleep apnoea. The increased prevalence of asthma among obese children has been reported in some studies, but the association of asthma and obesity is not unequivocal (Santamaria et al. 2007). Excess weight stresses the musculoskeletal system, which may cause impaired mobility and musculoskeletal discomfort and even lead to slipped capital femoral epiphysis and tibia vara in childhood (Taylor et al. 2006). Obesity seems also to lead to lower D-vitamin concentrations, which may partly mediate the adverse consequences of obesity (Vimaleswaran et al. 2013).

Since childhood obesity often tracks into adulthood, it is a strong risk factor for cardiovascular diseases in adults (Eriksson et al. 2001, Owen et al. 2009, de Kroon et al. 2010, Andersen et al. 2010, Tirosh et al. 2011). Children who are overweight between the ages of 2 and 4 have a five-fold risk of being overweight by the age of 12 years compared to normal weight peers. The earlier a child becomes overweight, the stronger the risk of becoming an overweight adult is (de Kroon et al. 2010). There is evidence of a positive correlation of childhood BMI and adult intima media thickness (Freedman et al. 2008).

The results from four large cardiovascular risk factor studies' following children to adulthood showed that overweight and obese children who were also obese as adults had an increased risk of type 2 diabetes, hypertension, dyslipidemia and carotid artery atherosclerosis (Juonala et al. 2011). These risks were higher than in obese adults who were a normal weight in childhood. A positive finding in this study was that if children became non-obese by adulthood, they did not have an increased risk of those outcomes compared to adults who had never been obese.

The risk of cancer in later life, especially breast cancer risk, seems to be increased as a consequence of childhood obesity (Reilly and Kelly 2011). In a study among American Indian children with a BMI in the highest quartile at the mean age of 11.3 years, the risk of premature death from endogenous causes before age 55 years was more than double compared to children with a BMI in the lowest quartile (Franks et al. 2010). However, that study was not powered to analyse the effects on more specific categories of endogenous causes of death. Similarly premature mortality rates in adulthood have been found in other studies (Reilly and Kelly 2011).

2.4 Early life risk factors for childhood obesity

2.4.1 Genetic factors

The increased prevalence of obesity during recent decades is mainly due to changes in lifestyle and environment. A strong determinant for this trend is the human genome, which is not able not adapt to those changes rapidly. The human ability to effectively store energy was formerly an advantage, but in today's society this easily leads to excess adiposity, especially in those genetically prone (Eckel 2003). There is racial and familial clustering of obesity.

Children of overweight or obese parents have a high risk of developing obesity (Jääskeläinen et al. 2011). The risk of overweight that is mediated by parental excess weight is due to shared genes, societal and physical environment and diet (Silventoinen et al. 2007a, Silventoinen et al. 2007b). If both parents are obese, the offspring's obesity risk has been shown to be from six- to 15-fold (Price et al. 1990, Jääskeläinen et al. 2011). The risk of an obese mother passing obesity on to her children is stronger than that for an obese father (Danielzik et al. 2002, Öhlund et al. 2010). Some racial groups, such as Pima Indians, African-Americans and Hispanic people, are susceptible to obesity (Knowler et al. 1991, Maligie et al. 2012). In twin and non-twin sibling studies, it has been shown that genetic factors contribute between 40 and 70% of the variation of susceptibility to excess adiposity (Hebebrand et al. 2003, Bell et al. 2005, Silventoinen et al. 2010).

Epigenetics is a newer area of heritability under intensive research. Environment in foetal and infant life can induce the up- or down-regulation of changes in expression of the child's genotype, changes which are capable of potentiating offspring's risk for obesity (Godfrey et al. 2011, Hochberg et al. 2011). Monogenic obesity is rare, of which MC4R (Melanocortin-4 receptor) mutations are the most frequent, affecting about 5% of the severely obese (Lubrano-Berthelier 2006). The number of genes known to be associated with obesity is now over forty; however, these seem to explain only a minor portion of the differences in adiposity risk (Speliotes et al. 2010). The knowledge of the heritability of obesity is expected to take a huge step forward with next-generation sequencing techniques (Manco and Dallapiccola 2012).

2.4.2 Prenatal environment

2.4.2.1 Mother's weight

According to epidemiological studies, mother's obesity and excessive gestational weight gain are strong determinants of the offspring's obesity risk (Salsberry and Reagan 2005, Wrotniak et al. 2008). At present, pregnant mothers are often obese, which means that

children often encounter an obesinogenic environment prenatally (Barker and Clark 1997, Whittaker 2004, Ornoy 2011, Catalano et al. 2012). Maternal excessive weight gain during pregnancy has been shown to increase birth weight independently of genetic factors (Ludwig and Currie 2010). Deierlein et al. (2012) showed that maternal weight gain exceeding recommendations during pregnancy resulted in faster weight gain and higher weight-for-length until the age of three years in offspring. Newborns of overweight and obese women with normal glucose tolerance have increased fat mass in comparison with those of lean or average weight women (Sewell et al. 2006). Maternal pre-pregnancy BMI and foetal adiposity have positive correlation with newborn insulin resistance (Catalano et al. 2009). Kral et al. (2006) reported that the prevalence of obesity was 52% lower among the same age offspring born to mothers after bariatric surgery and weight loss, compared to offspring born before that procedure. Smith et al. (2009) found a 3-fold lower prevalence of obesity among offspring born after the mother's bariatric surgery compared to offspring born before this surgical procedure; these offspring also had more advantageous metabolic profiles concerning several metabolic markers than children born before bariatric surgery. In the prospective longitudinal Northern Finland Birth Cohort of 1986 study, a 2.6-fold risk of overweight at age of 16 years was found if the mother was overweight before pregnancy (Pirkola et. al. 2010a). Offspring exposed to maternal obesity during foetal life also appear to have a higher risk for type 2 diabetes (Dabalea et al. 2008, Pirkola et al. 2010b).

2.4.2.2 Gestational diabetes mellitus

Gestational diabetes mellitus has become a frequent complication of pregnancy as a consequence of an increased prevalence of overweight and obesity among women of a fertile age (Harlev and Witznitzer 2010, Simmons 2011). There is evidence of the mother's GDM increasing the risk of obesity in childhood and adolescence (Gillman et al. 2003, Hillier et al. 2007, Vääräsmäki et al. 2009, Chandler-Laney et al. 2011). Maternal hyperglycaemia, even lower than gestational diabetes levels, is capable of inducing changes in foetal metabolism resulting in e.g. higher birth weight (The HAPO Study Cooperative Research Group 2008, Catalano et al. 2012, Mäkelä et al. 2013). This risk seems to be partly independent of the newborn's birth weight and also of maternal pre-pregnancy weight (Gillman et al. 2003, Rogers et al. 2006, Lawlor 2011, Baptiste-Roberts et al. 2012). In addition to increasing the risk of excess weight gain in the offspring, mother's GDM has been shown to increase their fat mass (Rogers et al. 2006, Chandler-Laney 2011). The obesinogenic effect of GDM on the offspring's weight gain is often not seen during the first years of life, but rather after toddler years (Pettitt et al. 2010, Crume et al. 2011, Baptiste-Roberts et al. 2012). In the Northern Finland Birth Cohort study, the mother's GDM seemed to increase the offspring's risk of overweight in adolescence only if the mother was overweight before pregnancy (Pirkola et al. 2010a).

Mother's GDM causes foetal insulin resistance, hyperinsulinism and excessive growth, which induce adverse metabolic consequences in the offspring (Bush et al. 2011).

2.4.2.3 Newborn birth weight

Both high and low birth weights have been associated with an increased risk of childhood and adult obesity (Yu et al. 2011). Barker and Clark (1997) presented a hypothesis that impaired foetal growth induces permanent changes in offspring metabolism during this critical period, which increases the risk for adiposity and other metabolic adverse outcomes. This assumption has subsequently been confirmed in other studies and been extended similarly to overgrowth of the foetus (Barker et al. 2002, Eriksson et al. 2003, Li et al. 2003, Bush et al. 2011). In the study of Wei et al. (2007), low birth weight was associated with a higher risk of diabetes, whereas high birth weight was associated with higher obesity and diabetes risks. Newborn macrosomia has been shown to increase the risk of overweight and obesity in several studies (Gillman et al. 2003, Araujo et al. 2009, Weng et al. 2012). Oldroyd et al. (2011) showed that high birth weight increased the risk of overweight or obesity in both girls and boys, but low birth weight seemed to decrease this risk only in girls. A recent report by Sparano et al. (2012) found a positive correlation with newborn macrosomia and childhood overweight or obesity in both boys and girls, which was not related to the mother having GDM. The importance of optimal prenatal growth was strengthened in a recent systematic review and meta-analysis, which concluded that low birth weight is associated with a decreased risk of later overweight, and that high birth weight correlates with an increased risk of overweight (Schellong et al. 2012).

2.4.2.4 Metabolic consequences

The mechanisms mediating the obesinogenic effect of the prenatal environment are not well known. There are several mechanisms thought to be responsible for the associations of pregnant mothers' obesity, gestational diabetes and the risk of obesity in offspring. There are specific intrauterine factors affecting developing foetus that are not explained by genetic susceptibility, shared lifestyle or environment. It is suggested that a hyperglycaemic prenatal environment may induce oxidative stress in foetal mitochondria leading to adverse consequences in foetal metabolism (Fröhlich et al. 2012). The hyperglycaemic environment of obese or overweight mothers seems to mediate the overgrowth of the foetus, probably by increasing foetal insulin production (Catalano et al. 2009, Bush et al. 2011). Foetal hyperinsulinism is suspected to mediate intrauterine programming via metabolic imprinting, which can induce changes in appetite regulation and also in energy regulation and metabolism (Barker 1997, Cripps et al. 2005). Hyperinsulinemia is adipogenic and animal studies have suggested that it has

the potential to induce permanent changes in such regions of the brain that regulate metabolism and body weight (Dörner et al. 1994, Ornoy 2011).

Mothers of macrosomic newborns have been shown to have higher plasma concentrations of free fatty acids and triglycerides than mothers of normal weight newborns. Placental lipase hydrolyses triglycerides to free fatty acids providing the foetus with excess lipids, which could also increase foetal adiposity by increasing the number, size or lipase activity in fat cells (Schaefer-Graf et al. 2008). Mother's hyperglycaemia is suggested to also result in higher newborn leptin concentrations possibly causing leptin resistance or altered leptin signalling, which may promote excess adiposity later in life (Simmons and Breier 2002, Dabalea and Crume 2011).

The alterations in foetal metabolism resulting from maternal obesity and/or GDM may induce epigenetic changes in offspring's genome. Epigenetic mechanisms alter the expression of genes without changing the DNA sequence. The developing foetus is susceptible to epigenetic changes because of rapid DNA synthesis during foetal growth. These changes may permanently alter genes that are responsible for energy regulation and balance resulting in adverse metabolic influences in the offspring (Bouchard et al. 2010, Godfrey et al. 2011, Dabalea and Crume 2012).

2.4.3 Mother's smoking during pregnancy

Mother's smoking during pregnancy seems to incontestably increase overweight and obesity in children and adults (Dubois and Girard 2006, Oken et al. 2008). In a meta-analysis, the pooled adjusted odds ratio was 1.52 for overweight or obesity among smoking mothers' offspring aged 3–33 years compared with non-smoking mothers' offspring (Ino 2010). In another study, the odds ratio of being overweight at the age of 7 years was 1.24–2.22 depending on how heavy the mother's smoking was during pregnancy, and also whether the infant was breast fed or not (Wen et al. 2012). Al Mamun et al. (2006) found in their study that mothers motivated to stop smoking during pregnancy see a favourable effect in their offspring: the risk of overweight and obesity among adolescent offspring whose mothers stopped smoking during pregnancy, but smoked at other times during the child's life, was similar to those among offspring whose mothers had never smoked. The mechanisms behind the risk of obesity and maternal prenatal smoking are not clear, but e.g. foetal undergrowth with subsequent rapid postnatal weight gain and low leptin concentration in cord blood have been suggested (Oken et al. 2008). In a study of low income families, children in smoking families were found to have diets with high levels of fat and low levels of fibre, suggesting that the environment in smoking families may be promoting excess weight gain in the offspring (Johnsson et al. 1996).

2.4.4 Nutrition

2.4.4.1 Infant feeding

Modifications of diets in infancy appear to reduce subsequent obesity risks (Lanigan and Singhal 2009). Exclusive breastfeeding during infant's first months has been reported to moderately reduce later obesity risk in several studies (Owen et al. 2005). The protective effect of breastfeeding against obesity has been somewhat conflicting, and was not found in all studies (Huus et al. 2008, Weng et al. 2012). Boys that were fully breastfed for more than 17 weeks appeared to see a protective effect against overweight if the mother was overweight; however, no such advantage was seen in girls and in neither gender if the mother had normal weight (Buyken et al. 2008). Crume et al. (2012a) reported that the offspring of diabetic or non-diabetic mothers who had breastfed for at least six months had a slower rise in BMI during infancy and childhood up to 13 years. They also reported recently that breastfeeding for at least six months resulted in lower levels of adiposity in the offspring being in the highest levels of BMI and fat depositions (Crume et al. 2012b).

Breastfeeding has been shown to increase satiety signals in infants, which could partly mediate healthier weight gain in later childhood (Brown and Lee 2012). Slower weight gain of breastfed infants may protect against overweight and obesity (Griffiths et al. 2009, Singhal et al. 2010). Furthermore, the offspring may adopt dietary preferences even via flavour in breast milk (Mennella et al. 1994). In their review, Moorcroft et al. (2011) concluded that no clear association was found between the age of introduction of solid foods and obesity. However, in a recent prospective pre-birth cohort study concerning formula-fed infants or infants weaned before 4 months-of-age, the introduction of solid foods before the age of 4 months was associated with increased odds of obesity at age of 3 years (Huh et al. 2011). The lack of parental perception of infant's hunger and satiety cues has been reported to increase overfeeding and overweight in infants and children (Baughcum et al. 1998, Worobey et al. 2009).

2.4.4.2 Preschoolers

The feeding practices in families have a significant effect on offspring's dietary habits and thus on their weight development (Clark et al. 2007). The food introduced in the family and other eating practices of the family have strong effects on the food consumption of infants, who progress to the same diet as the rest of the family (Cullen et al. 2003). Children's eating patterns are influenced by characteristics of both the physical and social environment. Children are more likely to eat foods that are available and easily accessible, and they tend to eat more when larger portions are provided. Food choices and behaviour adapted in childhood seem to track into adulthood (Mikkilä et al. 2005).

Parent's behaviours, attitudes, and feeding styles influence their children's eating patterns. The eating pattern has a significant impact on the food consumption (Patrick and Nicklas 2005). Children who frequently eat family meals have been reported to have a lower risk of obesity (Anderson and Whitaker 2010, Hammons and Fiese 2011). The availability and consumption of fruits and vegetables by parents are found to correlate with consumption of the same by children and adolescents (Talvia et al. 2006, Pearson et al. 2009). Adding fruits and vegetables to meals reduces the energy intake in children; higher fruit and vegetable intakes are reported to correlate with lower BMI in children (Leahy et al. 2008, Johnson et al. 2008, Wosje et al. 2010, Acharya et al. 2011). High protein intakes during complementary feeding in infancy and during the transition to the family diet were found to be associated with an unfavourable body composition at the age of 7 years (Gunther et al. 2007).

According to The Feeding Infants and Toddlers Study, over 50% of 12–15 month-old toddlers in the USA were consuming high-energy density foods like desserts, sweets, cookies and sweetened beverages; that level of consumption tended to remain constant throughout the toddler years, thus increasing the risk of excess weight gain already during preschool years (Dubois et al. 2007, Malik et al. 2009, Siega-Riz et al. 2010). In Finland, children's daily energy intake seemed to increase with age during preschool years, and the diet of 2–6 year-olds contained excess saturated fat and sucrose compared with the current Nordic Nutrition Recommendations (Kyttälä et al. 2010). Eating out of the home has been reported to increase the risk of becoming overweight or obese in childhood in a number of studies (Lachat et al. 2012).

2.4.5 Infant and preschool age rapid weight gain

Rapid weight gain during the first year of life is a risk factor for developing overweight/obesity in later years (Ong and Loos 2006, Leunissen et al. 2009, Andersen et al. 2012, Weng et al. 2012). In the recent meta-analysis of Druet et al. (2012), each weight-for-age SDS unit increase between 0 and 12 months conferred a two-fold higher risk of childhood obesity and a 23% higher risk of adult obesity. In the STRIP Study, children who were overweight at age 13 years, gained weight more rapidly than normal weight peers from 2 or 3 years onward (Lagström et al. 2008). In a longitudinal study of Blair et al. (2007), rapid growth during preschool years was independently associated with adiposity at 7 years. The adiposity rebound is a period of increasing body mass index after the early childhood nadir occurring between 3 and 7 years of age. At adiposity rebound, fat cells start to increase in number after an earlier phase of increasing and then decreasing in size (Rolland-Cachera 2002). An early age at adiposity rebound is known to be a risk factor for later obesity (Rolland-Cachera 1984). The children growing rapidly during preschool years meet their adiposity rebound at an earlier age, thus exposing them to overweight in later life (Taylor et al. 2005).

2.4.6 Sleep duration

Short sleep duration in childhood has been related to risk for overweight (Locard et al. 1992, Anderson and Whitaker 2010, von Kries et al. 2002). Sleep duration shorter than 12 hours per day in infancy increased the risk for overweight and adiposity in preschool age children (Taveras et al. 2008). Nevarez et al. (2010) reported that maternal depression during pregnancy, the early introduction of solid foods, infant TV viewing, and attendance at child care was associated with shorter infant sleep duration. Sleep patterns assumed in infancy have a tendency to track into later life, which emphasises the importance of adequate sleep duration in early childhood (Jenni et al. 2007). Subjective sleep duration was studied by Al-Disi et al. (2010) in relation to dietary intake and hormonal outcomes. They reported that a long and uninterrupted sleep was associated with a lower intake of carbohydrates as well as a higher level of adiponectin and a lower concentration of ghrelin, as markers of a more advantageous metabolic profile. Preschool aged children sleeping for shorter periods were reported to be at risk of hyperglycaemia (Tian et al. 2010). In a large Australian cohort study, no association between sleep duration and obesity in preschool aged children was found (Hiscock et al. 2011) indicating that more research linking childhood obesity and sleep duration is needed.

2.4.7 Physical activity and sedentary time

Adequate time spent being physically active on a daily basis can prevent rapid weight gain in early childhood, thus decreasing the risk of obesity. The early years comprise a critical period for the development of active lifestyle behaviours (Timmons et al. 2012). It is recommended that preschool age children should get at least two hours of brisk physical activity (PA) each day (Ministry of Social Affairs and Health 2005). Hinkley et al. (2012) recently found that the majority of children aged 3–5 years were not adequately physically active and were spending excessive amounts of time with screen-based entertainment. A systematic review by Tucker (2008) on PA levels among children aged from 2 to 6 years found that only 54% of the studies included reported that children in this age group met the recommended PA levels. In Finland, more than 60% of 1 to 6 year-old children spend their days in kindergartens (THL 2012). In Finnish kindergartens there is a routine to spend 45–60 minutes twice a day outdoors, which could fulfil the daily PA requirement during weekdays (Siren-Tiusanen 1996). However, when evaluating the time spent on PA in kindergartens, it seems to be below the eligible time (Jämsén 2012). With the increased sedentary activity among families, this suggests that many Finnish children are receiving less PA than recommended.

Although several studies have reported an inverse association between the time spent in active play or PA and the risk for excess weight gain, knowledge of the health

impact of PA in early childhood is insufficient (Sääkslahti et al. 1999, Sääkslahti et al. 2004, Nelson et al. 2006, Janz et al. 2009, Kimbro et al. 2011). Timmons et al. (2012) concluded in their review that there was evidence of variable quality on the relationship between increased or higher PA and improved measures of adiposity in children aged 0–4 years. Further research is needed to evaluate the relationship between the frequency, intensity, time, and type of PA needed to adequately prevent excessive weight gain in young children.

Time spent sitting in front of the TV or electronic games has increased during recent decades even among the toddler age group, and at least in some countries more than half of children under two years of age watch television daily, although television viewing is not recommended at all for children younger than 2 years of age in many countries (Zimmerman et al. 2007). For children who have reached 2 years of age, it is not recommended to spend more than two hours daily watching TV or with electronic games (= screen time) (American Academy of Paediatrics 2001). In Finland, there are no recommendations for daily screen-time for preschool age children (Kaikkonen et al. 2012). Early life screen time patterns tend to persist to later childhood (Certain and Kahn 2002). There is strong evidence of an association between time spent watching TV or other screens and the increased risk of excess weight gain and adiposity among toddler and preschool-age children, probably via increasing sedentary time and diminishing time spent in active play and other physical activities (Mendoza et al. 2007, Lumeng et al. 2006, Dennison et al. 2002). Children spending more time watching television have also been reported to have more energy-dense diets causing a cumulative effect on the risk of overweight (Lissner et al. 2012).

2.5 Studies to prevent childhood obesity in preschool age children

This chapter covers intervention studies targeting children of preschool age (up to seven years of age) at baseline. Intervention studies included in this section have reported outcomes on children's weight or adiposity. The studies were published between years 1998 and 2012 (Table 1, Appendix 1). To date, there are still only a few primary prevention studies targeting preschool age children, but this study area is rapidly growing as evidence on the importance of early preventive actions to prevent obesity has become stronger. There are several studies ongoing of which the study protocols have been published: e.g. "Prevention of Overweight in Infancy study" targeting parents with infants and aiming to modify breastfeeding, early food preferences, PA and sleep behaviour (Taylor et al. 2011), and "Stockholm Obesity Prevention Program" targeting overweight or obese parents and their infants with a multifaceted prevention program (Sobko et al. 2011).

Table 1. Summary of overweight/obesity prevention studies.

Author, year	Target behaviour	Design Number of participants	Age of participant children at baseline	Measure of adiposity or weight gain	Statistically significant results
Kramer et al. 2007	Breastfeeding	Cluster RCT 7108/6781	Newborn – 16 months	BMI, waist or hip circumference, triceps or sub-scapular skin-fold thickness	-
Simell et al. 2000, Lagström et al. 2008	Diet	RCT 541, ~ 50% contr.	7 months	BMI	-
Daniels et al. 2012	Early feeding	RCT 273/293	4–6 months	BMI z-score	+
Mo-Suwan et al. 1998	PA	Cluster RCT 147/145	Mean 4.5 years	BMI, triceps skin-fold thickness	Girls +, Boys -
Reilly et al. 2006	PA	Cluster RCT 245/259	Mean 4.2 years	BMI z-score	-
Bayer et al. 2009	Diet + PA	Cluster RCT 866/463	Mean 5.7 years	Proportion of overweight and obesity	-
Dennison et al. 2004	Diet + PA	Cluster RCT 43/34	2.6–5.5 years	Triceps skin-fold thickness, BMI	-
Eliakim et al. 2007	Diet + PA	RCT 54/47	5–6 years	BMI percentile, fat percent by skin-folds	+
Fitzgibbon et al. 2005 and 2006	Diet + PA	Cluster RCT 146/154, 171/160	2–5 years	BMI	2005: +, 2006: -
Harvey-Berino and Rourke 2003	Diet + PA	Cluster RCT 20/20	14–30 months	Weight-for-height z-scores, weight-for-height percentile	-
Jouret et al. 2009	Diet + PA	Cluster RCT 556/410, 697/410	2.5–5 years	Prevalence of overweight, BMI z-score and change in BMI z-score	+ (in under-privileged areas)
Kafatos et al. 2007	Diet + PA	CCT 85/91	5.5–6.5 years	BMI z-score	+
Keller et al. 2009	Diet + PA	RCT 49/134	4–7 years	BMI z-score	+

Table 1...

Author, year	Target behaviour	Design Number of participants	Age of participant children at baseline	Measure of adiposity or weight gain	Statistically significant results
Manios et al. 1998	Diet + PA	CCT 231/162	5.5–6.5 years	BMI, Suprailiac, biceps, triceps, and subscapular thicknesses	+
Manios et al. 2002	Diet + PA	CCT 356/285	5.5–6.5 years	BMI, Suprailiac, biceps, triceps, and subscapular thicknesses	+
Plachta-Danieltzik et al. 2007	Diet + PA	CCT 345/1419	6 years	BMI z-score	+
Warren et al. 2003	Diet + PA	RCT 42/42	Mean 6.1 years	Proportion of overweigh/obese	-
Wen et al. 2012	Feeding + family nutrition + PA	RCT 255/242	Newborn	Mean BMI	+
Brotman et al. 2012	Behavioural	RCT 19/21, 106/40	Risk group, 3–5 years	BMI z-score, Proportion of obese children	+
Wake et al. 2011	Behavioural (sleep)	Cluster RCT 101/92	7–8 months	BMI z-score, proportion of obese/ overweight, waist circumference	-
Kavanagh et al. 2008	Feeding + behavioural	RCT 38/57	3–10 weeks formula-fed	Weight gain (g/week)	-
Paul et al. 2011	Feeding, behavioural or both	RCT 29/30, 29/30, 22/30	Newborn	Weigh-for-length percentile	+ If received both interventions
Puder et al. 2011	Diet+PA + media use + sleep + environment	Cluster RCT 333/292	Mean 5.1 years, high-migrant	BMI, percentage body fat, sum of skin-folds, waist circumference	BMI - Adiposity + Waist circ.+
Gillman et al. 2010	Treating impaired glucose tolerance during pregnancy	RCT + follow-up 94/105	Foetus	BMI z-score	-

PA, physical activity; BMI, body mass index; RCT, randomised controlled trial; CCT, controlled clinical trial

2.5.1 Methods used in prevention studies

The design of most of the intervention studies reviewed here is either an RCT or Cluster RCT study. Four of those are controlled clinical trials (Kafatos et. al 2007, Manios et al. 1998 and 2002, Plachta-Danieltzik et al. 2007). The contents of the interventions, participants, anthropometric outcomes and sample size at the time of measurement are described in Appendix 1 and as a summary in Table 1.

These preschool age interventions were mainly attributed to parents, which is critical when trying to modify lifestyle or behaviour in early childhood. Four of the studies addressed only children (Mo-Suwan et al. 1998, Eliakim et al. 2007, Plachta-Danielzk et al. 2007, Puder et al. 2011). These studies targeted children during kindergarten or school days by lessons on healthy nutrition and PA sessions. One of these interventions was purely aiming at increasing PA (Mo-Suwan et al. 1998). In two of these interventions, lessons on nutrition and PA were given with structured PA. The intervention program of Puder et al. (2011) was multifaceted and targeted diet, PA, media use and sleep behaviour.

There were two studies that started during pregnancy. The primary aim of the study of Gillman et al. (2010) was to effectively treat impaired glucose intolerance during pregnancy by dietary advice, glucose monitoring and insulin if needed. They followed up the offspring's weight gain until 4–5 years of age. Wen et al. (2012) started their intervention program in late pregnancy and continued until the age of 24 months. Their aim was to promote breastfeeding, appropriate timing for the introduction of solid foods, active play, and also the diet and PA of rest of the family.

In addition to the study of Wen et al. (2012), six other interventions targeted parents with infants (Daniels et al. 2012, Harvey-Berino et al. 2003, Kavanagh et al. 2008, Kramer et al. 2007, Paul et al. 2011, Simell et al. 2000, Lagström et al. 2008, Wake et al. 2011). These interventions addressed promoting breastfeeding, recognising infant's satiety cues and/or sleep strategies. Kavanagh et al. (2008) targeted caregivers having infant on formula-feeding and had a program to promote awareness of satiety cues. The STRIP Study (Simell et al. 2000, Lagström et al. 2008) was aimed at decreasing the risk of cardiovascular disease. They gave individual counselling on the healthy fat content of diet first addressing only parents with infants and preschool age children, and later also separately children up to 13 years.

The intervention programs targeting older preschool age children with their parents were mainly promoting both healthy eating and PA (Bayer et al. 2009, Dennison et al. 2004, Fitzgibbon et al. 2005 and 2006, Kafatos et al. 2007, Keller et. al 2009, Manios et al. 1998 and 2002, Warren et al. 2003). Brotman et al. (2012) targeted minority group children with behavioural problems and in risk of obesity. They promoted effective parenting and child's behavioural regulation without addressing dietary or PA issues at all. The intervention program of Jouret et al. (2009) gave counselling on appropri-

ate sedentary activity in addition to dietary and PA counselling. Reilly et al. (2006) attempted to increase PA and decrease sedentary time.

In the majority of these intervention programs, several methods were used to deliver the counselling. Lessons to groups on health-related beneficial behaviours were the most commonly used methods, given either to parents and children together, only to parents or only to children during school or kindergarten days. In most intervention programs, additional material was given to parents in written form e.g. in form of newsletters or "tip cards". An educational internet platform was offered in some studies. Individual counselling by health care personnel, often by a nurse, was used in several studies. Counselling was also given at home, when the targets were families with infants. PA sessions structured to children were held in several kindergarten- or school-based programs, in addition to the other methods described above.

In four of these preventive intervention studies, the theoretical model of the counselling procedure was described (Warren et al. 2003, Fitzgibbon et al. 2005 and 2006, Kavanagh et al. 2008). In the majority of these studies, only a cursory description of the training process for the counselling was given, if at all. Some evaluation of the success of the counselling event was reported in three of these intervention studies (Warren et al. 2003, Kavanagh et al. 2008, Daniels et al. 2012).

2.5.2 The results on weight gain and adiposity in prevention studies

The four studies targeting only children showed some positive results in weight gain or adiposity. The primary school-based dietary and PA counselling study of 14 weeks increased daily PA and found a significantly slower increase of BMI among the intervention group children compared to the control group (Eliakim et al. 2007). The 7-month exercise-promoting program of Mo-Suwan et al. (1998) had no effect on BMI, although the girls in the intervention group were less likely to have an increasing BMI slope at the end of the intervention. A CCT targeting children with diet and PA lessons during first school year resulted in a lower incidence of overweight in the intervention group four years after the intervention, but the effect was only found in families with high socioeconomic status (Plachta-Danielzk et al. 2007). A multidimensional one year intervention targeting high migrant population children (parent born outside Switzerland) in preschool reported that the intervention group had a lower percentage of body fat and WC at the end of the intervention (Puder et al. 2011).

The effective treatment of impaired glucose tolerance during pregnancy had no effect on offspring BMI z-score at age of 4–5 years, although macrosomia at birth was significantly reduced in the intervention group compared to the routine care group (Gillman et al. 2010). In the other intervention with a multifaceted approach starting during pregnancy and continuing until the offspring were aged 2 years, the BMI was

significantly lower in the intervention group offspring at the end of the intervention (Wen et al. 2012).

The intervention of Daniels et al. (2012) giving anticipatory guidance in early feeding practices to parents with 4–6 months infants for 3 months seemed to result in lower BMI-for-age z-scores and slower weight gain at 6 months after intervention compared to the control group infants. The small RCT promoting healthy feeding practices and appropriate sleep duration of infants during infants first month showed lower weight-for-length percentiles at the age of one year compared to the conventional health care group (Paul et al. 2011). The other four studies targeting parents with infants showed no significant positive results on adiposity or weight gains (Harvey-Berino et al. 2003, Kavanagh et al. 2008, Kramer et. al 2007, Wake et al. 2011).

The purely behavioural intervention of Brotman et al. (2012), which promoted effective parenting and behavioural regulation of children with problems in that respect, found that children in the intervention group had lower BMI z-scores; the intervention group also had lower rates of obesity compared to the control group five years after the intervention, except for the group with only girls. Dietary and PA counselling targeting children and parents in the kindergarten setting seemed to slow the BMI z-score increase measured at the end of two years intervention; also, prevalence of overweight was lower among the intervention group children, but these positive results were only seen in underprivileged areas (Jouret et al. 2009). The same primary school-based PA and dietary intervention targeting both children and parents was used in controlled clinical trials of Manios et al. (1998 and 2002) and Kefatos et al. (2007). Manios et al. (1998 and 2002) reported significantly smaller increases in the suprailiac skin fold thickness and BMI in the intervention group after 3 and 6 years of intervention. Kefatos et al. (2007) reported follow-up results 4 years after the end of the 6 year intervention: the BMI z-score had increased more in the control group, while it had decreased slightly in the intervention group. The rest of the reviewed interventions had no significant effect on children's adiposity or weight gain (Table 1, Appendix 1).

In most studies described here, at least partly, the targeted behaviour had changed towards healthier after the intervention; this is despite the fact that the studies often failed to show positive results on weight gains or adiposity. Only 10 of the 24 reviewed studies failed to show any positive results on adiposity or weight gain in intervention group children compared with the control groups, which gives hope to the potential of various behavioural, dietary or PA interventions starting during preschool years to diminish overweight or obesity prevalence in children. However, the follow-up periods after interventions were either lacking or short in many studies in respect of assessing obesity risk, leaving long-term results unknown (Appendix 1). The variation in settings, methods used, duration of the interventions and age of the target child further complicate the comparison of the effectiveness of these interventions.

Given that in most of the obesity prevention studies there was a lack of description of the success of the counselling event, the evidence of the efficacy of the intervention counselling to promote healthy weight gain in children is insufficient. The failure of the intervention study to show an effect on child's weight development may lay partly on the failure of the counselling process to promote changes in health-related behaviour, as well as on the unwillingness of the study participants to change these behaviours. Training of the health care personnel providing the counselling and the process evaluation of the counselling constitute an important element in behavioural intervention studies (Salmela et al. 2009). Success of an intervention trial to turn in favourable changes in health-related behaviours lays much on the intervention event and on the success of the interaction of the counselling performer with the client (Whitlock et al. 2002). Counselling that is aimed at lifestyle changes is assumed to be more effective if it is based on behaviour change models; these models specify factors required for behaviour change and maintenance, such as changes in knowledge, attitude, motivation, self-confidence and skills (Elder et al. 1999). There are six theoretical models of behaviour change, which are most often cited concerning lifestyle interventions (Whitlock et al. 2002). The trans-theoretical model-based interventions have been reported to be more effective than the corresponding control interventions (Whitelaw et al. 2000). This model describes the behavioural change as an on-going process with multiple stages; the task of the health care providers is to assist the client to progress to the next stage by recognising the current stage and individualising the counselling strategy (Salmela et al. 2009). Applying relevant theoretical models to behavioural counselling interventions contributes to the strengthening of the research in this area (Smedley et al. 2001). Equally important is assessing how well the intervention performers have adapted the aimed intervention strategy (Salmela et al. 2009).

Some review articles on obesity prevention studies in children less than 7 years of age have been published during the past few years. Hesketh and Campbell (2010) evaluated interventions in 0–5 years of age children. Monasta et al. (2010) reviewed RCT interventions in preschool age children. Ciampa et al. (2010) assessed the evidence for interventions designed to prevent or reduce overweight and obesity in children younger than 2 years. The reviewers concluded that limited evidence suggests that interventions may improve dietary intake, PA and parental knowledge about nutrition for children in this age group. They also stated that, for a clinically important and sustainable effect, future research should focus on designing rigorous interventions targeting young children and their families. The latest Cochrane review on interventions for preventing obesity in children showed that obesity prevention studies targeting the ages of 0 to 5 years clearly had the strongest positive effect on weight gain compared with older age groups of 6–12 and 13–18 years (Waters et al. 2011).

2.6 Summary of the literature

The prevalence of overweight and obesity during childhood has more than doubled during the past few decades in industrialised countries. There are reports that the increasing trend of obesity is levelling off, but the prevalence numbers are still high in preschool age children. The reasons for this worldwide trend are thought to be the easy availability of energy-dense food, while the need and motivation to be physically active has greatly reduced. A child is obese when she or he has excess body fat in a degree that her/his wellbeing and health is at risk of being impaired. Obesity has several adverse psychological and physical disadvantages in childhood. The most threatening health risk is the increased incidence of cardiovascular diseases in adulthood, which often result in increased morbidity and thus in a lower quality of life and shorter life span. For these reasons obesity is not only a health burden, but also an economic burden to society. Overweight or obesity often has its origin in preschool years; therefore, it is very difficult to reverse once it has been established and it also tends to track into adulthood. To break this track and avoid adverse consequences of obesity, preventive actions should start in early life.

In addition to genetic predisposition, there are several known factors that increase the risk of obesity in childhood. During foetal life, mother's overweight or obesity before pregnancy, excessive weight gain, impaired glucose tolerance or smoking during pregnancy increase this risk. The knowledge of mechanisms mediating this risk in still insufficient, but e.g. epigenetic changes and foetal hyperinsulinemia inducing permanent changes in energy metabolism and appetite regulation are suspected to be in the background. Also, rapid weight gain during infancy increases the child's risk of being overweight or obese. Factors affecting infant growth include the duration of breastfeeding, formula-feeding and the age at introducing solid foods, as well as sleep duration and patterns. Breastfeeding for long enough and not introducing solids to infants before six months of age seem to slightly protect from excessive weight gain. Dietary habits and time spent in active play or physical activity have a major impact on weight gain during preschool years. The practices learned during these years tend to track into later life. To prevent obesity before it has emerged, predisposing and modifiable factors during preschool years should be targeted.

There are few intervention studies that have targeted this age group. The methods used in those are counselling on infant feeding practices, promoting a healthy diet, increasing physical activity and diminishing sedentary time, as well as influencing sleep patterns and effective parenting. Some of them have been seen to slightly promote healthy weight gain and decreased adiposity, but long-term effects are mainly unknown. The recent Cochrane review on interventions for preventing obesity in children showed that studies targeting children younger than five years of age had the

strongest positive effect on weight gain compared with the older age groups (Waters et al. 2011). Multifaceted programs seem to be the most effective, along with programs that target risk groups. Obesity prevention studies especially focusing on the youngest age groups with longer follow-up periods are needed to fill in the gaps in evidence in this field.

3 AIMS OF THE STUDY

The aims of this study were to evaluate whether three different behavioural interventions implemented in maternity and child health care clinics could have the potential to decrease offspring's risk of overweight or obesity in preschool age children, and also to describe the protocol of a primary prevention study to prevent childhood overweight or obesity in these settings in detail.

The specific goals were

1. to assess whether the intensified dietary and physical activity counselling given to mothers during pregnancy has an effect on offspring weight gain by the age of 4 years.

2. to assess if dietary and physical activity intervention targeted at mothers with infants aged 2–10 months have an effect on children's weight gain by the age of 4 years.

3. to describe the protocol of a pragmatic childhood obesity primary prevention study conducted in maternity and child health care clinics.

4. to report pregnancy, newborn and infant weight gain outcomes of the childhood obesity primary prevention study started during the first trimester of pregnancy in maternity health care clinics.

4 PARTICIPANTS AND METHODS

4.1 Study settings

The settings of these studies were the maternity and child health care clinics in the cities of Tampere, Hämeenlinna (I–II) and Vaasa (III–IV) in Finland. In Finland, there is a primary health care-based system to regularly evaluate pregnant mothers and children's health and well-being and promote the whole family's health and health behaviour. The services are paid by public tax revenue and are free of charge to families and widely accepted and used by Finnish families; only exceptionally are they not used. During pregnancy there are 11–15 visits to the maternity health care clinic (MHC) public health nurse (PHN) and usually three visits to physicians, as well as one home visit during the newborn's first weeks. By the age of one year the child will have visited a child health care clinic (CHC) PHN 9–10 times and a physician 3 times for health control. Routinely, there is one visit to the CHC around 18 months of age and thereafter one visit yearly until six years of age. The families visit the health care clinic, which is located at their residential area.

4.2 Study designs and participants

This dissertation contains two different study designs and groups of participants. The lifestyle interventions in the NELLI follow-up studies (NELLI, Neuvonta, elintavat ja liikunta neuvolassa; Counselling, lifestyle and physical activity in maternity or child health clinics) (I–II) were controlled clinical trials (CCT). The VACOPP Study (III–IV) is a pragmatic controlled clinical trial. There are two different groups of intervention target mothers. In follow-up studies I–II, the participants were first-time mothers without any special risk characteristics with their offspring, and in VACOPP Study (III–IV), the participant mothers were at risk of developing GDM during pregnancy with their infants.

4.2.1 The NELLI follow-up studies (I–II)

The NELLI pilot intervention trials were conducted in six maternity and child health care clinics in Finland in the cities of Tampere and Hämeenlinna between 2004 and 2006. The allocation was performed at clinic level. Three of the clinics volunteered to be intervention clinics and the remaining clinics were treated as control clinics. The clinics were a convenient sample of the clinics in Tampere and Hämeenlinna, as they were selected based on the clinics' administrative personnel's suggestion for suitable clinics.

The primary aim of the NELLI pilot trial was to evaluate the feasibility and effects of the lifestyle intervention in preventing excessive gestational weight gain and postpartum weight retention (Kinnunen et al. 2007a, 2007b and 2008). The intervention was addressed during five visits to maternity (I) or child health care (II) clinics. The inclusion criteria of participant mothers were mothers without previous deliveries, over 18 years of age, and no type 1 or type 2 diabetes mellitus (GDM excluded), twin pregnancy, physical disability preventing exercise, otherwise complicated pregnancy, substance abuse, treatment or clinical history for any psychiatric illness, inadequate language skills in Finnish or intention to change residence within 3 months. The PHNs recruited mothers either during their first visit to MHC (I) or mothers with infants when visiting their home after delivery or at their first visit to the childcare centre (II). All participants provided written informed consent for participation.

A postal questionnaire on their offspring's growth measurements was sent in 2010 to mothers who had participated in the intervention trial either during pregnancy or during infant's first year. This questionnaire was chosen for data gathering as direct access to the child health clinic records would have entailed maternal permission, and the mothers also have the same information on their offspring's growth in the child's health booklet that is in the health clinic records.

4.2.2 The VACOPP Study (III–IV)

The VACOPP Study is a controlled pragmatic trial, which is aimed at the primary prevention of childhood obesity. The trial is conducted in maternity and child health care clinics in the city of Vaasa in the Western part of Finland. As a pragmatic trial, the study is implemented in normal municipal health care practice, and the study practitioners are the ordinary health care staff. All maternity clinics in the town were involved in recruitment. The PHNs recruited the intervention group mothers during first visit to MHC in the beginning of the pregnancy from February 2009 to April 2010.

The control group was recruited by the research nurse among families who had been clients of the same maternity clinics one year earlier (2008). The eligibility criterion was a mother at risk of gestational diabetes: body mass index ≥ 25 kg/m^2, mac-

rosomic newborn in any previous pregnancy, immediate family history of diabetes and/or age ≥ 40 years. This group of mother's with their offspring was selected for the target group, because offspring of mothers with GDM or BMI in the range of overweight or obesity before pregnancy are at risk of excessive weight gain during childhood. Furthermore, this group of mothers is also at risk of gaining excessive weight during pregnancy, and may have a genetic as well as lifestyle predisposition to obesity, which they may pass on to their offspring. These both features are also known to increase the risk of childhood obesity.

Our study was designed to be integrated in routine health care practice and to maximise the applicability of results to the usual care setting. The intervention begins during the first trimester of pregnancy and continues until the child is 5 years old. The duration of follow-up is planned to be until the offspring's age of 6 years. In this dissertation, the protocol of the study and the outcomes of intervention in MHC until the infant reached one year of age are described.

4.3 Contents of the interventions

For the NELLI pilot intervention, the PHNs and public health dietician and physiotherapist were educated before the interventions started. PHNs had been trained to carry out the intervention by the research group during sessions lasting 12 hours in total (Kinnunen et al. 2007a, 2007b and 2008). Both the control and intervention clinic PHNs had also been trained for study arrangements. The PHNs had written material in the form of a handbook describing the tasks the intervention included. A researcher or two also visited the clinics on a monthly basis for meetings held separately to control and intervention groups.

In the VACOPP Study (III–IV), the PHNs, public health dietician and physiotherapist were schooled before the intervention started. The schooling was carried out in the form of several 1.5 to 2 hour lectures or meetings and one whole day schooling session. During study intervention and follow-up, the PHNs were also given a revision of study procedures, phases of study and other study information at least twice a year. The contents of the schooling were the background of the study, study arrangements and intervention procedures held by the researcher and the research nurse. The PHNs received a one day schooling session by The Finnish Heart Association on their "Smart family – exercise and nutrition guidance method" (Appendix 2).

4.3.1 The NELLI follow-up studies (I–II)

The NELLI interventions preceding follow-up studies reported in this dissertation included individual counselling on physical activity and diet either during pregnancy or when the child was 2–10 months old. The purpose of the intervention had been to

promote leisure time physical activity (PA) and healthy dietary habits, aiming to support participants' appropriate weight gain during pregnancy or to return to their pre-pregnancy weight by 10 months after delivery.

The PA counselling consisted of a primary counselling session before the 10th week of pregnancy and four brief additional sessions until the 37th week, or at the infant's age of 2–10 months. The counselling was based on the model introduced by Laitakari and Asikainen (1998). 30 minutes of moderate-intensity physical activity five times a week was considered sufficient for health and 40 minutes of high-intensity physical activity three times a week for fitness. The PHN boosted the counselling with the help of a counselling card. The participants had the option of attending structured group exercise sessions of 45–60 minutes weekly.

The dietary counselling was based on recommendations focused on four topics that could help the participants to prevent excessive gestational weight gain or return to their pre-pregnancy weight (Ministry of Social Affairs and Health 2004). The dietary focus was set for each participant to achieve or maintain a regular meal pattern, to eat at least 5 portions of vegetables, fruit or berries per day, to favour fibre-rich bread and to restrict the intake of high-sugar snacks. For the dietary counselling there was one 20–30 minute primary counselling session and three additional sessions in relation to visits to the MHC or CHC beginning from 16–18 weeks to the 37th week of gestation, or from 3 to 10 months after delivery. In the control clinics, the nurses continued their usual counselling practices on PA and diet. The intervention, which was performed earlier, is described in more detail by Kinnunen et al. (2007a, 2007b and 2008).

4.3.2 The VACOPP Study (III–IV)

The intervention began at the MHCs during the first trimester of pregnancy and continued at CHCs until the child reached five years of age. The intervention used was multifaceted, focusing on several behavioural factors known to increase the risk of child's overweight or obesity. During pregnancy, the intervention targeted appropriate PA and healthy diet. Mothers were offered two group counselling sessions: one during both the first and the second trimester of pregnancy. 1.5 hour sessions were given by a physiotherapist and dietician employed in the public health centre. During these sessions, the dietician gave information on nutrition recommendations during pregnancy, especially on the appropriate use of fibre, energy content, quality of carbohydrates and fat in diet (Ministry of Social Affairs and Health 2004). The physiotherapist gave information on suitable and sufficient amount of exercise during pregnancy (Aittasalo et al. 2008). Information was also given on the effect of healthy diet, exercise and appropriate weight gain during pregnancy on the risk of having GDM, offspring's perinatal problems and obesity risk. At the end of these sessions, the mothers participated in a brief session of exercise that is suitable to do at home.

The mothers also received written educational material on healthy diet and physical activity during pregnancy. The written information was according to the Finnish Heart Association and the material on PA according to UKK Institute for Health Promotion (Finland) (Suomen Sydänliitto ry, UKK-instituutti). This counselling was repeated more briefly by the PHNs during the 13 routine visits to maternity clinics. After delivery, a PHN gave the mother a written information leaflet reminding that breastfeeding up to 6 months of age is recommended for promoting healthy weight gain in the infant.

The intensified counselling during CHC follow-up was aimed at a healthy age-appropriate diet, PA according to recommendations, suitable time spent at sedentary activities (screen time especially) and sufficient sleep time of children. The intervention during childhood is mostly delivered by PHNs at yearly appointments, but the families were also offered to participate in a 1.5 hour structured group counselling session when the child is 1 to 2 years of age, which is held by a physiotherapist and a dietician regarding healthy diet recommendations to children under school age, as well as advice on suitable physical exercise, sleep and screen time at that age. The physical activity and dietary recommendations were according to those of the Ministry of Social Affairs and Health (2004 and 2005). Intervention group children are given appointments with the PHN in CHC at routine yearly control visits at 1, 2, 3, 4 and 5 years of age that are 30–60 minutes longer compared to control group children. Dietary and PA issues, as well as advice on age-appropriate sleep and screen time, are addressed. These issues are addressed with the help of The Finnish Heart Association's "Smart family - exercise and nutrition guidance method" (Appendix 2). In this method, the family estimates its own habits regarding lifestyle and it functions as a tool for motivational interview. The method includes motivational and simplifying pictures and written information about healthy diet and physical activity, which are obtained together with the PHN. The timing of interventions is presented in Table 2.

The control group receives the usual counselling used in Finnish maternity and child health care clinics.

Table 2. The VACOPP Study (III – IV). Timing of the intensified counselling in maternity and child health care clinics.

Intervention during pregnancy

Gestational weeks 10–17	Gestational weeks 18–28	Gestational weeks 20–32	Gestational weeks 28–40
Counselling session by physiotherapist and dietician 1.5 hours and 2 routine visits to PHN with intensified counselling concerning diet and physical activity	3 routine visits to PHN with intensified counselling concerning diet and physical activity	Counselling session by a trained physiotherapist and dietician 1.5 hours	8 routine visits to PHN with intensified counselling concerning diet and physical activity

Intervention in child health clinics

0–6 months	1 year	1–2 years	2 years	3 years	4 years	5 years
Information leaflet on breast-feeding	Intensified counselling by PHN at child health care centre with "The Smart Family- exercise and nutrition guidance method"	Intensified counselling by PHN at child health care centre with "The Smart Family- exercise and nutrition guidance method"	Intensified counselling by PHN at child health care centre with "The Smart Family- exercise and nutrition guidance method"	Intensified counselling by PHN at child health care centre with "The Smart Family- exercise and nutrition guidance method"	Intensified counselling by PHN at child health care centre with "The Smart Family- exercise and nutrition guidance method"	Intensified counselling by PHN at child health care centre with "The Smart Family- exercise and nutrition guidance method"

PHN = public health nurse

4.4 Outcomes and data collection

The main outcomes of all of the studies in this dissertation are weight-for-length/height SDS or BMI-for-age and -gender SDS, and the differences and changes with time in those parameters of weight gain among the study group offspring. The PHNs measured the weight and length/height of the children at CHC visits and also entered these measures in the child's own health booklet. The children's weight was measured to the nearest 0.01 kg without clothes until one year of age, and thereafter to the nearest 0.1 kg on a standard electronic scale with light clothing. Children under 2 years of age

were measured in recumbent position and thereafter in standing position to the nearest millimetre with a standard stadiometer.

4.4.1 The NELLI follow-up studies (I–II)

In the follow-up studies, we analysed a secondary outcome of the intervention study: the weight development of the offspring. The primary outcomes (functioning as intermediate outcomes in the follow-up studies) reported earlier were the proportion of mothers exceeding the weight gain recommendations during pregnancy or returning to their pre-pregnancy weight by 10 months after delivery. The dietary and PA outcomes reported by Kinnunen et al. (2007a, 2007b and 2008) showed changes in meal patterns, the overall intake of vegetables, fruit and berries, use of high-fibre bread and the intake of high-sugar snacks, and metabolic equivalent minutes.

In 2010, the mothers who had participated in the intervention trial, and whose children were then about five years old, received a postal questionnaire asking the results of their offspring's growth measurements (weight, length/height, head circumference) from birth up to 5 years of age. The mothers transferred the information on their offspring's growth measurements from child's health booklet to the questionnaire. In the questionnaires, the mothers were also asked whether their children had any long-term illnesses affecting growth, duration of breast-feeding and the child's age when starting solid foods.

4.4.2 The VACOPP Study (III–IV)

During pregnancy, the intermediate outcomes of the intervention were gestational weight gain and keeping weight gain within the recommended ranges, and mother's glucose tolerance at 26–28 weeks' of gestation measured as 2 hours 75 grams glucose load oral glucose tolerance test (OGTT) and the proportion of mothers with GDM (Institute of Medicine and National Research Council 2009, American Diabetes Association 2010). The samples for OGTT were capillary plasma samples, using the cut-off-levels for GDM corresponding to the above mentioned cut-off-levels: 0 h ≥ 5.3 or 1 h ≥ 11.0 or 2 h ≥ 9.6 mmol/l.

Mother's pre-pregnancy weight and weight at 36–37 weeks' of gestation, blood pressure (BP), sleep duration, mother's own estimate about weekly physical exercise (out of breath level) during pregnancy, and results of 2-hour OGTT at 27-28 weeks of pregnancy were recorded in questionnaires filled in partly by the PHN and partly by the mothers during the first, second and third trimester of pregnancy. The PHN measured and recorded the physical measures in the questionnaires, except for the control group's measures during pregnancy, which were filled in by the mothers themselves.

The pregnancy-related physical measures of the control group were entered into the study questionnaire by mothers from their maternity card, which was completed by a PHN during pregnancy. If necessary, we were able to check the data from the health care records.

The time point of the final primary outcome measure (BMI and weight-for-height z-score) will be at six years of age in the offspring, but the weight gain anthropometry is reported until one year of age in this dissertation. Pregnancy-related measures and duration of exclusive breast-feeding are reported here as intermediate and secondary outcomes. Secondary outcomes of the offspring are duration of exclusive breastfeeding, frequency of offspring's dietary intake of "junk food", sugary beverages, pastry, sweets, fruit, berries, vegetables, type of butter or margarine used and the frequency of eating takeaway food, eating pattern, the average daily screen and sleep time, and time spent physically active. PA time is a parent's estimate of how the child spends time outdoors, in moderate intensity or structured PA by hours/day or week. As secondary outcomes, the following objective measures are gathered: WC and BP at 2, 3, 4, 5 and 6 years of age. The metabolic markers (fasting triglycerides, HDL-cholesterol, glucose, insulin and alaninaminotransferase) are measured at 2, 4 and 6 years of age.

The offspring data are recorded in self-administered questionnaires, which are completed at yearly appointments with the PHN. Long-term illnesses affecting growth are also investigated. The anthropometric data was/is gathered at 4 and 6 months of age and thereafter at 1, 2, 3, 4, 5 and 6 years of age. The PHNs add growth measurements to the questionnaires. WC is instructed to be measured on the midpoint between the lower costal border and the iliac crest. BP is measured by PHN using an automated BP monitor (Omron M6) under standard conditions with two repeated measurements. The newborn's ponderal index was assessed by dividing weight in kilograms by length in meters cubed (kg/m^3). Large-for-gestational-age (LGA) was assessed as birth weight above the 90th percentile and small-for-gestational-age (SGA) for birth weight below the 10th percentile, both of which were adjusted for gestational age based on birth weight percentiles of Medical Birth Registry information on Finnish children born during 2004–2006 by method of Kramer et al. (2001).

The children's dietary intakes measured as average consumption/day or week and other secondary outcomes recorded are filled in by the mother or father of the child. Fasting blood samples are collected in the local medical laboratory used by the health centre in Vaasa (Vaasa Central Hospital) and analysed using standard automated techniques. Laboratory results are recorded by the researcher directly from the laboratory score sheet. The timing of questionnaires, physical measurements and laboratory tests are listed in Table 3.

Table 3. Timing of questionnaires, physical measurements and laboratory tests (III).

Maternity health care			
Weeks' gestation			
8–12	**26–28**	**37**	**After childbirth**
Mother's age Mother's education Father's education Mother's weight and height before pregnancy Mothers chronic illness Fathers weight and height History of GDM History of newborn > 4500 g Smoking during pregnancy Previous deliveries Immediate family history of DM 2, CAD, hypertension, obesity and hypercholesterolemia Mother´s average sleep h/d Mother's average physical activity h/d Blood pressure	Mother's average sleep h/d Mother's average physical activity h/d Blood pressure Oral glucose tolerance test	Mother's average sleep h/d Mother's average physical activity h/d Blood pressure Mother's weight	Gestation week of childbirth Birth weight Birth length Birth head circumference
Child health care			
1 year of age	**2, 4 and 6 years of age ***	**3 and 5 years of age**	
Chronic illness Weight and length at 4 and 6 months Weight Length	Chronic illness Consumption of beverage, fruits, vegetables, berries, sweets, pastry, bread, yoghurt, eating at takeaway restaurant Regularity of meals Sleep time h/d Daily physical activity/outdoor activities Daily screen time Weight Height Waist circumference Blood pressure fP-glucose fP-insulin fP-cholesterol fP-HDL-cholesterol fP-triglycerides P-ALAT	Chronic illness Consumption of beverage, fruits, vegetables, berries, sweets, pastry, bread, yoghurt, eating at takeaway restaurant Regularity of meals Sleep time h/d Daily physical activity/outdoor activities Daily screen time Weight Height Waist circumference Blood pressure	

* At these time points the parents are offered to have their weight, waist circumference, blood pressure, fP-glucose, fP-cholesterol, fP-HDL-cholesterol and fP-triglycerides measured by health care centre; fP = fasting plasma; GDM = gestational diabetes mellitus; DM = diabetes mellitus; CAD = coronary artery disease; P-ALAT = plasma alaninaminotransferase

4.5 Ethical aspects

The NELLI follow-up studies were approved by the Ethics Committee of Pirkanmaa Hospital District. The ethical approval for the VACOPP Study was granted by the Ethics Committee of Vaasa Hospital District. The informed written consent was provided by all participant mothers prior to baseline assessments of the studies. The children participating in blood tests are offered a local anaesthetic before blood sampling.

4.6 Statistical methods

Characteristics of the study participants are described using means or frequencies and 95% confidence intervals (CI). Normality was evaluated with the Kolmogorov-Smirnov test. Student's t-test (normally distributed) or Mann-Whitney U-test (non-normally distributed) was used to evaluate the differences between the groups. Categorical variables were tested using the Chi-square test or Fisher's exact test. Corresponding 95% CI for continuous variables were calculated using formula mean ± (1.96 * standard error of the mean) and for categorical variables using the Wilson score method without continuity according to Newcombe (1998) (IV).

The child's weight gain was analysed using weight and length/height converted to weight-for-length/height or BMI-for-age and -gender (Saari et al. 2011) and their SDSs (z-scores) according to the recently updated Finnish growth reference. The within-child correlation between repeated measures was taken into account by using a two- or three-level mixed-effects linear regression models for analysing the association of BMI-for-age and/or weight-for-length z-score over time by group (intervention/control). In three-level mixed-effect models, the fixed effects of groups, child's age in months, non-linear effects (Age^2 and Age^3) and interaction between groups and age and random effects (measurements within child within centre) were analysed (I–II). These models allow for a difference between the groups at baseline, linear changes of z-scores over time and the difference in weight development between the groups, which can be viewed as the intervention effect (i.e. interaction term). The parameter estimates were presented with 95% CI and p-values. The exact age of the child was used in all analyses. In studies I and II, we analysed maternal age and pre-pregnancy BMI, and gender of the child as possible confounders, but the p-value for interactions did not become statistically significant in any of these. In study IV, we added potential confounding variables to the model: mother's education, parity, smoking during pregnancy, pre-pregnancy BMI, gender of the child and target height, which were not significant, thus the final model includes only the above mentioned three factors. The goodness-of-fit of the model was evaluated by normal probability and residual plots and also tested by the

normality of the residuals (Kolmogorov-Smirnov test). The likelihood-ratio test was used in evaluating the change in model fit when including Age^2 and Age^3 in the models.

All analyses were performed using STATA software (version 12.0 for Windows, StataCorpLP, Texas, USA).

5 RESULTS

5.1 Participants in the studies (I, II, IV)

5.1.1 The NELLI follow-up studies

Response rate to the follow-up questionnaire among gestational intervention study mothers (I) was 66.1% (N= 72/109) (Figure 1). There were no obese women with BMI ≥ 30 kg/m^2 in the control group, whereas in the intervention group three mothers were obese before pregnancy. The proportion of normal weight (BMI < 25 kg/m^2) mothers was higher among the control group mothers, but the mean pre-pregnancy BMI did not differ between the groups (p-value 0.17). The proportion of macrosomic infants was slightly higher among the control mothers than among the intervention mothers (0.0% vs. 13.2%, p-value 0.056).

71.9% (N=64/89) of the mothers in the postpartum intervention group responded to the questionnaire on child's growth data (II). The proportion of missing mother/child dyads due to non-response was similar among the intervention (N = 14) and the control (N = 11) groups (Figure 2). The intervention mothers were slightly older than the control mothers (mean age 29.6 vs. 28.4 years, p-value 0.20). There were no obese mothers (BMI ≥ 30 kg/m^2) in the control group, whereas in the intervention group, there were two mothers who were obese before pregnancy, but the mean pre-pregnancy BMI did not differ between the groups (p-value 0.40).

Analyses to compare mothers lost to follow-up and those who responded were performed: no statistically significant differences in maternal pre-pregnancy BMI, education, marital and employment status and smoking before pregnancy were found.

Figure 1. Original sample and the follow-up of the offspring, respondents and non-respondents (The NELLI Study I).

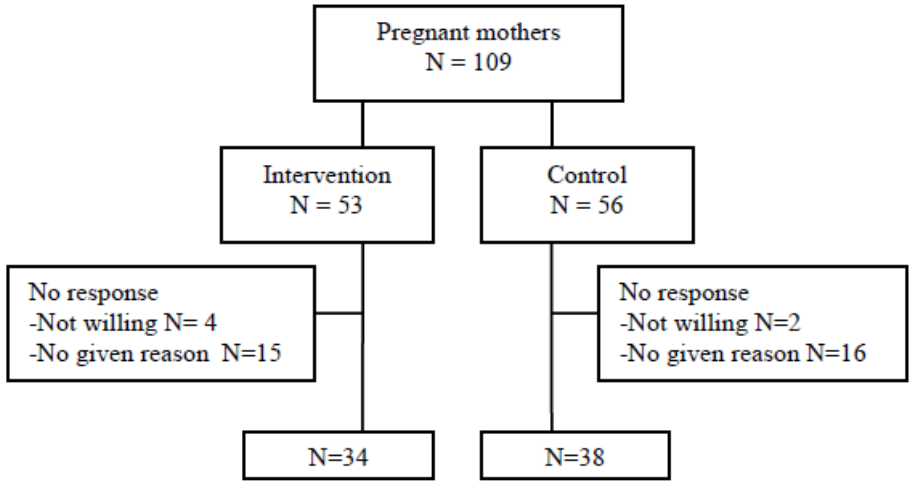
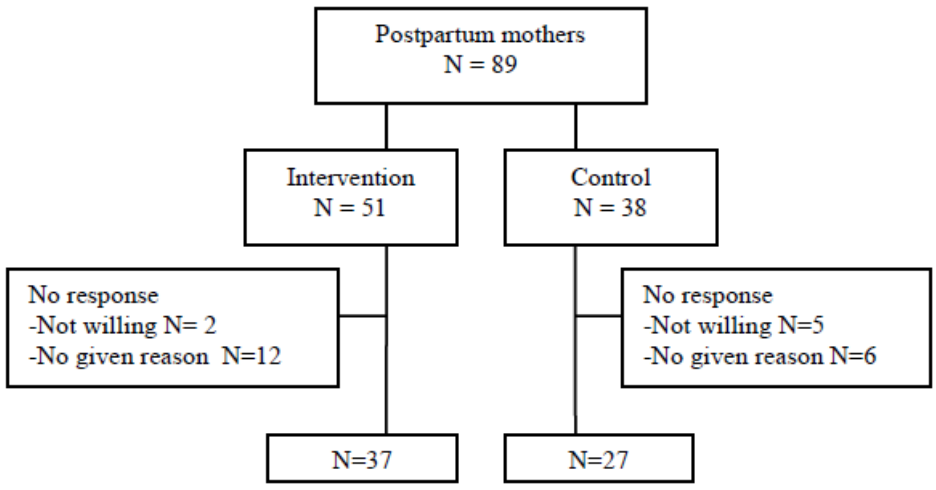


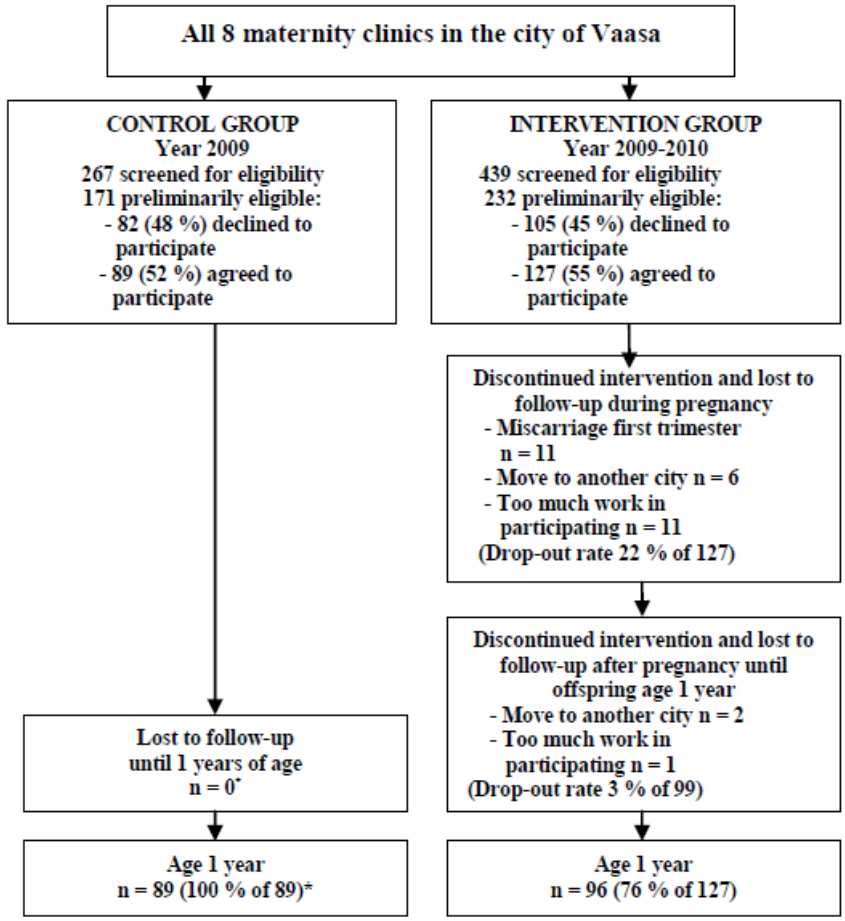
Figure 2. Original sample and the follow-up of the offspring, respondents and non-respondents (The NELLI Study II).



5.1.2 The VACOPP Study

For the control group, 171 of 267 mothers who had given birth in 2008 and visited targeted maternity health care clinics during their pregnancy were eligible for the study. Of those mothers, 89 (52%) agreed to participate. 439 mothers visiting these MHCs in 2009–2010 were screened for eligibility for the intervention group: 232 of those were eligible and 55% (N = 127/232) agreed to participate. 22% of the intervention group mothers discontinued the intervention during pregnancy, mostly due to moving to another city or suffering a miscarriage. There were no drop-outs until one year of offspring age in the control group, because the recruiting took place between birth and one year age. The study flow is described in Figure 3.

Figure 3. The flow chart of the VACOPP Study (IV).



* Because of one year retrospective recruitment

5.1.3 The baseline characteristics

Several factors capable of confounding offspring weight gain were analysed at baseline (I, II, IV). There were no statistically significant differences in these characteristics between the groups (Table 4).

Table 4. Baseline characteristics in the studies I, II and IV (mean or frequency (%)).

	Follow-up study I		**Follow-up study II**		**The VACOPP Study**	
	Intervention	Control	Intervention	Control	Intervention	Control
N	34	38	37	27	96	89
Age of the mother (years)	28.7±4.2 (2)	29.1±3.6	29.6±3.6	28.4±4.0	30.9±5.8	30.1±5.3
Mother's education (N of high, medium, low)	8, 7, 17 (2)	11, 3, 24	8, 7, 21	8, 3, 16	31,42, 23	25,41, 23
Father's education (N of high, medium, low)	-	-	-	-	33, 35, 7 (1)	30, 39,16 (4)
Mother's pre-pregnancy BMI (kg/m^2)	23.3±3.4(3)	22.2±2.1 (1)	22.4±3.7 (1)	21.8±2.4	27.5±4.7	26.6±4.1
Proportion of obese mothers (BMI ≥ 30 kg/m^2)	9.7%	0.0.%	5.6%	0.0%	26.0%	19.1%
Father's BMI (kg/m^2)	-	-	-	-	27.3±4.1 (2)	27.1±4.1 (6)
Proportion of obese fathers (BMI ≥ 30 kg/m^2)	-	-	-	-	20.2% (2)	16.9% (6)
Mother, Type 2 Diabetes	-	-	-	-	0.0% (1)	1.1%
Father, Type 2 Diabetes	-	-			1.1% (2)	1.1% (2)
Proportion of obese grandparent (BMI ≥ 30 kg/m^2)	-	-	-	-	56.8% (8)	63.1% (5)
Proportion of a grandparent having type 2 Diabetes	-	-	-	-	39.1%	43.2%
Parity						
Primiparous	100%	100%	100%	100%	57.3%	43.8%
History of newborn > 4500 grams	-	-	-	-	2.1% (1)	3.4%
Mother smoking during pregnancy	0.0.% (4)	5.3%	11.1%	22.2%	5.2%	11.2%
Gender of the child (boy)	47.1%	47.4%	56.8%	59.3%	51.0%	50.6%
Newborn > 4000 grams	0.0%	13.2%	13.5%	11.5%	-	-
Duration of exclusive breastfeeding (months)	4.4±1.6	4.5±1.7 (1)	4.0±1.8	3.5±2.4	Assessed as outcome	
Age at start of solid foods (months)	5.0±1.2	5.0±1.0 (1)	4.8±1.0	4.8±1.3	-	-

Number of missing values in the group is shown in parentheses. All differences between the intervention and control groups were non-significant. BMI, body mass index

5.2 The NELLI intervention and offspring's weight development

The weight development of the intervention target mothers' offspring was analysed in this study. The primary outcomes of the study have been reported earlier. These were the proportion of pregnant mothers exceeding the recommended level of gestational weight gain or the proportion of women returning to their pre-pregnancy weight by 10 months postpartum, changes in mothers' meal patterns, overall intake of vegetables, fruit and berries, the use of high-fibre bread and the intake of high-sugar snacks (Kinnunen et al. 2007a and 2007b). Physical activity outcomes also reported earlier were metabolic equivalent minutes (Aittasalo et al. 2008).

Maternal age, pre-pregnancy BMI and gender of the child were analysed as possible confounders for both postpartum and gestational intervention effects, but p-value for interaction did not become statistically significant in any of these.

5.2.1 Intervention during pregnancy (I)

When the lifestyle intervention was given during pregnancy (I) weight-for-length/height z-score between birth and 48 months or BMI z-scores between 24 and 48 months did not differ statistically significantly between the intervention and control group offspring (95% CI -0.01 to 0.01, p = 0.75, and 95% CI -0.03 to 0.01, p = 0.34) (Table 5, Figure 4). Mean weight-for-height z-score at 4 years of age did not differ significantly between the groups (-0.33 vs. -0.14, p-value 0.47).

*Figure 4. The NELLI follow-up study concerning intervention during pregnancy (I): Weight-for-length/height z-scores at 0-48 months (upper) and BMI z-scores at 24-48 months (lower). P-values denote the significance of intervention effects (interaction between group and child's age in months). Linear model including age of the child, and interaction between group*age.*

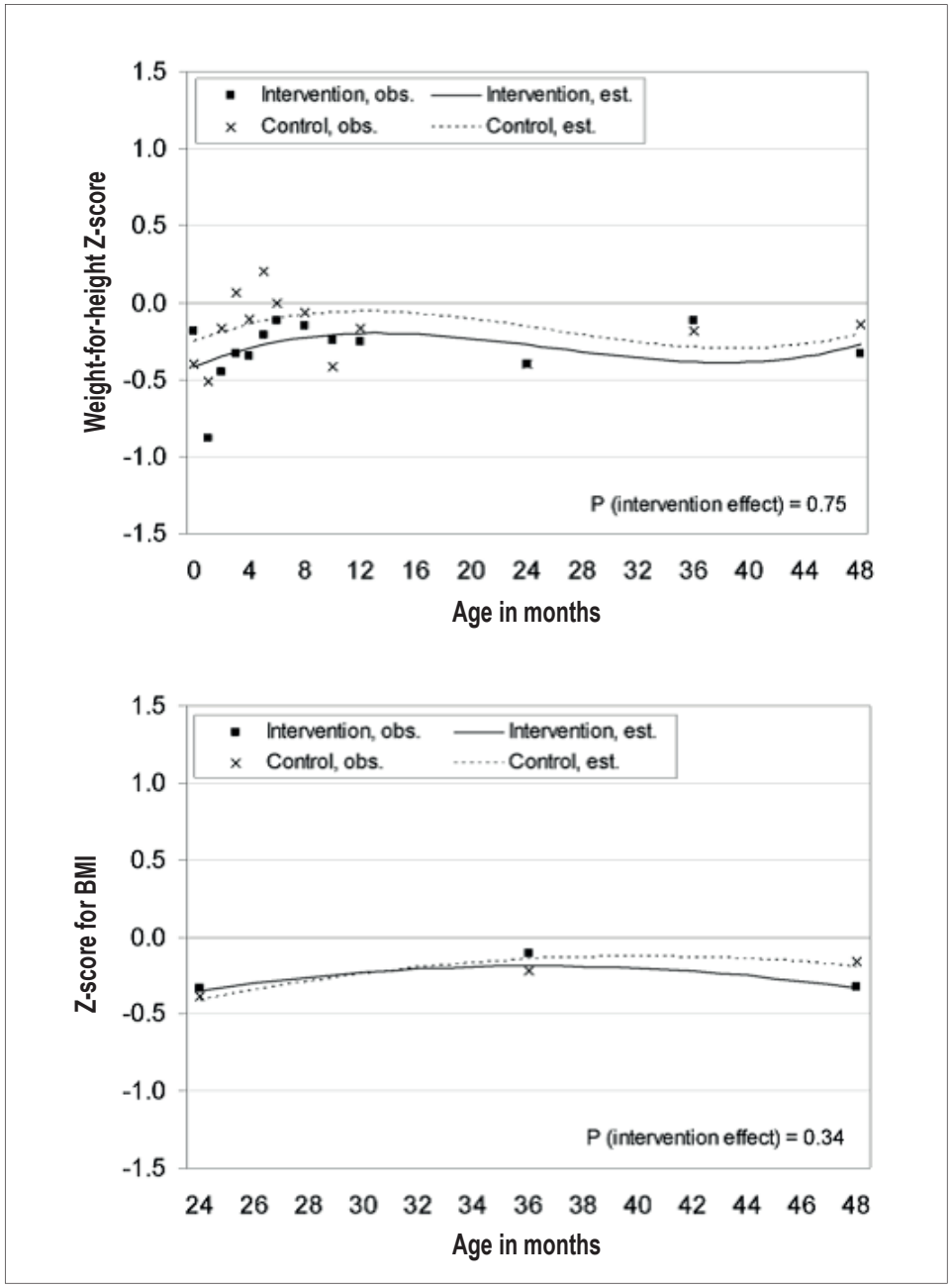


Table 5. The NELLI follow-up study concerning intervention during pregnancy (I): Offspring weight development and confidence intervals. Estimates and 95% confidence intervals for z-scores for weight-for-length/height and body mass index. Results from separate multilevel mixed effects linear regression models, including group, age of the child and interaction between age of the child and group. Non-linear relationship between z-score and age of the child was modelled using polynomials Age^2 and Age^3.

	Coefficient	95% CI	p-value
Weight-for-length/height z-score from 0 to 48 months of age			
Group	-0.163	-0.563 to 0.237	0.42
Age	0.036	0.008 to 0.064	0.013
Age^2	-0.002	-0.003 to -0.000	0.009
Age^3	0.000	0.000 to 0.000	0.016
Group * Age	0.002	-0.010 to 0.014	0.75
BMI z-score from 24 to 48 months of age			
Group	0.255	-0.611 to 1.121	0.56
Age	0.086	0.021 to 0.151	0.010
Age^2	-0.001	-0.002 to -0.000	0.016
Group * Age	-0.008	-0.025 to 0.009	0.34

5.2.2 Intervention during infancy (II)

The weight gain from birth to 48 months of age was measured as weight-for-length/height using multilevel mixed effect linear regression model. Weight gain did not differ significantly between the groups within this time frame (p-value 0.23) (Figure 5). The BMI z-scores of this intervention group children in these models had a slower slope of increase from 24 to 48 months of age compared to the control group (-0.034 to -0.002, p-value 0.028) (Table 6, Figure 5). Also weight-for-height z-scores showed slower weight gain during this age period among the intervention group children (-0.035 to -0.004, p-value 0.012).

Figure 5. The NELLI follow-up study concerning intervention during infancy (II): Weight-for-length/ height z-scores from birth to 48 months (upper) and BMI z-scores from 24-48 months (lower). P-values denote the significance of intervention effects (interaction between group and child's age at months). Linear model including group, age of the child, non-linear terms age^2 and/or age^3 and interaction between group and age of the child.

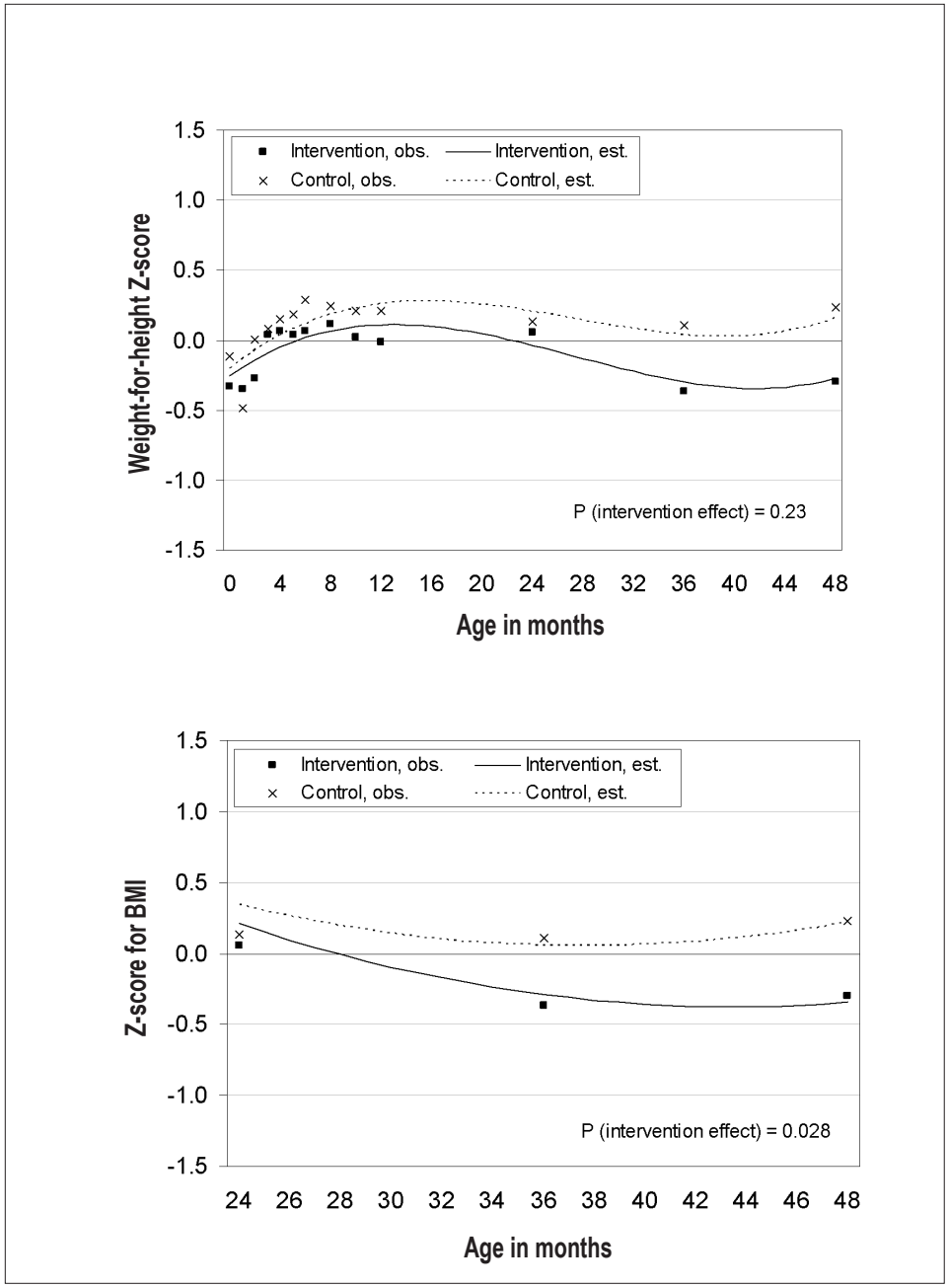


Table 6. The NELLI follow-up study II: Estimates and 95% confidence intervals for z-scores for weight-for-length/height and body mass index. Results from separate multilevel mixed-effects linear regression models, including group, age and interaction between age of the child and group. Non-linear relationship between z-score and age of the child was modelled using polynomials Age^2 and Age^3.

	Coefficient	95% CI	p-value
Weight-for-length/height z-score from 0 to 48 months of age			
Group	-0.056	-0.487 to 0.375	0.80
Age	0.071	0.044 to 0.098	<0.001
Age^2	-0.003	-0.005 to -0.002	<0.001
Age^3	0.000	0.000 to 0.000	<0.001
Group * Age	-0.008	-0.021 to 0.005	0.23
BMI z-score from 24 to 48 months of age			
Group	0.308	-0.480 to 1.095	0.44
Age	-0.115	-0.174 to -0.057	<0.001
Age^2	0.002	0.001 to 0.002	<0.001
Group * Age	-0.018	-0.034 to -0.002	0.028

5.3 The VACOPP Study (IV)

84/96 (87.5%) of the intervention group mothers participated in the first trimester counselling session held by a dietician and a physiotherapist, and 57/96 (59.4%) in the corresponding session during the second trimester. The participation rate with regard to the PHN counselling was almost 100% since the counselling was held in relation to routine visits to the MHCs.

5.3.1 Neonatal and pregnancy outcomes

The duration of pregnant mother's self-reported moderate intensity exercise during the second and third trimesters of pregnancy did not differ statistically significantly between the groups. GWG (gestational weight gain) until 37 gestational weeks did not differ between the groups, although there was a slight tendency towards the intervention group gaining less weight during pregnancy than the control group (11.4 vs. 12.7 kg; 95% CI 10.4 to 12.5 kg vs. 11.5 to 14.0 kg, p-value 0.11). Minimum and maximum

weight gains also pointed slightly towards the intervention group gaining less weight (-4.9 to 27.2 kg vs. -1.0 to 34.7 kg) (Table 7). Proportions of mothers keeping within the recommended total weight gain range, mothers below it and mothers exceeding the range according to Institute of Medicine of National academics (IOM) criteria were analysed (IOM 2009). The proportion of mothers exceeding the recommended range in the intervention group was 43.6% and in the control group was 47.2%; the difference was not statistically significant (p-value 0.83). The differences in the proportion of mothers maintaining or below the recommendations were not significant between the groups. The association of exceeding GWG recommendations and abnormal OGTT result was not statistically significant (p-value 0.10).

The mothers in the control group had a significantly higher proportion of abnormal OGTT results compared with the intervention group (29.2% vs. 14.6%; 95% CI 20.8 to 39.4% vs. 8.9 to 23.0%, p-value 0.016). No differences in the proportion of mothers having regular delivery between the groups were found. There was no difference either in newborn weight, ponderal index, large-for-gestational age status, or small-for-gestational age status (Table 7). The mean blood pressure level of mothers in the first and the third trimesters of pregnancy did not differ between the groups (Table 7).

Table 7. The VACOPP Study (IV). Maternal and neonatal outcomes in the trial groups (mean, frequency, or 95% CI).

	Intervention	Control	p-value	Missing
N	96	89		
Maternal				
First trimester				
Systolic blood pressure (mmHg)	119.1 (116.9 to 121.2)	116.5 (114.3 to 118.7)	0.10 [a]	4, 5
Diastolic blood pressure (mmHg)	73.9 (72.4 to 75.4)	72.1 (70.0 to 74.1)	0.14 [a]	4, 5
Second trimester				
Physical exercise (h/week)	4.2 (3.6 to 4.7)	4.5 (3.6 to 5.4)	0.62 [b]	2, 5
OGTT (Gest. weeks 26-28)				
0 h (fasting) (mmol/l)	4.8 (4.7 to 4.8)	4.9 (4.8 to 5.0)	0.12 [b]	-
1 h (mmol/l)	8.7 (8.4 to 9.0)	9.0 (8.7 to 9.4)	0.21 [a]	-
2 h (mmol/l)	6.8 (6.6 to 7.1)	6.9 (6.6 to 7.1)	0.77 [a]	-
Abnormal OGTT result (cP-gluc)	14.6%	29.2%	0.016[c]	
(0 h≥5.3 or 1 h≥11.0 or 2 h≥9.6 mmol/l)	(8.9% to 23.0%)	(20.8% to 39.4%)		
Third trimester				
Systolic blood pressure (mmHG)	122.4 (120.1 to 124.6)	122.5 (120.0 to 125.0)	0.79[b]	3, 4
Diastolic blood pressure (mmHG)	77.8 (76.1 to 79.5)	75.2 (73.2 to 77.3)	0.052[a]	3, 4
Physical exercise (h/week)	3.4 (3.0 to 3.8)	3.2 (2.5 to 3.9)	0.11[b]	4, 4
Gestational weight gain until 37 weeks' (kg)	11.4 (10.4 to 12.5)	12.7 (11.5 to 14.0)	0.11[a]	2, 0
Min – Max weight gain	-4.9 to 27.2	-1.0 to 34.7		
Neonatal				
Non-complicated vaginal delivery	77.1% (67.7% to 84.4%)	75.3% (65.4% to 83.1%)	0.77[c]	-
Gestational age at birth (weeks)	39.8 (39.4 to 40.1)	39.4 (39.2 to 39.7)	0.084[b]	-
Gender of the newborn (boy)	51.0% (41.2% to 60.8%)	50.6% (40.4% to 60.7%)	0.95[c]	-
Birth weight (grams)	3509 (3404 to 3615)	3507 (3417 to 3596)	0.97[a]	-
Ponderal index (kg/ m^3)	27.4 (26.9 to 27.9)	27.5 (27.0 to 27.9)	0.89[a]	-
Large-for-gestational age	7.3% (3.6% to 14.3%)	5.6% (2.4% to 12.5%)	0.64[c]	-
Small-for-gestational age	13.5% (8.1% to 21.8%)	6.7% (3.1% to 13.9%)	0.13[c]	-

[a]Independent Samples T-test, [b]Mann-Whitney U-test, [c]Chi-Square Test, [d]Fisher's Exact Test, OGTT=Oral glucose tolerance test (75 g, 2-hour); CI, Confidence interval; cP-gluc, capillary plasma glucose

5.3.2 Breastfeeding and infant growth outcomes

Duration of exclusive breastfeeding did not differ between the groups (3.0 vs. 2.8 months, p-value 0.52) (Table 8).

The offspring's growth, assessed as length-for-age SDS, weight-for-age SDS or weight-for-length SDS at ages of 0, 4, 6 and 12 months, did not differ between the groups. Absolute BMI was compared at the age of 12 months and did not differ between the groups (Table 8). According to the mixed effect linear regression model, the weight-for-length z-score slopes did not differ significantly between the intervention and control groups (p= 0.71) (Table 9). The mixed effect linear regression model included group and age of the child and interactions between the group and age of the child. Adding gender and the target height of the child, mother's pre-pregnancy BMI, smoking during pregnancy, parity and mother's education level to the models did not induce significant differences in the results, and they were not included in the reported results.

The proportion (expressed as percentage value deviation from the mean weight-for-length value according to Finnish definition of preschool-age overweight and obesity) of overweight (≥ + 10% weight-for-length) or obese (≥ + 20% weight-for-length) infants at the age of 12 months was not significantly different in the groups, although the control group had a slight tendency towards a higher proportion of overweight infants (Table 8).

Table 8. Anthropometric data in study groups during offspring's first year (mean ± SD or frequency and %). The VACOPP Study (IV).

	Intervention	Control	p-value	Missing
N	96	89		
Weight-for-length SDS				
0 months	-0.08 ± 0.96	-0.07 ± 0.93	0.94[a]	
4 months	0.05 ± 0.99	0.17 ± 1.10	0.46[a]	
6 months	0.13 ± 1.02	0.20 ± 1.18	0.65[a]	
12 months	0.09 ± 1.06	0.06 ± 1.11	0.85[a]	3, 0
Body mass index (kg/m^2)				
0 months	13.8 ± 1.3	13.8 ± 1.1	0.93[a]	
4 months	17.0 ± 1.4	17.2 ± 1.6	0.32[a]	
6 months	17.4 ± 1.5	17.6 ± 1.7	0.58[a]	
12 months	17.2 ± 1.4	17.2 ± 1.6	0.89[a]	3, 0
Weight-for-length ≥ +10% [d]				
12 months	16 (17.2%)	18 (20.2%)	0.60[b]	3, 0
Weight-for-length > +20% [e]				
12 months	3 (3.2%)	1 (1.1%)	0.62[c]	3, 0
Duration of exclusive breastfeeding (months)	3.0 (2.5 to 3.4)	2.8 (2.3 to 3.2)	0.52[b]	8, 0

[a]Independent Samples T-test , [b]Chi-Square Test, [c]Fisher's Exact Test, [d]assessed as overweight, [e]assessed as obese

Table 9. Estimates and 95% confidence intervals for weight-for-length SDS from multilevel mixed-effects linear regression models (IV). Non-linear relationship between z-score and age of the child was modelled using polynomial Age in months^2.

Weight-for-length SDS from 0 to 12 months of age	**Coefficient**	**95% CI**	**p-value**
Group (intervention/control)	-0.71	-0.31 to 0.16	0.56
Age in months	-0.06	0.02 to 0.01	0.002
Age in months ^{2}	-0.004	-0.007 to -0.002	0.002
Group * Age	-0.006	-0.023 to 0.034	0.71

6 DISCUSSION

6.1 Main results of the studies

6.1.1 Pregnancy outcomes in the VACOPP Study

The lower proportion of mothers with abnormal OGTT results in the intervention group suggests that the intervention could have the potential to improve glucose tolerance in pregnant mothers, and, as a result, a possibility to modify the foetal environment. Positive long-term effects in diminishing the offspring's risk for overweight or obesity and type 2 diabetes can be induced via better maternal glucose tolerance (Gillman et al. 2003, Hillier et al. 2007). The intervention given during pregnancy had no significant effect on mother's weight gain during pregnancy, although a tendency towards lower weight gain was seen among the intervention group mothers. No significant differences between the groups were found in self-reported PA during pregnancy. No differences were found either in the newborn birth weights, ponderal index, or in the proportions of non-complicated delivery.

Previous intervention studies using dietary and/or PA counselling during pregnancy have often failed to show any positive effects on maternal glucose tolerance, GWG or newborn weight, but also suggested that favourable effects can be achieved (Adamo et al. 2012). In the intervention studies aimed to prevent GDM, dietary, rather than PA, counselling has been found to decrease the prevalence of GDM (Oostdam et al. 2011). The NELLI intervention study, which targeted women at risk of GDM during pregnancy, was effective in lowering the proportion of large-for-age newborns, but no significant differences in the proportions of mothers with GDM was found (Luoto et al. 2011). However, their intervention resulted in an increased intake of dietary fibre and polyunsaturated fatty acids, and a decreased intake of saturated fatty acids and saccharose (Kinnunen et al. 2012). Also, a non-significant effect on the increase in PA was found (Aittasalo et al. 2012). In a recent study aimed at increasing PA during pregnancy, an improvement in gestational glucose tolerance was found (Barakat et al. 2012).

A lower proportion of abnormal OGTT results at 26–28 gestational weeks in the VACOPP intervention group could be the result of dietary improvements. We did not gather dietary records during pregnancy, since the control group had completed their

pregnancy at the time of recruitment, and also as the primary outcomes are the offspring outcomes. We can only speculate that the possible increase in fibre intake, which was one of the aims of the counselling, and which has the potential to improve glucose tolerance, could be responsible for the improved glucose tolerance in the study group. Differences in energy gains or consumptions between the groups seem more unlikely, since there were only suggestive differences between weight gains during pregnancy and no significant differences in self-reported moderate intensity PA. The influence of the intervention on mothers' glucose tolerance during pregnancy is possible, since the first group intervention was given at the latest at the 20th gestational week, and PHNs gave intensive counselling at routine visits to maternity clinics beginning in the first trimester.

Many lifestyle intervention trials, which have aimed to prevent GDM, have failed to decrease GDM incidence despite a feasible intervention method (Korpi-Hyövälti et al. 2011, Luoto et al. 2011). The improved glucose tolerance among the VACOPP intervention mothers compared to controls could be partly due to the higher motivation of mothers to carry out the dietary changes, because the primary aim of the study to prevent excess weight gain of the children was heavily emphasised to pregnant mothers. They were also informed that their unborn children are considered to be at a higher risk of unhealthy weight gain, because of their own risk factors for GDM.

The effective treatment of GDM may have diminished the intervention effect on GWG, newborn weight and type of delivery. At the time when the gestational intervention was ongoing, the mothers with abnormal OGTT results suggesting GDM were referred to the Central hospital for further evaluation and treatment; this was also true if the mother had several abnormal plasma glucose values in her self-monitoring after OGTT. All mothers with abnormal OGTT result were given dietary advice contributing to better glucose balance and a glucose meter to monitor their glucose values. Insulin treatment was started if the target glucose values were not achieved by above mentioned means. However, the higher prevalence of GDM in the control group could also be a biased result induced by the insufficient power of the sample, type 1 error or a chance. The continued follow-up of the children will show whether the improved glucose tolerance during pregnancy among the intervention group mothers has a positive effect on their children's weight gain.

6.1.2 Offspring's weight gain

The 24–48 month old children whose mothers had received intensified counselling (NELLI intervention) from 2 to 10 months after delivery had slower weight gain measured as BMI and weight-for-height z-scores compared to control group children. When the same intervention targeted pregnant mothers, there were no significant differences found between the groups in the offspring's weight gain until four years of

age. This counselling was previously reported to be feasible, to favour mothers' intake of fibre-rich bread, berries and fruits, and to help the mothers to maintain the PA level during pregnancy, but not to increase the level of PA, and to help the mothers to return to their pre-pregnancy weight (Kinnunen et al. 2007a, 2007b and 2008, Aittasalo et al. 2008). Considering that the intervention has been found to be effective in enhancing a healthy lifestyle, it is possible that the advantageous sequel on the offspring weight gain is seen only if the intervention is given after pregnancy.

There are very few reported intervention studies which have targeted pregnancy or infancy with follow-up of the child's weight gain. Of these, three resemble the intervention delivered in our studies (Appendix 1). One of those is the recent home-based RCT study of Wen et al. (2012), including almost 700 participants. They addressed families from late pregnancy to the offspring age of 2 years with counselling on breastfeeding, appropriate timing of the introduction of solid foods, active play, as well as family nutrition and PA; at 2 years of age, the mean BMI was significantly lower in the intervention group. Harvey-Berino et al. (2003) conducted a small home-based cluster RCT study targeting overweight mothers with 14–30 month old children, and delivered training in child feeding and exercise and parenting support for 16 weeks. At the end of their intervention there was no difference in weight-for-height percentiles between the groups. The very short follow-up period, together with the small sample size, has probably influenced the results. Gillman et al. (2010) reported a follow-up study where the intervention had been to effectively treat impaired glucose tolerance during pregnancy with diet advice, blood glucose monitoring and insulin therapy if needed. They found no differences in BMI z-scores between the intervention and control groups at the offspring age of 4 to 5 years.

As previously discussed, mother's impaired glucose tolerance during pregnancy can induce metabolic changes in prenatal environment, and thus expose the offspring to later overweight or obesity (e.g. Chandler-Laney et al. 2011). Also, the rapid weight gain during preschool years seems to increase the tendency to unhealthy weight gain (Blair et al. 2007, Lagström et al. 2008). Dietary and PA counselling targeted at mothers with small children may favour the offspring's healthy weight gain via the healthier lifestyle adopted by their mothers. The role of parents is crucial in introducing healthy behaviour among their offspring, and preschool age is an important period in the acquisition of food preferences and physical activity habits (Cullen et al. 2003, Timmons et al. 2012). For example, children who eat more fruits and vegetables in their meals have lower energy intake (Leahy et al. 2008), and eating more fruits and vegetables is reported to correlate with a lower BMI in children (Acharya et al. 2011). Thus, the NELLI intervention, which had been used in the follow-up studies, has theoretical potential for long-term benefit in maintaining offspring's normal weight. This potential is suggested by the slower weight gain of the offspring in the intervention group from 2 years of age onwards, when the intervention target group was mothers with infants.

In the STRIP Study, children who were overweight at age 13 years gained weight more rapidly than normal weight peers from 2 or 3 years onward (Lagström et al. 2008), which is at the same age than the weight gain difference in our study emerged. This faster weight gain during preschool years has also been related to later overweight or obesity in other studies, as previously discussed (Taylor et al. 2005, Blair et al. 2007).

The VACOPP intervention during pregnancy did not have a significant effect on the infant weight gain up to one year of age, but a slight tendency towards the control group having a higher proportion of overweight offspring during the first year was seen. The intervention did not result in a longer duration of exclusive breastfeeding compared to the control group, which may be one explanation for not finding any differences in infant growth between the groups. No other intervention capable of modifying the infant's weight gain was given during the offspring's first year. Such interventions, according to the literature, could have given guidance on early feeding practices, infant satiety cues and advice on appropriate time of starting solid foods (Worobey et al. 2009, Singhal et al. 2010, Huh et al. 2011).

The NELLI intervention seemed to slower the weight gain in offspring only if the intervention was received after delivery. It is known from previous studies that mother's GDM does not influence the offspring's weight gain until late toddler years or school age (Crume et al. 2011). In the study of Lawlor et al. (2011b), they found that the effect of intrauterine environment on offspring's BMI was seen only when the mother had a high BMI. In the NELLI pilot study, the majority of participating mothers were of normal weight, which may have diminished the difference found in the offspring's weight gain: foetal conditions in normal weight mothers cannot be influenced as strongly as these conditions in mothers with excess weight when the diet changes towards lower glycaemic index. The proportion of overweight children tends to increase with age, and a longer follow-up time might have revealed increasing differences between the groups in the NELLI follow-up studies, as well as in the VACOPP Study, where we have so far only analysed offspring's weight gain until one year of age. The participant mothers in the VACOPP Study were at risk of having children with a tendency for excessive weight gain, which probably increases the possibility of finding favourable results in offspring weight gain if the intervention is effective. The VACOPP follow-up time will be up to six years of age, thus providing a fairly long-term follow-up. Although pregnant mothers are thought to be receptive to intervention aimed at the well-being of their offspring and themselves, it is possible that the dietary and PA habits are more likely passed on to their children when the counselling is given at a time when the child is born and maybe more in mother's focus than during pregnancy. It is however possible that the motivation to change behaviour is higher when the mother belongs to a risk group, as it was in the VACOPP Study but not in the NELLI pilot study.

6.2 Significance and possibilities of exploiting the results

The studies described in this dissertation are among the first reported lifestyle intervention studies targeting pregnant mothers or mothers of infants, using a follow-up of the offspring's weight development. Positive results capable of decreasing the risk of later overweight were found: Dietary and PA intervention (NELLI) given to mothers during child's first year seemed to induce slower weight gain in children aged 2 to 4 years, and the VACOPP intervention delivered to pregnant mothers beginning in the first trimester resulted in a decreased incidence of GDM. According to current knowledge on early childhood factors increasing the risk of obesity, these results may promote healthy weight gain, although the methodological limitations must be acknowledged (Weng et al. 2012).

The effect of these interventions should be repeated in other studies with a larger number of participants, targeting known risk groups, and with as good a methodological level as possible in a real-life setting in primary care. If these results can be repeated in other studies that are found to be feasible with the same type of intervention and setting at comparable periods of life, these programs should be implemented in maternity and child health care centres to reach a wide population with risk factors of obesity at those critical time frames in childhood. Combining these interventions during pregnancy and infancy could further potentiate the positive effect on offspring's weight gain. Such interventions could result in lower prevalence of obesity and its adverse health consequences.

6.3 Methodological considerations

6.3.1 Participants and settings

The participants in the NELLI follow-up study were healthy first-time mothers without any risk determinants for having overweight offspring, thus constituting a homogeneous group. The NELLI pilot study had a relatively small number of participants, since the main aim of the study was to develop a counselling method for a larger study. Possibly with a larger number of participants and thus enough statistical power, differences in offspring weight gain after intervention during pregnancy would have been stronger. The response rates to NELLI follow-up questionnaires were 66.1% in study I and 71.9% in study II, which should warrant a representative sample of the intervention participants. The respondents had a tendency to be more often highly educated and to have lower pre-pregnancy weight than the non-respondents, although no statistically significant differences were found. The slightly selective respondents may also have influenced the results by diminishing the intervention effect. In the VACOPP Study, the drop-out rate during pregnancy was 22%, of which 9% were mothers who found

participating too taxing. This 9% of mothers could have created a selection bias for participants, but the proportion is small. The rest of the drop-outs during pregnancy were due to miscarriages or relocating to another city. During the first year of life, the drop-out rate was minimal (3%). In the control group, there were no drop-outs until one year of age, possibly affected by the recruitment not occurring until 0–12 months of age. The sample size in the VACOPP Study was not based on sample size calculations and the number of participants may be small with respect to finding statistically significant subtle differences in children's weight gain.

In contrast to the NELLI pilot study, the participant mothers in the VACOPP Study were mothers at risk of GDM assumed to have a higher risk for overweight or obese offspring. The positive intervention effect is expected to be more likely than in cases of a study population without specifically sought risk characteristics.

The study groups in both NELLI and VACOPP studies were comparable at baseline with their control groups as there were no statistically significant differences in several characteristics known to modify the risk of offspring's excess weight gain. As such baseline characteristics, we analysed mother's age before pregnancy, pre-pregnancy BMI, gestational weight gain, level of education, smoking during pregnancy and parity. In the VACOPP Study, the father's BMI and level of education could also be evaluated, and no significant differences in the groups were found.

The study implementation of the both intervention studies in municipal MHCs and CHCs seems practical, since pregnant mothers and young families with an infant are favourable targets for adapting healthier lifestyles and passing this on to their children in receptive ages during crucial toddler years. The strength of both studies is that they are integrated in health care practice, thus having good prospects as a sustainable part of municipal health care if found to be effective. Also, the intervention costs are low, since the existing clinical staff can be the intervention practitioner.

6.3.2 Designs

The NELLI intervention was a controlled trial without randomised design. The intervention clinics volunteered to function as intervention clinics, because their clients had more targeted risk factors. This may have confounded the results in their offspring's weight development as well, but in a minor proportion, because there were no significant differences in baseline characteristics between the intervention and control groups. The design of the NELLI pilot study is discussed in earlier publications (Kinnunen et al. 2007a, 2007b and 2008, Aittasalo et al. 2008).

The design of the VACOPP Study is a controlled pragmatic trial. Obesity is a prevalent condition threatening the health and quality of life even in childhood, which supports the selected pragmatic design in order to be able to assess whether the intervention has an effect when implemented in normal health care practice. Pragmatic trials

are considered to have greater generalisability of the results than explanatory studies, but the reliability of the results may be lower instead (Godwin et al. 2003). This study was integrated into routine health care practice and is followed through by ordinary health care practitioners in order to ensure and pilot its applicability to usual care setting.

A limitation of the VACOPP Study is that we did not use randomisation of the participants. Randomisation is considered the best way to select the trial participants in pragmatic trials (Godwin et al. 2003). However, the randomisation process may reduce willingness to participate in a trial, especially in lifestyle interventions where problems in recruiting enough participants are usual. Case-control study design is considered the second best design in intervention studies when randomisation is not feasible, especially when the study groups are matched for the characteristics that may confound the results (Flay et al. 2005). A non-randomised design has been suggested to be acceptable when the key characteristics are equally balanced in the groups, as was the case in both the VACOPP and the NELLI studies (Raaijmakers et al. 2008).

Another limitation of the VACOPP Study is that the control group was recruited one year retrospectively; however, the control children have been in prospective follow-up from one year of age onward. It has also been stated however that retrospective recruitment can be used in primary care settings when non-acute conditions are studied (McCarney et al. 2002). The advantages of retrospective recruitment are that it shortens the recruitment time and reduces the workload of the practical staff. For those reasons, the control group was recruited by the research nurse and only the intervention groups by PHNs. We assume that recruiting the control group by the research nurse has not caused a significant selection bias of the participants.

Disadvantages of these above mentioned methods in the VACOPP Study include weaker control of bias or other unknown factors influencing the effectiveness of the trial. Those methods were chosen in order to get a larger sample size for the trial, which was planned to be performed in only one city and in a specific risk group. However, we estimated that the groups would be comparable as families living in the same city, recruited from the same risk population and visiting the same health care clinics. We also assumed that the one year retrospective control group would not induce bias in the results since there were no major changes in municipal health care practices or society during that period.

6.3.3 Interventions

The previously described and discussed NELLI intervention was primarily aimed at preventing excess weight gain during pregnancy or helping mothers to return to their pre-pregnancy weight by changes in the mother's dietary and PA habits during pregnancy or at 2–10 months postpartum. The counselling given is also suitable for pro-

moting healthy weight gain in children if it results in favourable changes in the prenatal environment of the child, as well as if the healthier behaviour is adopted by the mother permanently and passed on as a healthier lifestyle in the offspring. The strengths of the NELLI follow-up study include a counselling method which has been previously reported to be feasible and capable of changing mothers' dietary and PA habits (Kinnunen et al. 2008 and 2012, Aittasalo et al. 2008 and 2012). The NELLI counselling was based on a trans-theoretical model and the PHNs received a feedback session to evaluate their counselling skills (Whitelaw et al. 2000). A limitation of the VACOPP Study is that no specific feasibility evaluation was done concerning intervention during pregnancy. The reasons influencing this were that the study burden of PHNs in MHCs with recruitment and the extra paperwork was so significant in their busy timetable that the addition of feasibility assessments seemed not to be conceivable at that time. Many of the participant mothers found the counselling and paperwork similarly time-consuming, which is why the extra load with feasibility questionnaires was avoided in this project.

If the counselling event does not succeed to interact with the participants' needs in relation to induce changes in dietary and PA habits, the counselling cannot have an effect on the desired outcomes despite the counselling targeting the correct behaviour. The success of behavioural counselling to help the client make health-related changes in lifestyle partly depends on the adequate and appropriate training of the counselling provider, whose training success should also be monitored (Salmela et al. 2009). The use of a relevant theoretical model in behavioural intervention studies strengthens the relevance of the study results (Smedley et al. 2001). The intervention studies often lack these elements, which was the case in most of the prevention studies described in the literature review of this dissertation. In future intervention studies, these important elements should be taken into account. Similarly the lack of motivation of the target client to change diet or PA habits results in ineffectiveness of the otherwise feasible intervention. A limitation in the VACOPP Study was also that we did not have any record of adherence to the intermediate intervention aims during pregnancy.

The VACOPP Study is aimed at preventing overweight and obesity among a selected risk group of preschool age children. It has a multifaceted approach and addresses mothers with health behaviour counselling from the first trimester of pregnancy. The first of the two group counselling sessions during pregnancy had a high participation rate of 87.5%; there was a lower participation rate in the other session in mid-pregnancy (59.4%). The sessions were arranged in late afternoons as a compromise for health care staff working times and the study participants' time schedules in respect to their release from their work. However, the participants felt the timing of the sessions not optimal, because at that time the mothers usually prepared dinner for their family and were hungry themselves. The hunger of the mothers was tried to be accounted for by offering fruits as a snack during the sessions. The number of these sessions may have to be higher than two and may have to be started even earlier than

between 10–20 weeks of pregnancy in order to induce changes in health behaviour that also lead to appropriate weight gain during pregnancy and further improved glucose tolerance during pregnancy. However, it is questionable whether this is feasible, taking into account the mothers' opportunities to participate the counselling sessions. The PHNs performed a revision of the intensified counselling during the routine visits at MHCs. The intensity, motivation and compliance of the PHNs performing the intervention may have varied. This may result in a weaker reliability of the results, but the results of the intervention can be better extrapolated to usual primary health care settings.

After delivery, advice to favour breastfeeding was given to the intervention group mothers in the form of a written leaflet in order to promote also healthy weight gain in children. This was a very light intervention and more intense counselling is probably needed in order to bring about a longer duration of exclusive breastfeeding. At CHC visits, the parents are advised to help their child to adopt healthy food preferences, encourage their children to be physically active and minimise sedentary activity time, and are also reminded about the role of an appropriate amount of sleep in healthy weight gain. The intervention of the study is still on-going, and the final effects will be assessed at the offspring's age of six years.

The VACOPP intervention targets several behavioural factors that are known to affect the child's weight gain. Multifaceted intervention programs are thought to be suitable for pragmatic trials and to be the most effective in preventing overweight, since, in addition to genetic susceptibility, obesity is a result of many behavioural factors. Intervention starting during pregnancy has the potential to modify the energy regulation mechanisms of the foetus as part of overweight/obesity prevention, as discussed earlier. The intervention is planned to continue up to the age of five years, thus having a long duration and better chances of resulting in healthy weight gain. Some bias could be caused, as the same PHNs who perform the intervention take care of the usual counselling practice of the control group at CHCs, but that was not the case when the intervention was ongoing at MHCs. This possible bias is however reduced by the fact that the control group children have their visits of each age point one year before the intervention group.

The PHNs especially in MHCs felt the study recruiting, intervention and the paper work together taxing and time consuming, which probably affected the recruiting success of the intervention group, and the intensity and quality of the intervention given by them. Carrying out the intervention as a real-life program – without the demands of the study setting – the work load of PHNs would probably be moderate and acceptable by them.

As signs for safety of the VACOPP intervention, we interpret the findings that there were no differences in the proportions of mothers gaining weight less than rec-

ommended, durations of pregnancies, small-for-age status of the newborns or in the proportions of infants with slow weight gain between the groups.

The intervention was started in early life, during the period which is known to be a risk period for developing later overweight or obesity and thus a period when preventive actions must take place. We also offered the parents a chance to monitor their own weight, BP, WC and metabolic markers, which we thought would motivate the parents to continue in the study, and to function as a public health promotion act by helping to find parents at risk of cardiovascular diseases.

6.3.4 Outcome data

The measured growth data in the studies were based on repeated measurements by standardised methods at CHCs by PHNs, therefore providing reliable anthropometry of the offspring. The growth data was analysed by using z-scores of weight-for-length/height and BMI-for-age based on recently updated growth data on Finnish children (Saari et al. 2011), the weight status thus having an up to date reference. Weight gain of the offspring was analysed with mixed effect models, which allowed for a difference between groups at baseline, changes over time and intervention effects.

In the NELLI follow-up study, the data on durations of breastfeeding and the age when introducing solid foods may have recall bias, since this information was asked of mothers when the child was nearly five years of age. In the VACOPP Study, this data was gathered when the child was aged between one and one and half years, thus being a more accurate estimate.

In the VACOPP and NELLI Study, pregnancy-related physical measurements were performed by PHNs. The intervention group measurements and OGTT results were written into study questionnaires by PHN, thus providing reliable data. In the VACOPP Study, the corresponding data on the control group was transferred to study questionnaires by the mothers themselves from their maternity cards written by PHNs. We were able to check this data if necessary using the health care records. Only the mothers' pre-pregnancy weights were recorded by the mothers themselves, possibly resulting in inaccuracies.

In the VACOPP Study, the mother's PA was measured as their own estimate of moderate intensity exercise in hours per week. This type of PA estimate is susceptible to misinformation as it is difficult to accurately estimate the duration of weekly PA and also to evaluate the intensity of the PA. A significant deficiency of this study is the fact that we could not gather dietary records because the control group had completed their pregnancies by the time of recruitment.

6.4 Implications for future studies

The effect of the VACOPP intervention on children's weight gain will be evaluated at the end of this decade when the target children have reached six years of age. Hopefully, the drop-out rate of this study will remain moderate, although young families tend to change residence quite frequently. A follow-up of the NELLI Study on offspring growth is planned to be performed (Luoto et al. 2011). In that study there were a larger number of participants than the NELLI pilot studies described here, and the target group was mothers at risk of GDM.

There is still a lack of intervention studies aimed at the primary prevention of obesity, i.e. intervention starting in early life – in pregnancy or infancy – or at the latest during toddler years. A multifaceted approach with sufficient intervention time and targeting the whole family has the potential to lead to sustained results in weight gain.

Performing studies that report the model of the counselling method used will promote the evaluation of the quality of the counselling, as well as finding out which counselling method has the best possibility to induce positive health-related behavioural changes. Many of the intervention trial targets have low motivation to change their lifestyle despite the high health risks. These clients may either decline to participate the study, or when participating they may not change their behaviour in the desired way. This calls for studies that evaluate the participants' motivation to make health-related behavioural changes, their motivation to participate in the study and the success of the counselling event to interact with the special needs of the target client at issue.

The maternity and child health care clinics have a good opportunity to reach the risk population during life periods where the families are motivated to make behavioural changes in order to promote their children's health. Hopefully, primary prevention intervention studies with high enough methodological quality, adequate power and long enough follow-up times will be seen in the near future to find effective programs, which could be implemented in settings that widely reach young families.

7 CONCLUSION

The lifestyle intervention of the NELLI Study, which targeted mothers during child's first year (II), significantly reduced weight gain among the intervention offspring between 2 and 4 years of age compared to the control group offspring. The preschool age is considered a crucial growth period in relation to the later risk of overweight or obesity. Our results suggest that dietary and PA intervention targeted at mothers of infants may have an effect in promoting healthy weight gain in the offspring during their later life. When this same intervention targeted mothers during pregnancy, the offspring's weight gain velocity was not significantly reduced by the age of four years compared to control children. Whether the subtle effects of these studies on offspring's weight gain are affected by the small number of participants and too short follow-up time remains to be seen in other studies with similar settings. The dietary and PA intervention targeting pregnant mothers in primary health care setting and beginning from the first trimester of pregnancy (The VACOPP Study) seemed to improve glucose tolerance during pregnancy, suggesting its potential to have a positive effect on offspring weight gain. No effect was seen in the newborn birth weights or infant weight gains. However, cohort studies have shown that adverse effects of gestational diabetes on the offspring's weight gain tend to only develop later in childhood. The earliest age at which any effect of improved mother's glucose tolerance is expected to be seen is from two to three years of age, as previously discussed. These results must be assessed with caution, because of the small number of participants in the NELLI pilot studies and the lack of nutritional outcome data during pregnancy in the VACOPP Study.

Obesity, with its major health and economic burden, challenges society to start preventive actions. The most natural settings in primary health care for preventive interventions reaching the beginning of next generation are maternity and child health care clinics. Since obesity has its origin in the prenatal period and in early childhood, the preventive means should start early in life, as in studies described in this dissertation. Healthier lifestyles and weight gain in children suggests healthier weights of future pregnant mothers offering more favourable prenatal environments to the next generation. This is the most plausible way to eliminate the obesity epidemic.

The interventions described here have the potential to be integrated into routine municipal maternity and child health care practice with moderate costs to society, but the discussed limitations must be taken into account. There are several on-going early life intervention studies to prevent childhood obesity, but there is a need for additional studies implemented in existing health care systems with adequate methodological quality and power to confirm the effectiveness of the programs.

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Appendix 1. Intervention studies aiming at overweight/obesity prevention in preschool age children with outcome measure on weight gain or adiposity.

Author	Setting/Participants age at baseline, Design	Sample size at time of measurement Intervention/ Control	Intervention	Duration of the intervention	Follow-up	Outcome measure regarding weight or adiposity	Conclusion (regarding weight gain)
Bayer et al. 2009, Germany	Kindergartens, mean 5.7 years, Cluster RCT	866/463	Kindergarten teachers enhanced regular physical activity, healthy dietary habits and healthy drink consumption after training. Newsletters, Tipp Cards and internet platform with supporting information for families.	1 year	18 months after the start of the intervention	Proportion of overweight and obesity	Proportion of overweight and obesity: 0
Brotman et al. 2012, USA	Family, Minority group in risk risk of obesity and behavioural problems, 3-5 years, RCT	1) 19/21 (girls) 2) 106/40 (boys and girls)	Promotion of effective parenting and child behavioural regulation. 22 weekly, 90-minute concurrent groups for parents and preschoolers, 30 minutes of guided parent-preschooler interactions, 10 biweekly 90-minute home visits, and up to 6 additional family visits.	6–8 months	1) 5 years after intervention 2) 3 years after intervention	BMI z-score, Proportion of obese children.	1) + 2) Intervention groups in both studies had lower BMI at follow-up relative to controls. 2) Lower rates of obesity (BMI ≥95th percentile) among intervention children
Daniels et al. 2012, Australia	Community-based, Mothers of 4-6 months infants, RCT	273/293	Anticipatory guidance on early feeding practices. Group education 6 x 1-1.5 h delivered by a dietician and psychologist over 3 months.	3 months	At 6 months after end of intervention	BMI z-score	The control group infants had higher BMI z-score and were more likely to gain weight rapidly from the beginning of the intervention
Dennison et al. 2004, USA	Preschool-based, 2.6–5.5 years, Cluster RCT	43/34	Interactive sessions by an early childhood teacher and a music teacher to reduce television watching and promote healthy eating and PA. 7 x 20 min interactive education sessions (6 weekly sessions and a final session 1 month later) plus complementary materials and suggested classroom activities for staff and parents.	10.3 weeks	12 weeks after intervention	Triceps skin-fold thickness, BMI	BMI-difference and skinfold thickness: 0

Appendix 1...

Eliakim et al. 2007, Israel	Primary school, 5-6 years, RCT	54/47	Dietary and behavioural counselling during school days. 45 minutes structured PA during 6 days/week.	14 weeks	8 months	BMI percentile, fat percent by skinfolds	Slower gain of BMI and fat percent
Fitzgibbon et al. 2005, USA Fitzgibbon et al. 2006, USA	2–5 years, 24 preschools, Minority children Cluster RCT	2005:146/154 2006:171/160	Healthy eating and exercise intervention (40 min x 3/ week) by trained early childhood educators. 20-min lesson that introduced a healthy eating or exercise concept with an activity; and 20 min of on-going PA. Parents in the intervention group received a weekly newsletter including homework assignment.	14 weeks	2 years after intervention	BMI	2005: smaller increases in BMI in the intervention group 2006: BMI: 0
Gillman et al. 2010, Australia	Mothers with mild gestational diabetes (glucose intolerance in pregnancy) from 24–34 weeks onward, and their offspring in follow-up, RCT	94/105	Dietary advice, blood glucose monitoring, and insulin therapy if necessary. Individualized dietary advice from a dietician, which took into consideration a woman's prepregnancy weight, activity level, dietary intake, and weight gain; instructions to self-monitor glucose levels four times daily until the levels had been in the recommended range for 2 weeks.	After 24–34 weeks of gestation	At 4–5 years	BMI z-score, proportion of overweight	BMI z-score and proportion of overweight: 0
Harvey-Berino and Rourke 2003, USA, Canada	Home-based, Mother with BMI > 25 and 14 -30 months old child, Cluster RCT	20/20	Matemal training in child feeding, exercise and parenting support. The intervention was delivered one-on-one in homes by an indigenous peer educator. Control: parenting support only.	16 weeks	At end of intervention	Weight-for-height z-scores, overweight/ obesity	Overweight, obesity: 0 Weight-for-height z-scores: 0
Jouret et al. 2009, France	Kindergartens, 2.5-5 years, Cluster RCT	1) 556/410 2) 697/410	1) Parents and teachers received basic information on overweight and health. 2) In addition children received kindergarten-based education to promote healthy practices related to nutrition, PA and sedentary behaviours. A dietician and an education aide, conducted ten 20-min sessions (5/year).	2 years	At the end of intervention	Prevalence of overweight, BMI z-score and change in BMI z-score	Prevalence of overweight, BMI z-score and change in BMI z-score were significantly lower in intervention groups compared with controls in underprivileged areas.

Appendix 1...

Kafatos et al. 2007, Greece	Primary-school, Family, 5.5–6.5 years, CCT	85/91	Teacher conducted 13-17 hours dietary counselling each year. Increased lessons on PA: theoretical 4-6 hours/year and two 45 minutes active lessons/week. Parent meeting at baseline and twice yearly to inform about healthy diet and PA to promote health of children and parents.	6 years	4 years after the end of intervention	BMI z-score	BMI z-score increased more in the control group, BMI z-score of the intervention group slightly decreased.
Kavanagh et al. 2008, USA	Formula-feeding caregivers, infants aged 3–10 weeks, double-blind RCT	38/57	Intervention subjects received one 45-60 minutes' education session promoting awareness of satiety cues and discouraging bottles containing more than 6 ounces, a hand-out before 4 months of age. Intervention and control groups received education regarding introduction and feeding of solid food after 4 months of age.	One session 45–60 min	At 4–5 months of age	Weight gain (g/week)	Weight gain: intervention group gained more (g/week).
Keller et al., 2009, Germany	Health service, Home, 4–7 years, RCT	49/134	The paediatrician carried out a low threshold intervention consisted of an age-adapted nutrition and exercise program to inspire the awareness of the adequate nourishment and motion.	1 year?	1 year after intervention	BMI z-score	Intervention group stabilized their BMI z-score.
Kramer et al. 2007 Belarus	31 maternity hospitals and associated poly-dinics, Mothers with newborn infants, Cluster RCT	7108/6781	Baby-Friendly Hospital Initiative 18-h lactation management training course. The course emphasized methods to maintain lactation and promote exclusive and prolonged breastfeeding.	12–16 months	6.5 years	BMI, waist, hip circumference, triceps and sub-scapular skin-fold thickness	BMI, waist or hip circumference, triceps or subscapular skin-fold thickness: 0
Manios et al. 1998, Greece	Primary-school, Family, 5.5–6.5 years, CCT	231/162	Teacher conducted 13-17 hours dietary counselling each year. Increased lessons on PA: theoretical 4-6 hours/year and two 45 minutes active lessons/week. Parent meeting at baseline and twice yearly to inform about healthy diet and PA to promote health of children and parents.	3 years	At the end of intervention	BMI, Suprailiac, biceps, triceps, and subscapular thicknesses	Smaller increases in suprailiac skinfold thickness and body mass index in the intervention group.

Appendix 1...

Manios et al. 2002, Greece	Primary-school, Family, 5.5-6.5 years, CCT	356/285	Teacher conducted 13-17 hours dietary counselling each year. Increased lessons on PA: theoretical 4-6 hours/year and two 45 minutes active lessons/week. Parent meeting at baseline and twice yearly to inform about healthy diet and PA to promote health of children and parents.	6 years	At the end of intervention	BMI, suprailiac, biceps, triceps and subscapular skinfold thicknesses	Smaller increases in biceps, triceps, skinfold thickness and body mass index in the intervention group.
Mo-Suwan et al. 1998, Thailand	Kindergarten/ preschool, mean age 4.5 years Cluster RCT	147/145	Aerobic exercise program: 15-min walk before the morning class and 20-min aerobic dance session three times per week by specifically trained personnel.	29.6 weeks	At end of intervention	BMI, triceps skin-fold thickness	BMI: 0 Girls in the intervention group were less likely to have an increasing BMI slope.
Paul et al. 2011, USA	Community based, Parents with newborn, RCT	1) 29/30 2) 29/30 3) 22/30	Groups received both, one, or no interventions delivered at two nurse home visits. 1) Instructed parents on discriminating between hunger and other sources of infant distress in order to minimize feeding for non-hunger-related fussiness and to prolong sleep duration. 2) Taught parents about hunger and satiety cues, the timing for the introduction of solid foods, and how to overcome infants' initial rejection of healthy foods through repeated exposure. 3) Both interventions.	From 2 to 4 weeks after birth	At the age of one year	Weight-for-length	Infants who received both interventions had lower weight-for-length percentiles.
Plachta-Danieltzik et al. 2007, Germany	Primary school, 6 years, CCT	345/1419	6 hours series of lesions on diet and PA. After lesions 20 minutes PA session.	Within first school year	4 years after the start of the intervention	BMI, BMI z-score, triceps skinfold and waist circumference	Cumulative 4-year incidence of overweight was lower in intervention children from families with high socioeconomic status.

Appendix 1...

Puder et al. 2011, Switzerland	Preschool, High migrant population, mean age 5.1, Single-blinded cluster RCT	333/292	The multidimensional culturally tailored lifestyle intervention included a PA program (4 x 45 minute sessions of PA/week., motivating cards), lessons on nutrition, media use (22 sessions), and sleep and adaptation of the built environment of the preschool class.	11 months	At the end of intervention	BMI, percentage body fat, sum of skinfolds, waist circumference	BMI: 0 Intervention group had lower percentage body fat and waist circumference.
Reilly et. al. 2006, Scotland	Nurseries, Home, Mean age 4.2, Single blinded Cluster RCT	245/259	Enhanced PA program in nursery (three 30-min sessions /week over 24 weeks). Home-based health education aimed at increasing PA through play and reducing sedentary behaviour by health education leaflets.	24 weeks	12 months after start of intervention	BMI z-score	BMI z-score: 0
Simell et al. 2000 Lagström et al. 2008, Finland	Health service, 7 months, RCT	541, ~ 50% controls	Families of children in the intervention group received individualized counselling at 1- to 3-month intervals until the age of 2 years, biannually until the age of 7 years, and annually until the age of 13, to reduce intake of saturated fat and cholesterol while ensuring their total energy intake. After the age of 7 years children received additional separate counselling.	13 years	At end of intervention	BMI	BMI: 0
Wake et al. 2011, Australia	Population-based, Parents of 7-8 months infants with parent- reported sleep problems Cluster RCT	101/92	Behavioural sleep strategies delivered during one to three structured individual nurse consultations.	2 months	At age 6 years	BMI z-score, proportion of obese/ overweight, waist circumference	BMI z-score: 0 Proportion of obese/overweight: 0 Waist circumference: 0
Warren et al. 2003, UK	Primary school, families, mean age 6.1 years, RCT	42/42 (Diet) 46/42 (PA) 42/42 (Diet+PA)	25 minutes' lunchtime clubs with an interactive and age-appropriate nutrition and/or physical activity curriculum was delivered to children and parents.	20 weeks over 14 months	At 1 month after the intervention	Changes in the proportion of overweight or obese children	Changes in the rates of overweight and obesity: 0

Appendix1...

Wen et al. 2012, Australia	Home-based, Mothers with newborn, Single-blinded RCT	255/242	The nurse visited families eight times at home, once at 30-36 weeks' gestation and seven times after delivery. Promoting breastfeeding, appropriate timing of introduction of solids, and active play, as well as family nutrition and physical activity.	0–24 months	At age of 2 years	Mean BMI	Mean BMI was significantly lower in the intervention group.

The Smart Family

exercise and nutrition guidance method

Transforming recommendations and research results into practical activities

- The Smart Family programme of the Finnish Heart Association aims to promote good exercise and nutritional habits among children and families and to prevent obesity.
- The programme is based on Ministry of Social Affairs and Health recommendations on the activities of child welfare clinics and on an intervention study on the lifestyles of families with children in Turku (STRIP).
- The first phase of the Smart Family programme developed a family-centred exercise and nutrition guidance method to be used as part of the normal activities of maternity and child welfare clinics.
- Child welfare clinics are the easiest way to approach families with children under school age.
- During the second phase of the Smart Family programme, the method will be applied to school health care.

Family-centred guidance gives good results – working tools for public health nurses

- The tools help public health nurses to respect in their activities the individual needs of the families and to support their resources.
- The method supports and clarifies the role of the public health nurse in providing guidance and makes it easier to bring exercise- and nutrition-related lifestyle matters to the fore.

The family exercise and nutrition habits card

- The family's card forms the basis of the guidance method.
- The family have the same card throughout their period at the child welfare clinic.
- It includes questions on the mother's, father's and children's exercise and nutrition habits and allows the evaluation of one's own practices, the setting of goals and the monitoring of goal achievement.
- A simple traffic light system makes the answers easy to grasp.

Example questions relating to the parents' exercise and nutrition habits	Mother	Father
Exercise makes me feel good	●●●	●●●
I exercise at least 5 days a week for at least half an hour, so I get slightly out of breath (for example by brisk walking)	●●●	●●●
I have breakfast and at least one main meal every day	●●●	●●●
Example questions relating to children's exercise and nutrition habits		
The child likes exercise	●●●	
The child exercises every day for at least 2 hours and sometimes gets out of breath	●●●	
The child has breakfast every day and another 4 to 5 meals or snacks	●●●	

● = usualy
● = sometimes
● = very arely/never

Information pack

- An information pack for public health nurses, containing recommendations for matters relating to exercise and nutritional habits and some background information.
- Tips for the practical implementation of family-centred guidance methods in exercise and nutrition guidance.

From a programme to a national guidance method

- The Smart Family guidance method was piloted for six months in ten municipalities.
- The public health nurses who took part in the pilot study thought the guidance method was much needed, useful and a good tool to support their activities.
- The guidance method provided new tools for exercise and nutrition guidance and for the prevention of obesity.
- The aim is to introduce the use of the guidance method at all maternity and child welfare clinics in Finland.

Year 2011

- The Smart Family -method will expand to primary school health care and smoking will be included as a theme.

Image pack

- Easy-to-grasp material to support individualised exercise and nutrition guidance.
- The subject matters of the image pack support the questions on the exercise and nutrition habits card.

Continuing education

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- Finnish Osteoporosis Association.

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Lifestyle counseling during pregnancy and offspring weight development until four years of age: follow-up study of a controlled trial

Taina Mustila[1,2*], Jani Raitanen[3,4], Päivi Keskinen[5], Antti Saari[6] and Riitta Luoto[3,7]

Abstract

Background: Fetal conditions are known to be partly responsible for the child's risk for obesity. Our pilot study aimed to determine the effect of gestational lifestyle counseling on the offspring weight gain until 4 years of age and to estimate power for future studies.

Design and methods: First-time pregnant mothers participated in a controlled trial conducted in maternity health clinics during 2004 – 2006. The intervention included individual counseling on physical activity and diet, and an option to attend supervised group exercise sessions. The participant mothers (N = 109) received a follow-up questionnaire concerning 13 repeated growth measurements of their offspring. Response rate to the follow-up questionnaire was 66.1% (N = 72/109).

Results: The increase of BMI z-score between 24–48 months was not significantly slower among the intervention group offspring (95% CI −0.025 to 0.009, p = 0.34) compared to control group. Z-scores for weight-for-length/height did not differ between groups when the period 0–48 months was analyzed (95% CI −0.010 to 0.014, p = 0.75).

Conclusions: In this pilot study gestational lifestyle counseling did not significantly slow the weight gain of the offspring. Gestational intervention studies with at least 300 mothers per group are needed to confirm the possible effect on offspring's risk for obesity.

Trial registration: Current Controlled Trials ISRCTN21512277.

Keywords: Pediatric, Intervention, Primary prevention, Childhood obesity, Diet therapy, Exercise, Follow-up, Controlled trial

Background

Childhood overweight and obesity have reached epidemic proportions in the past three decades [1-3]. Genetic susceptibility contributes to risk of obesity, but the present epidemic of obesity is mainly attributable to societal and environmental changes, with changes in lifestyle [4]. A large proportion of pregnant mothers are obese, and their offspring meet an obesinogenic environment prenatally. Mother's prepregnancy BMI (body mass index), weight gain during pregnancy and glucose intolerance or gestational diabetes mellitus (GDM) seems to correlate with the offspring's risk for subsequent overweight and obesity [5-9]. These prenatal influences on obesity risk are thought to be mediated by intrauterine programming via metabolic imprinting [9-12]. So far the exact mechanism which mediates the obesity risk on offspring during fetal life is unclear. There is some evidence that the increase in birthweight is not the only potential factor increasing offspring obesity risk [8,13,14]. Evidence from animal and some human studies suggests that epigenetic changes in metabolic control genes during fetal life have potential to affect offspring appetite and energy regulation as well as metabolism [15,16]. Poston et al. (2011) note in a recent consensus statement regarding obesity in pregnancy and long-term consequences on child health that "randomized controlled trials are urgently needed to evaluate the effect of nutritional and behavioral interventions in pregnancy on short- and long-term outcomes in mother and child" [9]. So far it has been

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unclear at what age the effect prenatal environment starts to influence offspring weight gain. In a recent work diabetes exposure *in utero* started to show after 27 months of age in offspring BMI development [17], and in the HAPO study there was no difference in offspring weight regarding maternal glucose level during pregnancy at the age of two years despite the significant effect of maternal glucose level on birthweight [7,18]. In several studies prepubertal offspring of mothers with GDM or maternal excess weight gain during pregnancy had a greater risk for overweight and adiposity [14,19-21].

Successful treatment of obesity is difficult even in childhood and high BMI in childhood increases risk of cardiovascular disease in adulthood [22]. Since excessive weight gain begins already during preschool years, preventive interventions should start early, before pregnancy, and include pregnancy and infancy [23]. So far only few such intervention studies targeting the preschool years have been published. In these studies some positive effects on child's weight development have been found, but evidence of effective preventive means to reduce childhood obesity is still most insufficient [24-26]. To the best of our knowledge there are no published lifestyle counseling intervention trials targeting healthy pregnant women with follow-up of their offspring's weight gain. In a randomized controlled trial by Gillman et al. (2010) they studied pregnant women with mild gestational diabetes and found that treatment of mild GDM reduced macrosomia at birth, but did not result in a lower BMI among the intervention offspring at the age of 4–5 years of age [27].

We hypothesized that healthier lifestyle during pregnancy could alter the intrauterine environment via mother's more appropriate weight gain and also by improving mother's glucose tolerance during pregnancy. Also, a healthier lifestyle adopted by the mother during the intervention could have positive effects on toddler diet and increase the time spent physically active. The aim of this study was to investigate whether intensified individual counseling on diet and physical activity targeting first time mothers during pregnancy affects offspring weight gain by the age of four years, and also to estimate the number of participants needed in future studies.

Methods

Study design

A controlled trial was conducted in six primary care maternity health clinics in Finland in the cities of Tampere and Hämeenlinna between the years 2004 and 2006. The study protocol was implemented during five visits to maternity health care clinics. The intervention study targeting mothers during their offspring's first year has been reported earlier [28]. Feasibility of the study protocol and other details have been reported earlier [29-32].

The intervention study was conducted in six maternity care clinics, three of which volunteered to be intervention clinics and the remaining clinics were treated as control clinics. The allocation was performed at clinic level. The clinics were a convenience sample of the clinics in Tampere and Hämeenlinna as they were selected based on the clinics' administrative personnel's suggestion for suitable clinics. The nurses recruited pregnant women during their first visit to maternity health care. The eligibility of all potential participants was assessed and all eligible women were asked to participate in the study. The aim was to recruit at least 30 pregnant participants/clinic in the intervention and control clinics in August-October 2004.

For the original trial we used assumptions from previous literature resulting in 90% power and significance level $\alpha = 0.05$, which suggested 82 women per group, in total 164 [33]. In addition, a conservative estimation of the sample size would be at least 1.5 fold compared to this calculation, because cluster randomization was applied. The estimated dropout rate (25%) was also taken into account in the sample size calculations. With these requirements, at least 300–350 women should be recruited for the study. However, the purpose of a pilot study was to test whether the study protocol was feasible and develop the protocol further before initiating the main study. The statistical significance of the results was not a priority in our pilot study and we aimed to recruit at least 60 pregnant women. Of these women, approximately 15 pregnant women were assumed to discontinue the study because of miscarriage, pregnancy complications or for other reasons.

Participants

The nurses recruited pregnant mothers with no previous deliveries (Figure 1). The exclusion criteria were age under 18 years, type 1 or type 2 diabetes mellitus (but not gestational diabetes mellitus), twin pregnancy, physical disability preventing exercising, otherwise problematic pregnancy (determined by a physician), substance abuse, treatment or clinical history for any psychiatric illness, inadequate language skills in Finnish and intention to change residence within three months. All participants provided written informed consent to participation.

Intervention

The intervention included individual counseling on physical activity and diet at five routine visits to a maternity health care nurse starting at 8–9 weeks of gestation, and an option to attend supervised group exercise sessions once a week during pregnancy until 37 weeks' gestation. The content of the intervention is described in greater detail elsewhere [29,31]. The purpose of the intervention was to promote leisure time physical activity and healthy dietary habits, thereby supporting participants' to prevent

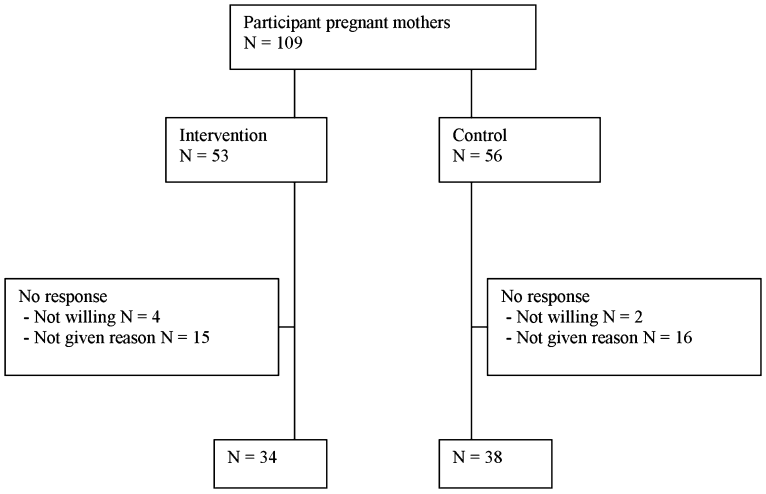

Figure 1 Original sample and the follow-up of the offspring, respondents and non-respondents.

excessive weight gain during pregnancy. In the control clinics, the nurses continued their usual counseling practices on physical activity and diet [31].

Outcomes

In this study we analyzed the secondary outcome of the intervention study, namely the weight development of the offspring. The primary outcomes of the study have been reported earlier: Dietary outcomes were changes in meal patterns, overall intake of vegetables, fruit and berries, use of high-fiber bread and intake of high-sugar snacks. Physical activity outcomes were MET(metabolic equivalent) minutes [29,32]. The proportion of pregnant mothers exceeding the recommended level of gestational weight gain was also of interest as a primary outcome.

Follow-up data collection

In 2010 mothers participating in the trial received a postal questionnaire on their offspring's weight development. This questionnaire was chosen for data gathering as direct access to the child health clinic records would have entailed maternal permission, and mothers have the same information on their offspring's growth as the child health clinic records. Finnish children attend child health care clinics several times in their first year and once a year thereafter. Children's weight was measured to the nearest 0.1 kg on a standard electronic scale. Children under 2 years were measured in recumbent position and thereafter in standing position to the nearest millimeter with a standard stadiometer. A nurse enters the height and weight measurements in the child's own health booklet for the mothers. The mothers entered these measurements in the postal questionnaire. The mothers were also asked whether their children had any long-term illnesses affecting growth (allergies or other chronic diseases), duration of breastfeeding and child's age when starting solid foods.

Statistical methods

The characteristics of the study participants were described using means and standard deviations or frequencies and proportions. The child's size during follow-up was analysed using weight and length/height converted to BMI (weight (kg)/height (m^2))-for-age and weight-for-length/height and their SDSs (z-scores) according to the recently updated Finnish growth reference [34-36]. The exact age of the child was used in all analyses.

Mixed-effects linear regression models were constructed to analyze the association of weight-for-length/height z-score and BMI z-score over time by group (intervention/control). Three-level mixed-effects models consisted of fixed effects (group, child's age in months, nonlinear effects $AgeInMonths^2$ and $AgeInMonths^3$ and interaction between group and age) and random effects (measurements within child within centre). These models allow for a difference between groups at baseline, linear changes of z-score over time and the difference in improvement between groups, which can be viewed as the intervention effect (i.e. interaction term). A likelihood ratio test was used for model selection. The parameter estimates were presented with 95% confidence intervals (95% CI) and p-values. The goodness-of-fit of the models was evaluated visually by normal probability and residual plots and also tested by the normality of the residuals (Kolmogorov-Smirnov test). All analyses were performed using STATA software (version 12.0 for Windows), StataCorp LP, Texas, USA. Likelihood-ratio test was used in evaluating the change in model fit when including $AgeInMonths^2$ and $AgeInMonths^3$ in the models. We also performed analyses

to compare mothers lost to follow-up and those who responded. Maternal prepregnancy BMI, education, marital and employment status and smoking before pregnancy were analyzed using Independent Samples *T*-test, Chi-Square Test or Mann–Whitney *U*-test. P-value for all these parameters between responders and non-responders were non-significant.

The study was approved by the Ethics Committee of the Pirkanmaa Hospital District.

Results

Response rate to the follow-up questionnaire was 66.1% (N = 72/109). According to the loss-to-follow-up analysis, there were no statistically significant differences between responders and non-responders in age, BMI before pregnancy, employment status, education or smoking before pregnancy. Responses were missing from 37 women who received counseling during pregnancy (Figure 1). Women in the intervention group who responded to the questionnaire, were similar in age than the control women (mean age 28.7 vs. 29.1 years). There were no obese women with BMI ≥ 30 kg/m^2 in the control group, whereas in the intervention group there were 3 women who were obese before pregnancy, and the proportion of normal weight (BMI < 25 kg/m2) mothers was higher among control group mothers (Table 1). There was no difference in the smoking status between the groups. The proportion of macrosomic infants was higher among the control mothers than among the intervention mothers (0.0% vs. 13.2%). Duration of breastfeeding or

Table 1 Baseline characteristics of the trial groups (mean ± sd or frequency and %)

	Intervention	Control	p value	Missing
N	34	38		
Age of the mother at delivery (years)	28.7 (4.2)	29.1 (3.6)	0.65 [1]	-
Pre-pregnancy weight (kilograms)	64.2 (9.7)	61.7 (7.2)	0.22 [1]	3, 1
Pre-pregnancy BMI (kg/m^2)	23.3 (3.4)	22.2 (2.1)	0.12 [1]	3, 1
Range	19.7 to 33.2	17.6 to 26.2		
Pre-pregnancy BMI			0.17 [4]	3, 1
<25 (kg/m^2)	24 (77.4%)	33 (89.2%)		
25-29.9	4 (12.9%)	4 (10.8%)		
30-	3 (9.7%)	-		
Gestational weight gain (kilograms)	13.6 (5.1)	14.1 (4.5)	0.69 [1]	3, 1
Weight gain recommendations during pregnancy			0.59 [3]	3, 1
Lower	11 (35.5%)	12 (32.4%)		
At the range of the recommendations	9 (29.0%)	15 (40.6%)		
Higher	11 (35.5%)	10 (27.0%)		
Education			0.25 [3]	2, 0
Low	8 (25.0%)	11 (28.9%)		
Medium	7 (21.9%)	3 (7.9%)		
High	17 (53.1%)	24 (63.2%)		
Employed	28 (84.8%)	30 (78.9%)	0.52 [3]	1, 0
Ever smokers	18 (54.5%)	18 (48.6%)	0.62 [3]	1, 1
Smoking during pregnancy	0 (0.0%)	2 (5.3%)	0.50 [4]	4, 0
Gestational age (days)	278.8 (10.7)	278.6 (8.4)	0.92 [1]	1, 1
Sex of the child – boy	16 (47.1%)	18 (47.4%)	0.98 [3]	-
Birthweight (grams)	3399 (313)	3388 (443)	0.91 [1]	-
Proportion of children with SGA	2 (6.1%)	5 (13.2%)	0.32 [3]	1, 0
Proportion of children with LGA	0 (0.0%)	0 (0.0%)	-	1, 0
Macrosomia, birthweight > 4,000 g	0 (0.0%)	5 (13.2%)	0.056 [4]	-
Breastfeeding (no other nutrition) (months)	4.4 (1.6)	4.5 (1.7)	0.66 [2]	0, 1
Partial breastfeeding (months)	7.2 (5.7)	7.5 (6.0)	0.95 [2]	0, 1
Age of the child receiving solid foods (months)	5.0 (1.2)	5.0 (1.0)	0.90 [1]	0, 1

SGA small for gestational age, *LGA* large for gestational age, [1] Independent Samples *T*-test, [2] Mann–Whitney *U*-test, [3] Chi-Square Test, [4] Fisher's Exact Test.

age when starting solid foods did not differ between the groups (Table 1).

Observed weight trajectories were slightly wider among girls than among boys until the age of 48 months (Figure 2). Weight-for-length/height z-scores did not differ significantly between the intervention and control groups at birth (Table 1). Intra-cluster correlation for z-scores in the height/length-for-weight final model was 0.57 and for ZBMI 0.93. Weight-for-length/height z-score between birth and 48 months or BMI z-scores between 24 – 48 months did not differ statistically significantly between intervention and control group offspring (95% CI −0.01 to 0.01, p = 0.75 and 95% CI −0.03 to 0.01, p = 0.34) (Table 2, Figure 3). As possible confounders we analyzed maternal age and prepregnancy BMI, and gender of the child, but p-value for interaction did not become statistically significant in any of these. Mean weight-for-height z-score at 4 years of age did not differ significantly in groups: intervention group −0.333 and control group −0.141, p-value 0.47.

Ordinary sample size calculation assumes that all data points are independent. With a multi-level structure, the ordinary sample size estimates needs to be inflated by the design effect $[1 + (n - 1)\rho]$, where n is the average cluster size and ρ is the estimated intra-cluster correlation coefficient (ICC). Sample size calculation proceeds by calculating the sample size for a naïve model, an ordinary model that assumes all observations are independent, and then inflating that sample size by multiplying it by the design effect, so that the sample size calculation applies to the multi-level model [37]. When comparing two groups of patients and 13 repeated measurements per child, the child is here considered as the cluster. Observed group means were −0.35 (intervention) vs. -0.15 (controls) and an intracluster coefficient = 0.57. Applying the design effect after calculating a sample size can be done in STATA (*sampclus)*. Thus we need 3,466 observations divided by the number of observations per child, 3466/13 = 266.6, or 267 child per group. When a drop-out rate of 20% is taken into account a sample size of at least 300 children in group is recommended in future studies.

Discussion

The main finding of our study was that lifestyle counseling during pregnancy did not significantly slow weight gain among the offspring. A greater number of study participants and a longer follow-up period are needed in future studies. Based on the current differences between the groups, at least 300 children per group are needed in similar experimental studies.

Childhood obesity leads to substantially increased risk for type 2 diabetes and cardiovascular diseases [22,38]. There is growing evidence for the important role of early preventive efforts since the unfavorable health consequences of obesity begin already during childhood and the treatment of childhood obesity tends not to lead to permanent results [4,39]. The higher prepregnancy BMI, gestational weight gain and GDM of the mother,have been shown to increase the risk for childhood obesity [7,8,20,21,40]. Mother's impaired glucose tolerance during pregnancy has been shown to increase offspring's risk for obesity and adverse metabolic changes in several studies [13,19]. The mother's glucose tolerance is influenced by diet and physical activity, as well as genetic factors and BMI. Our study was a controlled trial conducted in six maternity health clinics in primary care. The participants were first-time mothers without especially sought risk determinants for having

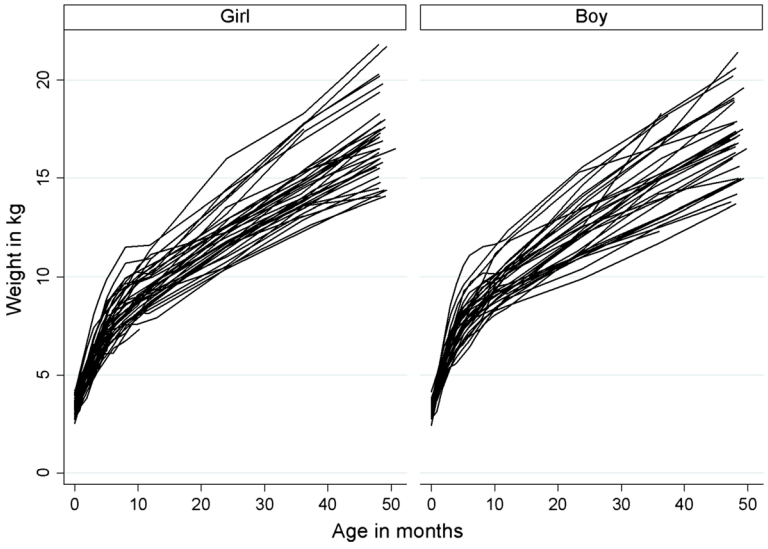

Figure 2 Growth trajectories by gender; exact age of the child and weight 0–48 months.

Table 2 Offspring weight development and confidence intervals

	Coefficient	95% CI	p value
Weight-for-length/height z-score from 0 to 48 months of age			
Group	−0.163	−0.563 to 0.237	0.42
Age	0.036	0.008 to 0.064	0.013
Age^2	−0.002	−0.003 to −0.000	0.009
Age^3	0.000	0.000 to 0.000	0.016
Group * Age	0.002	−0.010 to 0.014	0.75
BMI z-score from 24 to 48 months of age			
Group	0.255	−0.611 to 1.121	0.56
Age	0.086	0.021 to 0.151	0.010
Age^2	−0.001	−0.002 to −0.000	0.016
Group * Age	−0.008	−0.025 to 0.009	0.34

Estimates and 95% confidence intervals for z-scores for weight-for-length/height and body mass index. Results from separate multilevel mixed-effects linear regression models including group (intervention/control), age of the child and interaction between age of the child and group.

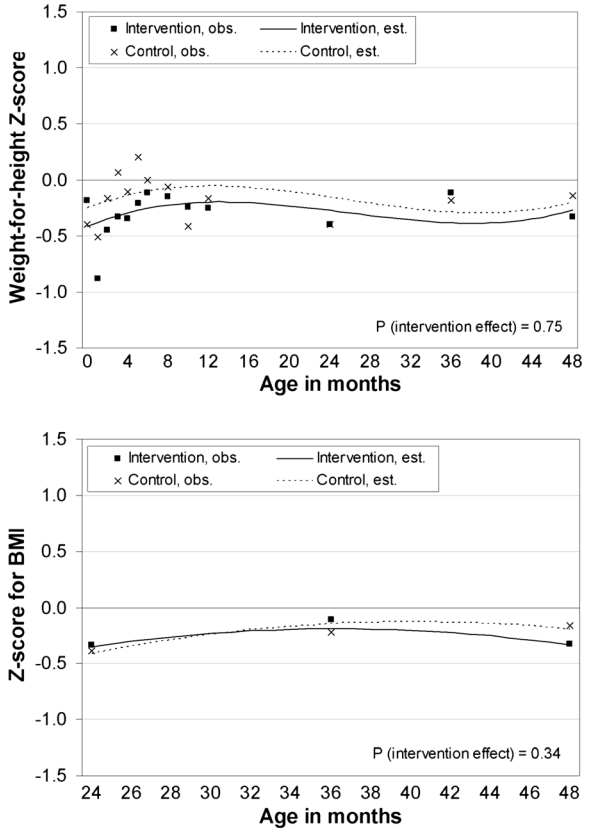

Figure 3 Effect of intervention on offspring weight development. Weight-for-length/height from birth to 48 months (upper) and BMI z-scores from 24–48 months (lower). P-values denote for the significance of intervention effects (interaction between group and child's age at months). Non-linear model including group, age of the child, non-linear terms age^2 and/or age^3 and interaction between group and age of the child.

overweight offspring. There were no statistically significant differences in factors known to affect offspring's risk of obesity between the two groups: mother's age before pregnancy, prepregnancy BMI, gestational weight gain, education, smoking during pregnancy and duration of breastfeeding. In the intervention clinics the mothers received intensified individual counseling on physical activity and diet, as well as an option to attend sessions of supervised group exercise once a week during pregnancy. The control group received conventional health care counseling. The intervention did not increase mother's physical activity or prevent excess weight gain during pregnancy, but the intensified counseling increased pregnant mothers' intake of fiber, vegetable and fruit (primary outcomes reported earlier) [29-32,41]. Thus this intervention could have an impact on the intrauterine environment via mother's healthier diet. Gestational lifestyle intervention can also potentially influence offspring's diet and time spent physically active via the healthier lifestyle adopted by their mothers. The role of parents is crucial in influencing lifestyle behavior among their offspring, and preschool age is an important period in the acquisition of food preferences and physical activity habits [23,42]. Previously published results from our data have shown a smaller proportion of macrosomic newborns in the intervention group than in control group [29]. Lawlor et al. (2011) showed in their recent study that the BMI of the offspring correlated with gestational weight gain if the mother was overweight or obese, but if the mother was of normal weight, the gestational weight gain had no correlation with offspring BMI, suggesting the role of intrauterine programming more clearly when the mother has high BMI [43]. In our study the majority of participating mothers were of normal weight, which may have influenced the results. In the study by Fraser et al. (2010) they found that any weight gain during the first 14 weeks of gestation was associated with increased offspring adiposity, but later in pregnancy only > 500 g/week weight gain increased offspring adiposity [40]. According to their result, the intervention targeting weight gain during pregnancy should start prior to conception rather than during the first trimester of pregnancy as in our study. The follow-up of the offspring of the HAPO study showed that maternal glucose at 28 weeks of gestation was not associated with offspring obesity at two years of age [18]. Crume et al. (2011) showed that intrauterine exposure to maternal gestational diabetes mellitus resulted in higher average BMI among the offspring only after 27 months of age and higher BMI growth starting at age 10 years and thus no differences in weight gain was seen in infancy or early childhood [17]. The follow-up

period in our study probably should have been longer than four years to see the effect of intrauterine influences on offspring weight gain.

One weakness of our study was that the participants did not belong to risk groups such as mothers at risk for gestational diabetes or exclusively overweight/obese mothers. Another weakness was the relatively small number of participants in this pilot study. Moreover, the effect of lifestyle intervention would probably show more marked results in the reduction of offspring weight gain if the follow-up period of offspring growth had been longer than four years. One weakness of the study is lack of randomized design, since the clinics volunteered as intervention clinics due to the magnitude of the problems in their clients. Thus the intervention clinic mothers presumably had more adverse weight gain than the control mothers, which may have confounded the results in their offspring weight development as well.

The strengths of our study include a feasible counseling method, a controlled trial setting and reliable growth data based on repeated measurements by nurses in primary health care. We also utilized the recently updated growth data on Finnish children by using z-scores of weight-for-length/height and BMI-for-age described in that growth data. Our sample included healthy first-time mothers, thereby constituting a more homogeneous group than mothers with earlier deliveries. We were also able to take into account confounding factors on childhood growth, such as smoking and mothers' prepregnancy BMI. A successful lifestyle intervention should create adequate motivation to change the lifestyle. Pregnancy is a suitable period to induce changes in lifestyle towards healthier, because pregnant mothers generally have good motivation to have a positive pregnancy outcome. Pregnant mothers have also regular contacts with health care nurses, and thus this kind of intervention is feasible. Our study was also integrated with primary health care follow-up of pregnancy. The intensified counseling helped pregnant mothers to increase the proportion of vegetables, fruit and fiber in their diet, as we have previously reported [25,28,41]. This change towards a lower glycemic index diet could improve mother's glucose tolerance below gestational diabetes level as well as lower mother's insulin levels. These metabolic changes may have beneficial sequelae in offspring weight gain by altering the intrauterine environment affecting the programming of offspring energy intake and metabolism.

Conclusions

In our study the lifestyle counseling targeting pregnant mothers in maternity clinics did not significantly reduce the velocity of weight gain among the offspring by four years of age. To the best of our knowledge this study is the first published controlled lifestyle intervention trial targeting healthy mothers during pregnancy with follow-up of their offspring growth. Larger randomized controlled trials with at least 300 children per group targeting this crucial period with a longer follow-up period of the offspring growth are needed to ascertain whether pregnancy is a period when it is worth investing in lifestyle counseling interventions to combat the obesity epidemic.

Abbreviations

BMI: Body mass index; GDM: Gestational diabetes mellitus; ICC: Intra-cluster correlation coefficient.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

RL is the guarantor of the study. TM, PK and RL planned the follow-up questionnaire to the mothers. TM coded the data together with research assistant. AS produced BMI-for-age statistics and participated to the interpretation of the BMI-for-age results. JR performed the statistical analyses. All contributors participated in drafting of the manuscript and approved the final manuscript. All authors had full access to all of the data (including statistical reports and tables) in the study and can take responsibility for the integrity of the data and the accuracy of the data analysis.

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Lifestyle counselling targeting infant's mother during the child's first year and offspring weight development until 4 years of age: a follow-up study of a cluster RCT

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ABSTRACT

Objective: To investigate the effect of intensified lifestyle counselling targeting infants' mothers on offspring weight development during the first 4 years of life.

Design and setting: Follow-up of a cluster-randomised controlled trial in primary care child health clinics during 2004–2006 in Finland. Participants received a follow-up survey during 2010 concerning weight and height measurements of their offspring. Number of clusters was six and the response rate to the follow-up 71.9% (N=64/89).

Participants: The participants (N=89) were mothers of infants aged 2–10 months.

Intervention: The intervention included individual counselling on diet and physical activity when the infant was 2–10 months of age and an option to attend supervised group exercise sessions.

Primary and secondary outcome measures: The authors analysed the secondary outcome of the intervention study: the weight development of the offspring. The primary outcome was the proportion of women returning to their prepregnancy weight by 10 months post partum, reported earlier.

Results: Multilevel mixed effect non-linear regression models included group, age of the child and interaction between group and age of the child. The increase of BMI z-score between 24 and 48 months was slower among the intervention group offspring (−0.034 to −0.002, p=0.028) as compared with control group. Z-scores for weight-for-length/height did not differ between groups when the period 0–48 months was analysed (p=0.23) but for the period of 24–48 months, between-group differences were significant (p=0.012).

Conclusions: Lifestyle counselling targeting mothers during the child's first year may be effective in slowing offspring weight gain until 4 years of age. However, larger studies are needed to confirm the findings which may have the potential in combatting the obesity epidemic.

Trial registration number: Current Controlled Trials ISRCTN21512277.

ARTICLE SUMMARY

Article focus

- Rapid preschool weight gain is known to increase risk for later obesity.
- There is lack of intervention studies targeting child's first year with follow-up of their weight gain.

Key message

- Results suggested that intensive lifestyle counselling targeting mother during child's first year may slower child's weight gain until 48 months of age.

Strengths and limitations of this study

- A feasible counselling method was used as well as a controlled trial setting and reliable growth data based on repeated measurements by nurses in primary child healthcare. We also utilised the recently updated growth data on Finnish children by using z-scores of weight-for-length/height and BMI-for-age described in that growth data.
- Since the study was a pilot study, number of participants and clusters was low. Also a longer follow-up period could reveal more clear influence of intervention on offspring weight development.

INTRODUCTION

The prevalence of childhood overweight and obesity has increased during the past three decades in the developed world and also in the developing world.[1–3] However, recent evidence suggests that the increase in childhood obesity prevalence may be abating.[4] Obesity has detrimental short- and long-term consequences to health, and successful treatment of obesity is difficult even in childhood. Effective preventive means are therefore needed.[4–6] Because overweight

tends to begin during preschool years, early primary preventive interventions are thought to be the most effective means to combat the obesity epidemic. However, only few randomised, controlled primary prevention lifestyle counselling trials have been reported targeting families during offspring's first year of life, to our knowledge none targeting only mothers and including both diet and physical activity counselling. Some of them have shown slightly positive effects on child's weight development, but evidence of effective preventive means to reduce childhood obesity is still insufficient.[7–9]

Obesity is partly a result of genetic susceptibility, but an obesity epidemic is mainly attributable to societal and environmental changes, with changes in lifestyle.[4] Pregnant mothers are also more often obese, and prenatally, a child may meet an obesinogenic environment.[10 11] Mother's prepregnancy BMI and weight gain during pregnancy correlate with the offspring's risk for subsequent overweight and obesity, and mother's glucose intolerance has been shown to increase the offspring's birth weight.[11–13] In some studies, higher birth weight seems to increase the child's risk for overweight and obesity, but the evidence is weak.[14 15] Children with rapid weight gain during their preschool years and children who reach their BMI rebound earlier are prone to obesity.[16–20] Modification of diet in infancy appears to reduce subsequent obesity risk.[21 22] Since excessive weight gain begins already during preschool years, preventive interventions should start early, before pregnancy, and include pregnancy and infancy.[23] So far, only few such intervention studies have been published.[4 7–9]

The aim of this study was to investigate whether individual counselling on diet and physical activity targeting first-time mothers with infants aged 2–10 months affects offspring weight gain by the age of 4 years.

METHODS

Study design, participants and methods

A controlled trial was conducted in six maternity and child health clinics in Finland in the cities of Tampere and Hämeenlinna between the years 2004 and 2006. Aim of the trial was to evaluate the feasibility and effects of a lifestyle intervention designed to prevent excessive gestational weight gain and postpartum weight retention. The study protocol was implemented during five visits to maternity or child healthcare clinics (figure 1). The prenatal intervention study will be reported elsewhere. Feasibility of the study protocol and other details have been reported earlier.[24–27]

The intervention study was conducted in six maternity and childcare centers, three of which volunteered to be intervention clinics and the remaining clinics were treated as control clinics. The allocation was performed at clinic level. The clinics were a convenience sample of the clinics in Tampere and Hämeenlinna as they were selected based on the clinics' administrative personnel's suggestion for suitable clinics. The participants consisted

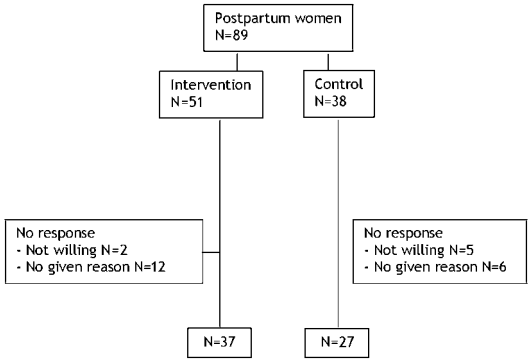

Figure 1 Original sample and the follow-up of the offspring, respondents and non-respondents.

of postpartum primiparous women. The exclusion criteria were age under 18 years, type 1 or type 2 diabetes mellitus (but not gestational diabetes mellitus), twin pregnancy, physical disability preventing exercising, otherwise problematic pregnancy (determined by a physician), substance abuse, treatment or clinical history for any psychiatric illness, inadequate language skills in Finnish and intention to change residence within 3 months. The nurses recruited postpartum women when visiting their home after delivery or at their first visit to the childcare center. The eligibility of all potential participants was assessed, and all eligible women were asked to participate in the study. All participants provided written informed consent for participation. The aim was to recruit at least 40 postpartum participants in the intervention and in the control clinics form August to October 2004.

For the original trial power calculations, we used assumptions from previous literature resulting at 90% power and significance level α=0.05, which suggested 82 women per group, in total 164.[28] In addition, a conservative estimation of the sample size would be at least 1.5-fold compared with this calculation because cluster randomisation was applied. The estimated dropout rate (25%) was also taken into account in the sample size calculations. With these requirements, at least 300–350 women should be recruited to the original intervention study. However, statistical significance of the results was not a priority in a pilot study and we aimed to recruit at least 60 postpartum women. Of these women, approximately 15 postpartum women were assumed to discontinue the study because of spontaneous abortion, pregnancy complications or for other reasons.

Intervention

The intervention included individual counselling on physical activity and diet when the child was 2–10 months old and an option to attend supervised group exercise sessions once a week. The content of the intervention is described in greater detail elsewhere.[25] The purpose of the intervention was to promote leisure time physical activity and healthy dietary habits, thereby supporting participants' return to their prepregnancy

weight during the study. In the control clinics, the nurses continued their usual counselling practices on physical activity and diet.[26]

Outcomes

In this study, we analysed the secondary outcome of the intervention study, namely the weight development of the offspring. The primary outcomes of the study have been reported earlier: the proportion of women returning to their prepregnancy weight by 10 months post partum. Dietary outcomes were changes in meal patterns, overall intake of vegetables, fruit and berries, use of high-fibre bread and intake of high-sugar snacks. Physical activity outcomes were MET (metabolic equivalent) minutes.[25 27]

Follow-up data collection

In 2010, mothers participating in the trial received a postal questionnaire on their offspring's weight development. This questionnaire was chosen for data gathering as direct access to the child health clinic records would have entailed maternal permission, and mothers have the same information on their offspring's growth as the child health clinic records. Finnish children attend child healthcare clinics several times in their first year and once a year thereafter. Children's weight was measured to the nearest 0.1 kg on a standard electronic scale. Children under 2 years were measured in recumbent position and thereafter in standing position to the nearest millimetre with a standard stadiometer. A nurse enters the height and weight measurements in the child's own health booklet for the mothers. The mothers entered these measurements in the postal questionnaire. The mothers were also asked whether their children had any long-term illnesses affecting growth (allergies or other chronic diseases), duration of breast feeding and child's age when starting solid foods.

Statistical methods

Characteristics of the study participants were described using means and SDs or frequencies and proportions. Observed weight trajectories by gender are shown in figure 2. The child's size during follow-up was analysed using weight and length/height converted to BMI (weight (kg)/height (m^2))-for-age and weight-for-length/height and their SDs (z-scores) according to the recently updated Finnish growth reference.[29–31] Exact age of the child was used in all analyses.

Mixed-effects linear regression models were constructed to analyse the association of weight-for-length/height z-score and BMI z-score over time by group (intervention/control). Three-level mixed-effects models consisted of fixed effects (group, child's age in months, non-linear effects AgeInMonths^2 and AgeInMonths^3 and interactions between group and age) and random effects (measurements within child within centre). These models allow for a difference between groups at baseline, linear changes of z-score over time

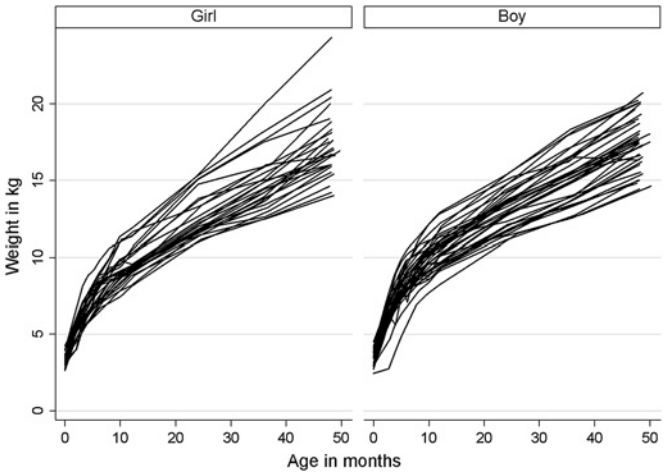

Figure 2 Growth trajectories by gender, exact age of the child and weight from birth to age of 48 months.

and the difference of improvement between groups, which can be viewed as the intervention effect (ie, interaction term). A likelihood ratio test was used for model selection. The parameter estimates were presented with 95% CI and p values. The goodness-of-fit of the models was evaluated visually by normal probability and residual plots and also tested by the normality of the residuals (Kolmogorov–Smirnov test). All analyses were performed using STATA software (V.12.0 for Windows), StataCorp LP.

Response rate to the follow-up questionnaire was 71.9% (N=64/89). We also performed an analysis to compare mothers lost to follow-up and respondents. According to the loss-of-follow-up analysis, mothers participating in the intervention and responding to the follow-up questionnaire reported significantly lower weight before pregnancy than non-responders (61.1 vs 66.3 kg, p=0.04). There were no differences in age, employment status or smoking before pregnancy, but the responding mothers tended to be more highly educated than non-respondents (highest education group 58.7% vs 33.3%, p=0.07).

We also estimated the power for the future studies using the current sample. With a multi-level structure, the ordinary sample size estimates need to be inflated by the design effect $(1+(n-1)\ \rho)$, where n is the average cluster size and ρ is the estimated intracluster correlation coefficient. When we have repeated measurements on the same child, the child is considered as the cluster. We applied the design effect after calculating a sample size (STATA, *sampclus*). New power estimates are shown in the Results section.

The study was approved by the Ethics Committee of the Pirkanmaa Hospital District.

RESULTS

Mothers in the intervention group who responded to the questionnaire were slightly older than the control mothers (mean age 29.6 vs 28.4 years, p=0.195). There

Table 1 Baseline characteristics of the trial groups (mean ± SD or frequency and %, difference between the groups and 95% CI)

	Intervention	Control	Difference (95% CI)	p Value	Missing
N	37	27			
Age of the mother at delivery	29.6±3.6	28.4±4.0	1.26 (−0.69 to 3.20)	0.195*	1, 0
Prepregnancy weight (kg)	61.8±11.1	60.1±8.1	1.64 (−3.19 to 6.47)	0.519*	1, 0
Prepregnancy BMI (kg/m^2)	22.4±3.7	21.8±2.4	0.68 (−0.85 to 2.21)	0.402*	1, 0
Range (kg)	18.1–35.4	17.3–27.9			
Prepregnancy BMI (kg/m^2)				0.593†	
<25	30 (83.3%)	25 (92.6%)	−9.3% (−24.9% to 6.4%)		1, 0
25–29.9	4 (11.1%)	2 (7.4%)	3.7% (−10.5% to 18.0%)		
30+	2 (5.6%)	–	5.6% (−1.9% to 13.0%)		
Gestational weight gain (kg)	15.8±5.5	16.0±5.0	−0.19 (−2.86 to 2.48)	0.888*	1, 0
Weight gain recommendations during pregnancy				0.965‡	
Lower	9 (25.0%)	6 (22.2%)	2.8% (−18.3% to 23.9%)		1, 0
At the range of the recommendations	10 (27.8%)	8 (29.6%)	−1.9% (−24.5% to 20.7%)		
Higher	17 (47.2%)	13 (48.1%)	−0.9% (−25.8% to 24.0%)		
Education				0.603‡	
Low	8 (22.2%)	8 (29.6%)	−7.4% (−29.3% to 14.5%)		1, 0
Medium	7 (19.4%)	3 (11.1%)	8.3% (−9.2% to 25.9%)		
High	21 (58.3%)	16 (59.3%)	−0.9% (−25.5% to 23.6%)		
Employed	32 (88.9%)	24 (88.9%)	0.0% (−15.7% to 15.7%)	1.000‡	1, 0
Ever-smokers	18 (50.0%)	17 (63.0%)	−13.0% (−37.4% to 11.5%)	0.306‡	1, 0
Smoking during pregnancy	4 (11.1%)	6 (22.2%)	−11.1% (−29.9% to 7.6%)	0.232‡	3, 1
Sex of the child—boy	21 (56.8%)	16 (59.3%)	−2.5% (−27.0% to 22.0%)	0.841‡	–
Proportion of children with SGA	7 (19.4%)	4 (15.4%)	4.1% (−14.9% to 23.0%)	0.680‡	1, 1
Proportion of children with LGA	1 (2.8%)	1 (3.8%)	−1.1% (−10.2% to 8.1%)	1.000†	1, 1
Macrosomia, birth weight >4000 g	5 (13.5%)	3 (11.5%)	2.0% (−14.5% to 18.5%)	0.817‡	0, 1
Breast feeding (no other nutrition) (months)	4.0±1.8	3.5±2.4	0.45 (−0.64 to 1.54)	0.391*	–
Partial breast feeding (months)	6.0±4.3	5.9±5.8	0.12 (−2.52 to 2.76)	0.657§	–
Age of the child receiving solid foods (months)	4.8±1.0	4.8±1.3	−0.03 (−0.64 to 0.58)	0.870§	1, 0

*Independent samples t test.
†Fisher's exact test.
‡χ^2 Test.
§Mann–Whitney U test.
LGA, large for gestational age; SGA, small for gestational age.

were no obese mothers (BMI ≥30 kg/m^2) in the control group, whereas in the intervention group, there were two mothers who were obese before pregnancy, but mean prepregnancy BMI did not differ between groups (p=0.40) (table 1). Smoking during pregnancy or duration of breast feeding did not differ significantly between groups (table 1). Number of mothers reporting children's allergies (two in intervention group, one in control group) or any chronic diseases (four children in intervention and five in control group) was low and did not result to exclusion of these children. Proportion of missing mother–child dyads due to non-response was similar among intervention (N=14) and control (N=11) groups (figure 1).

Observed weight trajectories were slightly wider among girls than among boys until age of 48 months (figure 2). The weight gain from birth to 48 months of child's age measured as weight-for-length/height was no significantly different between the groups (figure 3).

Multilevel mixed effect non-linear regression models included group, age of the child and interaction between group and age of the child. The increase of BMI z-score between 24 and 48 months was slower among the intervention group offspring (−0.034 to −0.002, p=0.028) as compared with control group. Z-scores for weight-for-length/height did not differ between groups when the period 0–48 months was analysed (p=0.23), but for the period of 24–48 months between-group differences were significant (p=0.012) (table 2 and figure 3).

Based on the current data, we also estimated the sample size of the study which should be needed to achieve sufficient power for the study. From the current sample, we assume group means (SDs) of −0.3 (1.1) vs 0.2 (1.2) and intracluster correlation coefficient of 0.63 for z-score on weight for height. For future studies, 730 observations are needed, divided by the number of observations per child, 730/13=56.2, 57 children per group.

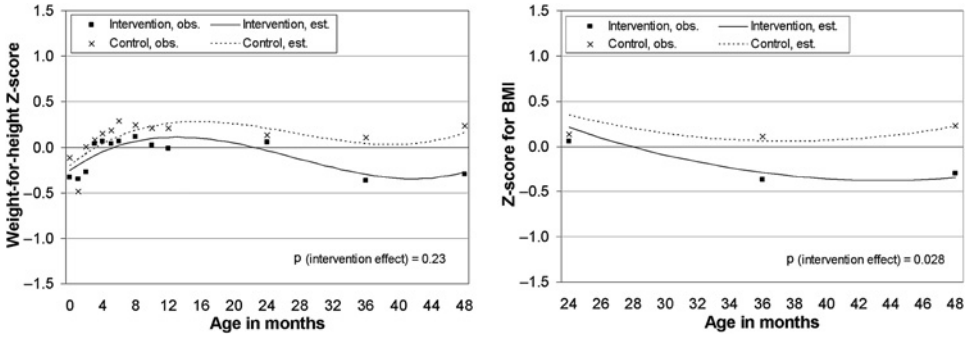

Figure 3 Weight-for-height from 0 to 48 months and BMI z-scores from 24 to 48 months. p Values denote for the significance of intervention effects (interaction between group and child's age at months). Non-linear model including age of the child and interaction between group × age. Obs., observed; est., estimated.

DISCUSSION

The main finding of our study was that the offspring of the mothers receiving intensified lifestyle counselling during the period from 2 to 10 months of infant's age may have slower weight gain measured as BMI z-scores between 24 and 48 months than the children in the control group. The STRIP Study showed that children overweight at 13 years had a steeper weight gain starting at 2 or 3 years.[18] Thus, our result suggests that the lifestyle intervention might reduce the risk for obesity.

Since the unfavourable health consequences of obesity already begin during childhood and the treatment of childhood obesity tends not to lead to permanent results, early preventive measures are needed.[4–6 23] One of the early determinants for obesity, type 2 diabetes and cardiovascular disease is rapid growth in early childhood.[16 18 19 32 33] Most of the evidence published so far on rapid early growth and subsequent increased risk for obesity has concerned infants, but there is also similar evidence regarding later preschool years.[18 19 34 35] To the best of our knowledge, no previous controlled intervention trials have targeted only mothers during child's first year and included both diet and physical activity counselling.[8 9] Our study was follow-up of a cluster-randomised trial conducted in child health clinics. The participants were first-time mothers without specifically sought risk determinants for having overweight offspring. There were no statistically significant differences between the groups regarding mother's age before pregnancy, prepregnancy BMI, gestational weight gain, education, smoking during pregnancy or duration of breast feeding. In the intervention clinics, the mothers received individual counselling on diet and physical activity and the option to attend supervised group exercise sessions once a week during the first 10 months of infant's life. The control group received conventional healthcare counselling.

Table 2 Estimates and 95% CIs for z-scores for weight-for-length/height and body mass index

	Coefficient	95% CI	p Value
Weight-for-length/height z-score from 0 to 48 months of age			
Group	−0.056	−0.487 to 0.375	0.80
Age	0.071	0.044 to 0.098	<0.001
Age^2	−0.003	−0.005 to −0.002	<0.001
Age^3	0.000	0.000 to 0.000	<0.001
Group × age	−0.008	−0.021 to 0.005	0.23
BMI z-score from 24 to 48 months of age			
Group	0.308	−0.480 to 1.095	0.44
Age	−0.115	−0.174 to −0.057	<0.001
Age^2	0.002	0.001 to 0.002	<0.001
Group × age	−0.018	−0.034 to −0.002	0.028

Results from separate multilevel mixed-effects non-linear regression models including group (intervention/control), age and interaction between age of the child and group.

The strengths of our study include a feasible counselling method, controlled trial setting and reliable growth data based on repeated measurements by nurses in primary child healthcare.[25 26] We also utilised the recently updated growth data on Finnish children by using z-scores of weight-for-length/height and BMI-for-age described in that growth data.[29] Our sample included healthy first-time mothers thereby constituting a more homogeneous group than mothers with earlier deliveries. We were also able to take account of confounding factors on childhood growth, such as mothers' smoking and prepregnancy BMI. We have shown earlier that intensified counselling both during pregnancy and postpartum results in changes in mother's dietary and physical activity behaviour.[24–27 36] Therefore, the beneficial sequelae in offspring weight gain found in this study are more probable than without an effective counselling method.

The weaknesses of our study include the relatively small number of participants and clusters. In spite of this, clinic level was taken into account in the models. The respondents were also more often highly educated and had lower prepregnancy weight than the non-respondents. Therefore, selective response may have influenced the result, and the abovementioned selection may have diminished the intervention effect. The possibility of Hawthorne effect cannot be denied either. Another reason for the small observed differences between groups may be that the participant mothers as a group had no special risk characteristics of having overweight children, such as obesity or low social class.[4] The proportion of overweight children tends to increase with age, and longer follow-up time might have revealed increasing differences between the groups.[4 37 38]

Power of the study was insufficient, but the primary aim of the original trial was to evaluate the feasibility of the counselling protocol. According to our estimates based on the current sample, at least 57 children are needed per group for future intervention studies concerning childhood obesity prevention.

The positive intervention effect on offspring weight gain is probably mediated by the healthier diet and increased physical activity adopted by the intervention mothers. The role of parents is vital in facilitating sustainable lifestyle behaviour in their offspring, and early childhood is a critical period in the acquisition of food preferences and physical activity habits.[23 39] The impact of the intervention via mother and her breast milk on infant's early nutrition could partly explain the effect of the lifestyle intervention on offspring weight gain: infants have been shown to acquire a flavour bridge through breast milk, which is influenced by mother's diet, making it easier for a child to accept these flavours in her diet.[40]

CONCLUSIONS

In our study, the intensified lifestyle intervention targeting mothers during child's first year may reduce weight gain in the offspring until 4 years of age. By slowing the weight gain, such an intervention targeting this crucial growth period could be one means of combating the obesity epidemic. To break this intergenerational circle of obesity and its complications, initiating early prevention programmes targeting mothers before, during and after pregnancy is essential, likewise community-based preventive actions.[4 5 23] Larger randomised controlled trials are needed to gather more evidence for selecting the most effective preventive programmes.

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Competing interests None.

Ethics approval The study was approved by the Ethics Committee of the Pirkanmaa Hospital District.

Contributors RL is the guarantor of the study. TM, PK and RL planned the follow-up questionnaire to the mothers. TM coded the data together with a research assistant. AS produced the BMI-for-age statistics and participated in the interpretation of the BMI-for-age results. JR performed the statistical analyses. All contributors participated in drafting the manuscript and approved the final manuscript. All authors had full access to all data (including statistical reports and tables) in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

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STUDY PROTOCOL Open Access

Behavioral counseling to prevent childhood obesity – study protocol of a pragmatic trial in maternity and child health care

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Abstract

Background: Prevention is considered effective in combating the obesity epidemic. Prenatal environment may increase offspring's risk for obesity. A child starts to adopt food preferences and other behavioral habits affecting weight gain during preschool years. We report the study protocol of a pragmatic lifestyle intervention aiming at primary prevention of childhood obesity.

Methods/Design: A non-randomized controlled pragmatic trial in maternity and child health care clinics. The control group was recruited among families who visited the same clinics one year earlier. Eligibility criteria was mother at risk for gestational diabetes: body mass index ≥ 25 kg/m^2, macrosomic newborn in any previous pregnancy, immediate family history of diabetes and/or age ≥ 40 years. All maternity clinics in town involved in recruitment. The gestational intervention consisted of individual counseling on diet and physical activity by a public health nurse, and of two group counseling sessions. Intervention continues until offspring's age of five years. An option to participate a group counseling at child's age 1 to 2 years was offered. The intervention includes advice on healthy diet, physical activity, sedentary behavior and sleeping pattern. The main outcome measure is offspring BMI z-score and its changes by the age of six years.

Discussion: Early childhood is a critical time period for prevention of obesity. Pragmatic trials targeting this period are necessary in order to find effective obesity prevention programs feasible in normal health care practice.

Trial registration: Clinical Trials gov NCT00970710

Keywords: Childhood obesity, Intervention, Lifestyle, Pragmatic, Prevention

Background

Obesity remains a worldwide costly health concern although the increase in prevalence of childhood obesity seems to be abating at least in some western countries [1,2]. Childhood obesity has several adverse outcomes during childhood, and since it often continues to adulthood, it increases cardiovascular morbidity among other health concerns in adult life [3,4]. Genetic susceptibility is a strong determinant for risk of being an obese child, but environment already starts to play a role during fetal life, infancy and preschool years [5-8] Once a child is obese it is difficult to reverse this adverse metabolic state with interventions [9]. This supports the rationale to find early preventive interventions. Since childhood obesity is a common health problem and concerns the whole community, the preventive methods should be applicable to normal health care practice and be cost-effective enough. Yet there are only few reported early interventions to prevent childhood obesity, and these are mostly not implemented in normal primary care practice. Many of these interventions especially those targeted at multiple factors affecting energy expenditure have resulted in some positive effects in weight development, but follow-up times have been short [10,11].

There is evidence that offspring of mothers gaining excessive weight and having impaired glucose tolerance during pregnancy are at higher risk for obesity [12-15]. Rapid weight gain in infancy and during preschool years

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is also a known risk factor for later obesity [8,16]. Breastfeeding may protect against obesity especially if the mother is overweight [17]. Parents have critical role in introducing healthy dietary habits to their offspring and food preferences often develop during preschool years [18]. Even preschool aged children spend a significant time in sedentary activities. Less physically active children are prone to obesity [8,19]. Reducing sedentary time has potential to mitigate childhood obesity risk [20]. Short sleep duration has been associated with greater risk for childhood obesity [21]. To reverse the obesity epidemic early intervention programs are thought to be an opportunity. An appropriate setting for these interventions would be municipal maternity and child health clinics, making it possible to reach the target population at moderate cost. Targeting preventive means at a risk group the cost-effectiveness of the intervention is presumed to be higher. The aim of this pragmatic multifaceted intervention programme is to prevent obesity in preschool children. In this paper we describe the protocol of the study.

Methods

Study objectives

The primary aim is to evaluate whether a multifaceted structured lifestyle intervention in primary care setting has potential to prevent overweight among preschool children belonging to a risk group. Additional aims include assessing changes in metabolic profile, waist circumference, blood pressure, dietary habits and time spent physically active, sleep and screen time of the offspring.

Hypothesis

Participant intervention group mothers at risk of gestational diabetes gain less excess weight and have better glucose tolerance during pregnancy via intensified counseling on healthier diet and physical activity. These goals are expected to favour normal offspring weight development. Continued counseling in child health care clinics concerning age-appropriate diet, physical activity, sedentary behaviour and sleep pattern is expected to further diminish offspring's risk for obesity.

Study design and setting

The study (VACOPP Study = VAasa Childhood Obesity Primary Prevention Study) is non-randomized controlled clinical pragmatic trial. The setting is eight municipal maternity and 14 child health care clinics in city of Vaasa in western Finland. All maternity and child health care clinics in the city participated in recruiting and intervention. The cohort of mothers who gave birth year 2008 and had risk factors for developing GDM and their offspring were the targets for recruiting the control group. Mothers pregnant during 2009–2010 with the same risk factors were targetted for the intervention group. The control group mothers were recruited retrospective, before their children had reached one year of age. Ethical approval for the study was granted by the Ethics Committee of Vaasa Hospital District.

Participants and recruitment

Informed written consent was provided by all participant mothers prior baseline assessments. The participants were mothers living in the city of Vaasa and belonged to a risk group for developing GDM. Criteria for belonging to this risk group were body mass index (BMI) ≥ 25 kg/m^2, macrosomic newborn (weight ≥ 4500 g) in any previous pregnancy, immediate family history of diabetes and/or age ≥ 40 years. This group of mothers are offered oral glucose tolerance test (OGTT) during pregnancy by the municipal maternity care. The offspring of these mothers are the target children. The exclusion criteria for the mothers were: multiple pregnancies, inability to speak Finnish, substance abuse or psychiatric illness fundamentally affecting ability to function. Recruitment of the control group was performed via telephone calls by a research nurse asking permission to send written research information and consent forms to subjects' homes. The intervention group recruitment took place in maternity clinics by public health nurses (PHN) at first contact. PHN gave the written research information and consent form. All mothers recruited were offered an opportunity to ask questions concerning the trial by telephone or e-mail of either the research nurse or the researchers. Since the study was a pragmatic trial, power calculations were not given priority. Due to the small number of expected participating mothers and retrospective control group the study would not reach statistical significance in a rigorous sense. The mean BMI z-score in the control group would be only a rough estimate thus making power calculations inaccurate [22].

Intervention in maternity health care clinics

The intervention started in the maternity clinics and continues in child health care clinics until the child is five years old. The intervention is intensified multifaceted lifestyle counselling. The intervention group mothers were offered two group counseling sessions: one during both first and second trimester of pregnancy. 1.5 hour sessions were given by a trained physiotherapist and dietician employed in public health centre. Information on diet was according to the nutrition recommendations of Ministry of Social Affairs and Health during pregnancy especially concerning appropriate energy content, fibre, quality of carbohydrates and fat [23]. The physiotherapist gave information about suitable and sufficient amount of exercise during pregnancy [24], and the mothers participated in brief session of gymnastics suitable to do at home. The

mothers also received information on the effect of healthy diet, exercise and appropriate weight gain during pregnancy on risk of having GDM, offspring's perinatal problems and obesity risk. Written educational material on healthy diet and physical activity during pregnancy was also given. This counseling was repeated more briefly by the PHNs during 13 routine visits to maternity clinics. After delivery the mothers were given a written information leaflet by a PHN reminding them that breastfeeding up to 6 months of age is also recommended for appropriate weight gain of the infant.

Intervention in child health care clinics

The families are offered to participate a 1.5 hour structured group counseling session when the child is 1 to 2 years old. It is given by physiotherapist and dietician employed in health care center and includes healthy diet recommendations to children under school age [23], as well as advice on suitable physical exercise at that age. The physical activity recommendations were according to those of Ministry of Social Affairs and Health [25]. Intervention group children are given a 30 to 60 minutes longer appointment with a PHN in child health care clinic at routine yearly control visits at 1, 2, 3, 4 and 5 years of age [Table 1]. During these visits counseling on healthy diet and amount of physical exercise/day is given as well as advice about age-appropriate sleep and screen time. These issues are addressed with help of the Finnish Heart Association's "The Smart Family- exercise and nutrition guidance method" [Additional file 1]. This method includes an interview card, a folder with e.g. informative images to be studied together with the family, and a separate information folder for PHNs. With the help of the card the family estimates its own habits regarding lifestyle and it functions as a tool for motivational interview. The folder contains motivational pictures and written information about healthy diet and physical activity. The PHNs in both maternity and child health care were trained in three separate group sessions for the intervention group intensified lifestyle counseling, and thereafter reminded about the intervention protocol at least once yearly by e-mail. The training of PHNs to use The Smart Family- exercise and nutrition guidance method was performed by Finnish Heart Association's educator in a whole day training session. The control group is getting the usual counseling used in Finnish maternity and child health care centers.

Measures

The primary outcomes of the intervention are difference and changes in BMI z-scores among the study group offspring, and the proportion of children being overweight according to the new Finnish cut-off-values for (percentile curve passing through BMI 25 kg/m^2) or obese (percentile curve passing through the BMI 30 kg/m^2) [26]. PHNs measure children's weight and length/height at 4 and 6 months of age and thereafter at 1, 2, 3, 4, 5 and 6 years of age.The final primary outcome measure time point will be at six years of age.

The secondary outcomes are duration of breastfeeding, frequency of offspring dietary intake of sugary beverages, pastry, sweets, fruit, berries, vegetables, type butter or margarine used and frequency of eating takeaway food as well as eating pattern are recorded yearly. Daily average screen and sleep time are recorded. Waist circumference

Table 1 Timing of the intensified counseling in maternity and child health care clinics

Intervention during pregnancy						
Gestational weeks 10-17	**Gestational weeks 18-28**		**Gestational weeks 20-32**		***Gestational weeks 28-40***	
Counseling session given by a trained physiotherapist and dietician 1,5 hours and 2 routine visits to PHN with intensified counseling concerning diet and physical activity	3 routine visits to PHN with intensified counseling concerning diet and physical activity		Counseling session given by a trained physiotherapist and dietician 1,5 hours		8 routine visits to PHN with intensified counseling concerning diet and physical activity	
Intervention in child health clinics						
0-6 months	**1 year**	**1-2 years**	**2 years**	**3 years**	**4 years**	***5 years***
Information leaflet on breastfeeding	*Intensified counseling by PHN at child health care centre with "The Smart Family-exercise and nutrition guidance method"*	*Intensified counseling by PHN at child health care centre with "The Smart Family-exercise and nutrition guidance method"*	*Intensified counseling by PHN at child health care centre with "The Smart Family-exercise and nutrition guidance method"*	*Intensified counseling by PHN at child health care centre with "The Smart Family-exercise and nutrition guidance method"*	*Intensified counseling by PHN at child health care centre with "The Smart Family-exercise and nutrition guidance method"*	*Intensified counseling by PHN at child health care centre with "The Smart Family-exercise and nutrition guidance method"*

(WC) and blood pressure (BP) are measured at 2, 3, 4, 5 and 6 years of age. Metabolic markers (fasting triglycerides, HDL-cholesterol, glucose, insulin and alaninaminotransferase) are measured at 2, 4 and 6 years of age.

Data collection

Mothers weight gain, BP, sleep duration, mother's own estimate about weekly physical exercise during pregnancy, results of 2-hour OGTT at 27–28 weeks of pregnancy were recorded in questionnaires filled in partly by the PHN and partly by the mothers once during the first, second and third trimester of pregnancy. The PHN measured and wrote down the physical measures in the questionnaires except for the control group's measures during pregnancy, which were filled in by the mothers themselves. The mothers transferred this data to study questionnaire from their maternity card, which was filled in by a PHN during pregnancy. The offspring data is recorded in questionnaires, which are filled in at the yearly appointment with the PHN. Long term illnesses affecting growth are recorded. The PHNs measure the length/height, weight, BP and WC of the child and add them to the questionnaire. The children's weight is measured to the nearest 0.01 kg without clothes until one year of age, and thereafter to the nearest 0.1 kg on a standard electronic scale with light clothing. Children under 2 years are measured in recumbent position and thereafter in standing position to the nearest millimetre with a standard stadiometer. WC is instructed to be measured on the midpoint between the lower costal border and the iliac crest. BP is measured by PHN using an automated BP monitor (Omron M6) under standard conditions with two repeated measurements. The children's dietary intakes are recorded yearly by questionnaires filled by mother or father of the child, and are measured as average consumption/day or week. The children's eating patterns are also recorded. The time children spend physically active is measured as parents estimate of time spent outdoors, moderate intensity or structured physical activity time as hours/day or week. Daily average screen time and sleep time are measured as parents' estimate yearly. Fasting blood samples are collected in the local medical laboratory used by health centre in Vaasa (Vaasa Central Hospital) and analysed using standard automated techniques. Laboratory results are recorded by the researcher directly from the laboratory score sheet. The timing of questionnaires, physical measurements and laboratory tests are listed in Table 2.

Statistical analysis

Characteristics of the study participants will be described using means and standard deviations or frequencies and proportions. The child's size during follow-up will be analysed using weight and length/height converted to BMI (weight (kg)/height (m^2))-for-age and weight-for-length /height and their SDSs (z-scores) according to the recently updated Finnish growth reference (26). Exact age of the child will be used in all growth analyses. Mixed-effects linear regression models will be used to analyse the association of weight-for-length/height z-score and BMI z-score over time by group (intervention/control). These models allow for a difference between groups at baseline, linear changes of z-score over time and the difference of improvement between groups, which can be viewed as the intervention effect (i.e. interaction term). The goodness-of-fit of the models will be evaluated visually by normal probability and residual plots and also tested by the normality of the residuals (Kolmogorov-Smirnov test). All analyses will be performed using STATA software (version 12.0 for Windows), StataCorp LP, Texas, USA.

Discussion

This pragmatic lifestyle intervention study aims to reduce the risk of obesity among a selected risk group of preschool children. It is based on following components: intensified diet and physical activity counseling during pregnancy; advicing mothers to favour breastfeeding and mother and father to help their child to adopt healthy food preferences; advicing parents to encourage their children to be physically active, minimizing sedentary activity time, and also reminding parents about the role of an appropriate amount of sleep in weight development. The intervention is still ongoing and the final feasibility and effectiveness of this trial will be assessed at offspring age of six years, but we will report also earlier preliminary results.

Pragmatic trials are considered to have greater external validity than do explanatory studies, but instead the internal validity is considered to be lower [27]. Our study was designed to be integrated in routine health care practice and to maximize the applicability of results to usual care setting. Practitioners who perform the intervention may vary in the way they deliver the planned counseling and the compliance of both practitioners and families may be variable. This results in weaker internal validity. For the internal validity randomization is considered the best way to select the trial participants also in pragmatic trials [27]. However, conducting a randomized controlled trial is not always feasible, and the randomization process may reduce willingness to participate in the trial especially in lifestyle interventions, where problems in recruiting enough participants are usual. Case control study design is considered the second best design in intervention studies when randomization is not feasible, especially when the study groups are matched for the characteristics that may affect the result [28]. Raaijmakers M et al. assessed randomized vs. non-randomized study with group matching

Table 2 Timing of questionnaires, physical measurements and laboratory tests

Maternity care	**Weeks' gestation**			
	8-12	**26-28**	**37**	**After childbirth**
	Mother's age	Mother´s average	Mother´s average sleep h/d	Gestation week of childbirth
	Mother's education	sleep h/d	Mother's average physical activity	Birthweight
	Father's	Mother's average	h/d	Birth length
	education	physical activity h/d	Blood pressure	Birth head circumference
	Mother's weight and height before pregnancy	Blood pressure	Mother's weight	
	Mothers chronic illness	Oral glucose		
	Fathers weight and height	tolerance test		
	History of GDM			
	History of newborn > 4500 g			
	Smoking during pregnancy			
	Previous deliveries			
	Immediate family history of DM 2, CAD, hypertension, obesity and hypercholesterolemia			
	Mother´s average sleep h/d			
	Mother's average physical activity h/d			
Blood pressure				
Child health care	**1 year of age**	**2, 4 and 6 years of age ***	**3 and 5 years of age**	
	Chronic illness	Chronic illness	Chronic illness	
	4 and 6 months weight and length	Consumption of	Consumption of beverage, fruits, vegetables, berries, sweets,	
	Weight	beverage, fruits,	pastry, bread, yoghurt, eating at takeaway restaurant	
	Length	vegetables, berries,	Regularity of meals	
		sweets, pastry, bread,	Sleep time h/d	
		yoghurt, eating at	Daily physical activity/outdoor activities	
		takeaway restaurant	Daily screentime	
		Regularity of meals	Weight	
		Sleep time h/d	Height	
		Daily physical	Waist circumference	
		activity/outdoor	Blood pressure	
		activities		
		Daily screentime		
		Weight		
		Height		
		Waist circumference		
		Blood pressure		
		fP-glucose		
		fP-insulin		
		fP-cholesterol		
		fP-HDL-cholesterol		
		fP-triglyserides		
		P-ALAT		

* At these timepoints the parents are offered to have their weight, waist circumference, blood pressure, fP-glucose, fP-cholesterol, fP-HDL-cholesterol and fP-triglycerides measured by health care centre; fP = fasting plasma; GDM = gestational diabetes mellitus; DM = diabetes mellitus; CAD = coronary artery disease; P-ALAT = plasma alaninaminotransferase.

design in their intervention and found that non-randomized appropriate matching resulted in 34% of their simulated trials in a more equally balanced distribution of their key characteristics compared with randomization, thus suggesting acceptability of non-randomized trials when the key characteristics are equally balanced in the groups [29]. It has also been stated that even retrospective recruitment could be used in primary care settings when non-acute conditions are studied [30]. In retrospective recruitment randomization is not possible and may make participant flow irregular, as it does in our study, too. The advantages of retrospective recruitment are that it shortens the recruitment time and reduces practical staff workload. Disadvantages of retrospective recruitment include weaker control of bias or other unknown factors influencing the effectiveness of the trial.

There are several methodological limitations in our study. We did not use randomizing and recruited the control group retrospectively in order to get a larger sample size for our trial planned to be performed in only one city and one risk group. The rationale behind this group selection was that it made the recruitment period shorter, the health centre staff's workload lower in recruiting, and we were able to recruit larger study groups in this small city willing to participate this long-term intervention study. Randomization is not possible when the control group is retrospectively recruited, but because motivation to participate trials is a problem, especially when lifestyle intervention is involved, the randomization could have further reduced families' willingness to participate in the study. However, we estimated that the groups would be comparable being families living in the same city and recruited from the same population. We also assumed that the one-year retrospective control group would not induce bias in the results since there were no major changes in municipal health care practices during that period. The retrospective control group could however cause bias, because the same PHNs who perform the intervention take care of the usual counselling practice of the control group in child health care clinics, but not in maternity clinics.

The strength of this study is that is designed to be a pragmatic trial integrated in health care practice thus having good prospect to be a sustainable part of municipal health care. The intervention costs are low since the existing clinical staff are the intervention practitioner. The follow-up time will be up to six years of offspring's age thus providing fairly long-term follow-up. Our intervention targeted several lifestyle factors that are known to affect the child's weight gain. Multifaceted intervention programmes are thought to be suitable for pragmatic trials and most effective in preventing overweight, since obesity is a result of many lifestyle factors in addition to genetic susceptibility. Moreover our intervention already starts during pregnancy and is planned to continue until the offspring is five years of age. This longer duration gives the intervention better chances of resulting in healthy weight gain. We are targeting mothers known to be at risk of having overweight or obese offspring. The positive intervention effect is more probable than in a trial targeting a population without specifically sought risk characteristics. We also offered the parents a chance to monitor their own weight, BP, WC and metabolic markers, which we thought would motivate the parents to continue in the study, and also to function as a public health promotive act by helping to find parents at risk of cardiovascular diseases.

Conclusion

Obesity originates prenatally and in early childhood. If overweight is already gained during the preschool years, the risk of becoming an obese adult is high. Thus preventive means should start early. The importance of pragmatic trials is that they help to define the best use of limited resources as well as policymakers and practitioners to make choices between customary care and the new counseling practice. Attempts to achieve methodological purity in explanatory trials can produce results that are not applicable in real life, but attempts to achieve full generalizability may also yield unreliable results. Pragmatic trials are not planned to study the contributors of its different components to the results and they should have long-term follow-up to ascertain whether the possible benefits are sustainable (27). Our intervention has potential to be integrated in routine municipal maternity and child health care practice with moderate costs to society.

Additional file

Additional file 1: Information on "the Smart Family"-exercise and nutrition guidance method.

Abbreviations

BMI: Body mass index; GDM: Gestational diabetes mellitus; OGTT: Oral glucose tolerance test; PHN: Public health nurse; WC: Waist circumference; BP: Blood pressure.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

TM and PK contributed to conception and design of the study. TM, RL and PK participated in drafting and revising the manuscript. All authors read and approved the final version of the manuscript.

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Pragmatic controlled trial to prevent childhood obesity in maternity and child health care clinics: pregnancy and infant weight outcomes (The VACOPP Study)

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Abstract

Background: According to current evidence, prevention of obesity should start in early life. Even the prenatal environment may expose a child to unhealthy weight gain; maternal gestational diabetes is known to be one of the prenatal risk factors that can promote obesity. The effects of dietary and physical activity counselling given during gestation on pregnancy and infant weight gain outcomes are reported here.

Methods: The study is a non-randomised controlled pragmatic trial aiming to prevent childhood obesity. The setting is municipal maternity health care clinics. The participants were mothers with a risk of developing gestational diabetes mellitus and their offspring. The children of the intervention group mothers were born during the years 2009–2010, and children of the control group during the year 2008. The intervention started between 10–17 gestational weeks. It consisted of individual counselling on diet and physical activity by a public health nurse, and two group counselling sessions by a dietician and a physiotherapist. The mothers also received a written information leaflet to motivate them to breastfeed their offspring for at least 6 months. We report the proportion of mothers with pathological glucose tolerance at 26–28 weeks of gestation, the mother's gestational weight gain (GWG) and newborn anthropometry. Infant weight gain from 0 to 12 months of age was assessed as weight-for-length standard deviation scores (SDS) and mixed effect linear regression models.

Results: Intervention group mothers had fewer pathological oral glucose tolerance test results (14.6% vs. 29.2%; 95% CI 8.9 to 23.0% vs. 20.8 to 39.4%; p-value 0.016) suggesting that the intervention improved gestational glucose tolerance. Mother's GWG, newborn anthropometry or infant weight gain did not differ significantly between the groups.

Conclusion: Since the intervention reduced the prevalence of gestational diabetes mellitus, it may have the potential to diminish the obesity risk in offspring. However, the results obtained in previous studies suggest that the possible effect on the offspring's weight gain is expected to be seen later in childhood.

Trial registration: Clinical Trials gov NCT00970710

Keywords: Childhood obesity, Gestational diabetes mellitus, Diet, Physical activity, Intervention, Prevention

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Background

The increase in obesity prevalence during past decades and the knowledge that obesity is difficult to reverse even in childhood has led to conclusion that the prevention of obesity is the most effective way to combat this major health problem [1]. Obesity tends to originate in early life: nearly 18% of 2-year-old Finnish children are overweight or obese and, according to recently reported prevalence data, nearly 19% of 12–24 month old children in the USA are obese [2,3]. The majority of obese pre-schoolers become obese schoolchildren and adults, which leads to an increased risk of cardiovascular diseases in adulthood [4,5].

Preventive efforts should start in early life. The prevention of obesity and its adverse health, social and economic consequences are a major public health priority. Primary health care is the most appropriate quarter to carry out the preventive intervention. Pragmatic trials are needed to find an effective preventive program that is applicable in existing health care settings [6].

Causes of obesity in pre-schoolers are multifactorial. Prevention programs should target known predisposing factors and behaviours. Known modifiable risk factors in early life are mother's obesity as well as excessive weight gain, impaired glucose tolerance and smoking during pregnancy [7-12]. Also, the type of infant feeding, sleep duration and rapid weight gain during the first year of life are known risk factors for childhood obesity [13-19]. High birth weight and ponderal index (weight in kilograms cubed, kg/m^3) have been shown to have some effect on subsequent obesity risk, but evidence is weak [20,21]. Mother´s gestational diabetes (GDM) appears to increase the risk of obesity in offspring, even if the birth weight is normal [20,22].

Early life is also considered a feasible period for the prevention of obesity because pregnant mothers and families with a preschool age child are often receptive to counselling on the health and well-being of their offspring. These families are easily reachable by primary health care. Furthermore, the offspring adopt dietary preferences during early life even via flavour in amniotic fluid and breast milk [23,24]. Dietary and physical activity habits are adopted during preschool years [25,26]. To improve the cost-effectiveness of a program that is carried out in health care system, it should be targeting families at risk of having obese offspring. One such risk group is the offspring of mothers at risk of developing GDM [20,22]. Mothers who are overweight or obese, those who have had gestational diabetes or a macrosomic newborn in a previous pregnancy, or those with an immediate family history of diabetes are considered to be at risk of GDM. These mothers often have a genetic predisposition to obesity and type-2 diabetes, which they may pass on to their offspring.

Only a few obesity prevention programs targeting pregnancy or infancy have been reported, and they have mostly had short intervention and follow-up periods [27,28]. Some of those have shown a positive effect on children's weight development [27-31]. Diet and physical exercise counselling, which targeted at mothers during the infant's first year seemed to result in slower weight gain in the offspring by the age of 4 years in a controlled pilot study [29], while the same intervention during pregnancy did not significantly reduce the offspring's weight gain [32]. Gillman et al. showed that treating mild GDM had no effect on the offspring's weight status by the age of 4–5 years [33]. In the follow-up of the HAPO Study, glucose levels during pregnancy were not found to significantly correlate with offspring's weight gain until two years of age [34].

The evidence from the reported obesity prevention programs has shown that multifaceted intervention is more effective compared with targeting a single behaviour [35,36]. A recent meta-analysis of gestational interventions concluded that the evidence was low to very low for preventing gestational diabe-

tes, but dietary and lifestyle interventions in pregnancy can reduce maternal GWG and improve outcomes for both mother and baby [37].

In this article we report the first results of a multifaceted controlled lifestyle intervention trial aiming at the prevention of childhood obesity (The VACOPP Study) [38]. The study is implemented in maternity and child health care clinics in the city of Vaasa in Western Finland. The intervention starts during the first trimester of pregnancy and first targets pregnant mothers at maternity health care clinics and then families until the offspring's age of five years. In this paper we report the intermediate outcomes of the intervention given during pregnancy, such as the prevalence of GDM, mother's GWG, newborn weight and infant weight gain in the groups.

Methods

Design and participants

The study was a non-randomised controlled clinical trial. All eight municipal maternity and 14 child health care clinics in the city of Vaasa in Western Finland participated in the recruitment and intervention. The intervention group mothers were recruited among the GDM risk group who were pregnant in the years 2009–2010; their offspring comprise the intervention target children. The control group was recruited among GDM risk group mothers and their offspring born in the year 2008 retrospectively before the offspring had reached the age of one year.

The mothers who fulfilled the following criteria were considered being at the risk of GDM: body mass index (BMI) ≥25 kg/m^2, macrosomic newborn (weight ≥4500 g) or GDM in any previous pregnancy, an immediate family history of diabetes and/or age ≥40 years. This group of mothers was routinely offered an oral glucose tolerance test (OGTT) during pregnancy in 26–28 weeks in Finland by primary health care. The children of these mothers were the primary target of the intervention effect. The mothers who had multiple pregnancy, were unable to speak Finnish, had substance abuse or severe psychiatric illness were excluded from the study recruitment.

Public health nurses (PHN) recruited the intervention group in maternity health care clinics at the first personal contact in the 12th gestational week at the latest, and gave the written research information and consent form to the mothers. Intervention group mothers' offspring were born during 2009 or 2010. The control group was recruited among mothers who had gone through OGTT in mid-pregnancy because of having a risk of GDM according to the above mentioned criteria. The deliveries of the control mothers were during year 2008. The control group mothers were identified by maternity care laboratory register review. Research nurses contacted them by telephone in 2009 and asked permission to send the written research information and consent forms to them. All recruited mothers were offered an opportunity to ask questions concerning the trial by telephone or e-mail to either the research nurse or the researchers. Informed written consent was provided by all participant mothers prior to the baseline assessments. Ethical approval for the study was granted by the Ethics Committee of Vaasa Hospital District.

Our study was a pragmatic trial; therefore, priority was not given to power calculations. Power calculations based on mean BMI z-score in the control group would be only an estimate and thus inaccurate [39].

Intervention

The intervention during pregnancy consisted of two group counselling sessions: one during both the first and the second trimester of pregnancy. 1.5-hour sessions were given by a trained physiotherapist and a dietician employed in public health care. Counselling on diet especially emphasised the recommended use of fibre, energy content, quality of carbohydrates and fat in the diet [40]. During counselling sessions pregnant mothers received information on the suitable and suf-

ficient amount of exercise during pregnancy. They also participated in a brief session of muscle tone exercise that was suitable to repeat at home. Mothers were advised to exercise for at least 2.5 hours/week (to get out of breath -level) and perform muscle tone training twice a week [41]. Information about the effect of healthy diet, exercise and appropriate weight gain during pregnancy on the risk of having GDM, offspring perinatal problems and offspring obesity was given to the participant mothers. Written educational material on healthy diet and physical activity during pregnancy was delivered during the sessions. During the 13 routine visits at maternity health care clinics starting from 10th week of gestation, the PHNs briefly repeated the same counselling information that was provided during the group sessions. At the first visit to the mother and baby the PHN gave mother a written information leaflet where breastfeeding up to six months of age was recommended also for the appropriate weight gain of the infant. The intervention is described in more detail in the protocol article [38].

Outcome measures

The secondary outcomes of the VACOPP Study until the offspring's age of one year are determined in this report. The primary outcome will be BMI and proportion of overweight or obese children at the age of six years [38]. Maternal outcomes were self-reported duration of moderate intensity (out of breath -level) exercise during the second and the third trimesters of pregnancy, OGTT results at 26–28 gestational weeks, and GWG until 37 weeks of pregnancy. The GWG was assessed at 37 weeks of gestation to obtain the last weight in the maternity clinic as comprehensively as possible for all mothers, and also because of the fact that weight later in pregnancy may be strongly influenced by swelling. The OGTT was performed with a glucose load of 75 gram. The plasma glucose values were analysed from capillary plasma samples at Vaasa Central Hospital laboratory. The following OGTT cut-off levels were used for capillary plasma glucose: 0 h ≥ 5.3 or 1 h ≥ 11.0 or 2 h ≥ 9.6 mmol/l [42]. The OGTT was considered abnormal if one of those values exceeded the cut-off level. Neonatal outcomes were the proportion of non-complicated vaginal delivery, birth weight, newborn ponderal index and large- or small-for-gestational age status. Infant outcomes reported here are the duration of exclusive breastfeeding, differences in weight-for-length SDSs and changes in weight-for-length SDSs at 0, 4, 6 and 12 months of age. We also report the absolute BMI differences in the groups, and the proportions of overweight and obese infants (overweight reaching or exceeding +10% and obese reaching or exceeding + 20% curves for weight-for-length above the mean weight-for-height of healthy Finnish children) according to the new Finnish growth reference [43]. The educational level of parents is defined as follows: "low" corresponds to education up to vocational school; "medium" indicates a higher vocational diploma and "high" denotes a university graduation.

Data collection

Mothers' weight was measured to the nearest 0.1 kg with light clothing on a standard electronic scale by maternity health care clinic PHNs. Maternal BP (blood pressure) was measured by the same PHN using an automated BP monitor (Omron M6) under standard conditions with two repeated measurements. Mothers' weight gain, BP, mother's own estimate on her weekly moderate-intensity (out-of-breath level) physical exercise during pregnancy, and results of 2-hour 75 gram OGTT at 27–28 weeks of pregnancy were recorded in questionnaires. The questionnaires were partially completed by the PHN and partially by the mothers during the first, second and third trimester of pregnancy during the maternity health care appointments of the intervention group. The PHN measured and wrote down the intervention group physical and laboratory measures for

the questionnaires. Newborn anthropometry was measured at the hospital by a hospital nurse immediately after delivery and the study questionnaires were completed by the PHN during the first visit after delivery.

Control group's measures during pregnancy were completed on the questionnaires by the mothers themselves 1–12 months after the end of pregnancy during 2008. The control mothers transferred data concerning physical measures and OGTT results to study questionnaires from their maternity card, which was filled in by a PHN during their pregnancy. The researcher was able to check OGTT results from the laboratory register if necessary. Fathers' and grandparents' anthropometry, possible diabetes diagnosis and educational level were reported by the participating mother for both groups.

Child health care clinic PHNs measured the infants' weight and length at 4, 6 and 12 months routine visits. The infant's weight was measured to the nearest 0.01 kg without clothes on a standard electronic scale. Infants' lengths were measured in recumbent position to the nearest millimetre with a standard stadiometer. Both intervention and control group infant anthropometric measures were completed on the questionnaires by the PHN during the one year appointment at the child health care clinic. Long-term illnesses affecting growth (e.g. severe food allergies) and duration of exclusive breastfeeding (months) were recorded in this questionnaire as well.

Statistical methods

Characteristics of the study participants are described using means or frequencies and 95% confidence intervals (Tables 1-3). Corresponding 95% confidence intervals (CI) for continuous variables were calculated using formula mean ± (1.96 * standard error of the mean) and for categorical variables using the Wilson score method without continuity according to Newcombe [44]. Differences between groups were evaluated by using Student's t-test or Mann-Whitney U-test for normally or non-normally distributed continuous variables. Normality was evaluated with the Kolmogorov-Smirnov test. Categorical variables were tested using the chi-square test or Fisher's exact test.

The child's weight gain was analysed using weight and length converted to weight-for-length and their SDSs (z-scores) according to the recently updated Finnish growth reference [43]. To investigate the effect of the intervention on child's weight, the outcome variable was the child's weight-for-length z-score at 0, 4, 6 and 12 months of age. In order to take into account the within-child correlation between repeated measures, we used a multilevel mixed-effects linear regression models to analyse the association of the weight-for-length z-score over time by group (intervention/control). The model included a variable (group) to indicate the difference between groups at baseline and a variable (time) to indicate the changes of weight-for-length z-scores over time. The difference in the change in z-scores across the intervention between the two groups was tested using an interaction term between group and time, which can be viewed as the intervention effect. In addition, we added potential confounding variables to the model: mother's education, number of gravidity, smoking during pregnancy, pre-pregnancy BMI, gender of the child and target height. None of these variables were significant, thus the final model only includes the three factors mentioned above. The goodness-of-fit of the model was evaluated by normal probability and residual plots and also tested by the normality of the residuals (Kolmogorov-Smirnov test). All analyses were performed using STATA software (version 12.0 for Windows), StataCorp LP, Texas, USA.

Results

The study flow is described in Figure 1. We analysed baseline characteristics that might interfere with offspring's weight development and found no statistically significant differences between the groups (Table 1). 84/96

(87.5%) of the intervention group mothers participated in the first trimester counselling session held by a dietician and a physiotherapist, and 57/96 (59.4%) in the corresponding session during the second trimester. The participation rate with regard to the PHN counselling was close to 100% since the counselling was held in relation to routine visits to the maternity health care clinics.

No statistically significant differences were found in the weekly duration of pregnant mother's moderate intensity exercise during the second and the third trimester of pregnancy or in GWG until 37 gestational weeks (p-value 0.11) (Table 2). We also analysed the weight gain in groups in relation to pre-pregnancy BMI according to IOM: mothers keeping within the recommended total weight gain range, mothers below it and mothers exceeding the range [45]. The proportion of mothers exceeding the recommended range in the intervention group was 43.6% and in the control group 47.2%, but the difference was not statistically significant (p-value 0.83, data not shown). The differences in the proportions of mothers keeping or below the recommendations were also not significant between the groups. We further analysed the association of exceeding GWG recommendations and pathological OGTT result and did not find it to be statistically significant (p-value 0.097, data not shown).

The control group mothers had a significantly higher proportion of abnormal OGTT results compared with the intervention group (29.2% vs. 14.6%, p-value 0.016) (Table 2). The proportion of mothers having a non-complicated delivery was similar in the groups. There was also no difference in the newborn anthropometry (birth weight, ponderal index, large-for-gestational age status, or small-for-gestational age status). No significant differences were shown between the groups for the mothers' pregnancy BP level, the proportion of mothers gaining less weight than recommended, the duration of pregnancies or the small-for-age status of newborns . Also, there was no significant difference in the proportions of infants with slow weight gain (Table 3). We interpreted the above mentioned results as signs for safety of the intervention.

Duration of exclusive breastfeeding did not differ statistically significantly between the groups (p-value 0.52) (Table 2). In addition, no statistically significant differences were found in length-for-age SDS, weight-for-age SDS, or weight-for-length SDS at 0, 4, 6 and 12 months of age between the groups (all data not shown). Proportions (expressed as percentage value deviation from the mean weight-for-length value according to Finnish definition of preschool-age overweight and obesity) of overweight (≥ + 10% weight-for-length) or obese (≥ + 20% weight-for-length) infants at ages 4, 6 and 12 months were not significantly different in the groups, although a slight tendency towards the control group having a higher proportion of overweight or obese infants was seen (Table 3) [43]. There were no differences in weight gain velocity assessed as change in weight-for-length ≥ 0.67 SDS or ≤ -0.67 SDS between the groups. Because of the lack of Finnish age- and gender-adjusted BMI reference for children under 2 years of age, we could not analyse BMI SDS. Absolute BMI was similar in the groups at the ages of 0, 4, 6 and 12 months (Table 3). Mixed effect linear regression models included group and age of the child and interactions between group and age of the child. Adding gender and the target height of the child, mother's pre-pregnancy BMI, smoking during pregnancy, number of gravidities and mother's education level to the models did not induce significant differences to the results, and they were not included in the reported results. According to a mixed effect linear regression model, the z-score slopes did not differ significantly between the intervention and control groups (p-value 0.71) (Table 4).

Discussion

The study results reported here suggest that the intervention in this trial may have the potential to improve glucose tolerance in pregnant mothers. A lower gestational glucose level can have a positive long-term effect in diminishing the offspring's risk of obesity and type-2 diabetes according to previous studies [10, 11, 20]. The intervention did not have a significant effect on mother's weight gain during pregnancy, although a slight tendency towards lower weight gain was seen among the intervention group mothers. No significant differences were found in the proportions of non-complicated delivery, the offspring's birth weight or ponderal index. Also, the duration of exclusive breastfeeding was similar in both groups. Offspring growth during the first year was not statistically significantly different between the groups, but a slight tendency towards the control group having a higher proportion of overweight or obese offspring during the first year was seen.

There is evidence of a favourable effect of lifestyle counselling during pregnancy on mother's diet, glucose tolerance and foetal growth. Luoto et al. showed that counselling on dietary and physical activity during pregnancy was effective in lowering the proportion of large-for-age newborns and the incidence of GDM in mothers who were adherent to the intervention aims [46]. They also showed that gestational intervention had a beneficial effect on several dietary aims, but only a non-significant effect on the increase in physical activity [46]. Barakat et al. recently found a reduction in the incidence of GDM in their physical activity intervention study during pregnancy [47]. We measured the mother's physical activity by self-reports, and no significant differences between the groups were found. The control group's physical activity was asked and recorded 1–12 months after the pregnancy; therefore, a recall bias cannot be excluded. Self-reports are also only rough estimates of the time spent physically active.

The lower proportion of pathological OGTT results at 26–28 gestational weeks in the intervention group could result from dietary changes. Since our main and secondary outcomes are the offspring's measures, we did not gather any dietary records during pregnancy, but only started to gather these during toddler years. An increase in fibre-rich food intake, which was one of the aims of the counselling, has the potential to improve glucose tolerance. Differences in energy consumptions between the groups seems more unlikely since there were only suggestive differences between weight gain during pregnancy and no significant differences in self-reported moderate intensity physical activity. The first group intervention was given at 20 gestational weeks' at the latest and PHNs gave intensive counselling at routine visits to maternity clinics beginning from 10 to 12 gestational weeks, making it possible that the intervention may have had a positive effect on OGTT results. The mothers were told that their lifestyle during pregnancy may have significant effects on the outcomes of the pregnancy and on their newborn, and also on the offspring's weight development. We believe that this knowledge may have motivated the intervention mothers to make healthy dietary changes during pregnancy.

The mothers who have abnormal OGTT results suggesting GDM and thereafter also abnormal plasma glucose values in own follow-up are referred to central hospital for further evaluation and treatment. All mothers having GDM are given dietary advice contributing to better glucose balance and a glucose meter to follow up glucose values at home. Insulin treatment is started if the target glucose balance is not achieved by these means. The effective treatment of GDM may have had an impact on the outcomes we measured: GWG, type of delivery and newborn weight. This could at least in part explain why there were no significant differences in these measures despite the higher prevalence of GDM among the control group mothers. However,

the higher prevalence of GDM in the control group could also be a biased result from the insufficient power of the sample, type 1 error or a chance.

The offspring's weight-for-length was analysed and adjusted with recently updated Finnish growth reference to get the SDS [43]. Weight gain velocity was analysed by assessing the proportions of infants whose change in weight-for-length was at least 0.67 SDS during their first 12 months. A weight-for-age difference of >0.67 SD has been defined as a clinically relevant rapid weight gain in infancy associated with risk of obesity later in childhood [15]. Weight gain during infancy was analysed with mixed effect models allowing for a difference between groups at baseline, changes over time and intervention effects. No significant differences between the intervention and control group offspring's weight gain during the first year were found. The intervention did not result in a longer duration of exclusive breastfeeding, which may result from the very light intervention in this issue. Improvements in foetal conditions such as mothers' lower glucose level during pregnancy have been shown to have no positive effect on the offspring's weight gain until the toddler years [10, 11, 20]. These above mentioned facts could explain why no differences in infant weight gains were seen despite the differences in mothers' glucose tolerance in mid-pregnancy.

The total drop-out rate among the intervention group during pregnancy was 22% (Figure 1). The most common reasons for dropping-out were an early miscarriage or the mother finding the study intervention too taxing. The miscarriages occurred during the first trimester of the pregnancies (except for one that was registered in the 20th gestational week), excluding the effect of the intervention on miscarriage rate. High drop-out rate is usual in lifestyle interventions; in that regard the drop-out rate in our study during pregnancy is moderate. It is possible that the mothers who were most motivated to make lifestyle changes and in the lowest risk for GDM were the ones who continued the intervention. This could have had an impact on GDM prevalence results in the groups.

The study groups were comparable at baseline as characteristics possibly interfering in the offspring's risk of obesity showed no statistically significant differences between the groups. However, we were not able to get reliable data on possible previous GDM that the mothers may have had. We targeted a group of mothers at risk of developing GDM, thus making the possibility of the intervention effect higher. The intervention was started during foetal and infant life, which are the periods known to be risk periods for the future development of obesity.

Our study has several limitations. It is not randomised and the control group was up to one year retrospective concerning outcomes in pregnancy, which could induce some bias to the results. The public health physiotherapist, dietician and maternity clinic PHNs only cared for the intervention group mothers, and the control group mothers' and infants' data was gathered when the control offspring was one year of age, that is one year before intervention was started, removing a possible Hawthorn effect on the control group.

The participation rate to group counselling sessions during pregnancy was good, although it was lower in the second session. Some of the public health nurses particularly felt that the recruiting of the intervention group and the paperwork of the study was burdensome, mostly because of their busy timetable. This may have reduced the success of recruiting in some maternity clinics. The motivation of the PHNs to perform intensive counselling may have varied, making the intervention uneven. However, this is common in real life implementations and the results are in this respect equivalent to these settings. Implementation in real-life practice has good potential to be a sustainable part of communal health care if proved to be effective and also the costs for society are moder-

ate. The maternity and child health care clinics have a good opportunity to reach the risk population for childhood obesity during a life period when the families are motivated to make changes in behaviour in order to promote their offspring's health.

Conclusions

Obesity with its great health and economic burden challenges society to initiate preventive actions. The most natural setting in primary health care for preventive interventions is maternity and child health care clinics, as this reaches the beginning of next generation. To find effective prevention programmes pragmatic trials in real-life setting are needed. Our study appeared to improve glucose tolerance during pregnancy, suggesting its potential to have a positive effect on offspring weight gain. We failed to find any effect on newborn birth weight or infant weight gain, but previous studies have shown that an adverse effect of gestational diabetes on the offspring's weight gain tends to develop only later in childhood. Several on-going early life intervention studies to prevent childhood obesity will provide more evidence on programmes worth for implementing in practice, including our intervention and follow-up continuing in child health care centres during preschool years.

List of abbreviations

GWG, gestational weight gain; SDS, standard deviation score; GDM, gestational diabetes mellitus; BMI, body mass index; OGTT, oral glucose tolerance test; PHN, public health nurse; BP, blood pressure; CI, confidence interval

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

TM and PK contributed to conception and design of the study. TM coded the data. TM, RL and PK participated in drafting and revising the manuscript. JR and TM performed the statistical analysis. AS produced weight-for-length statistics and participated to the interpretation of these results. All authors had full access to all of the data (including statistical reports and tables) in the study and can take responsibility for the integrity of the data and the accuracy of the data analysis. All authors read and approved the final version of the manuscript.

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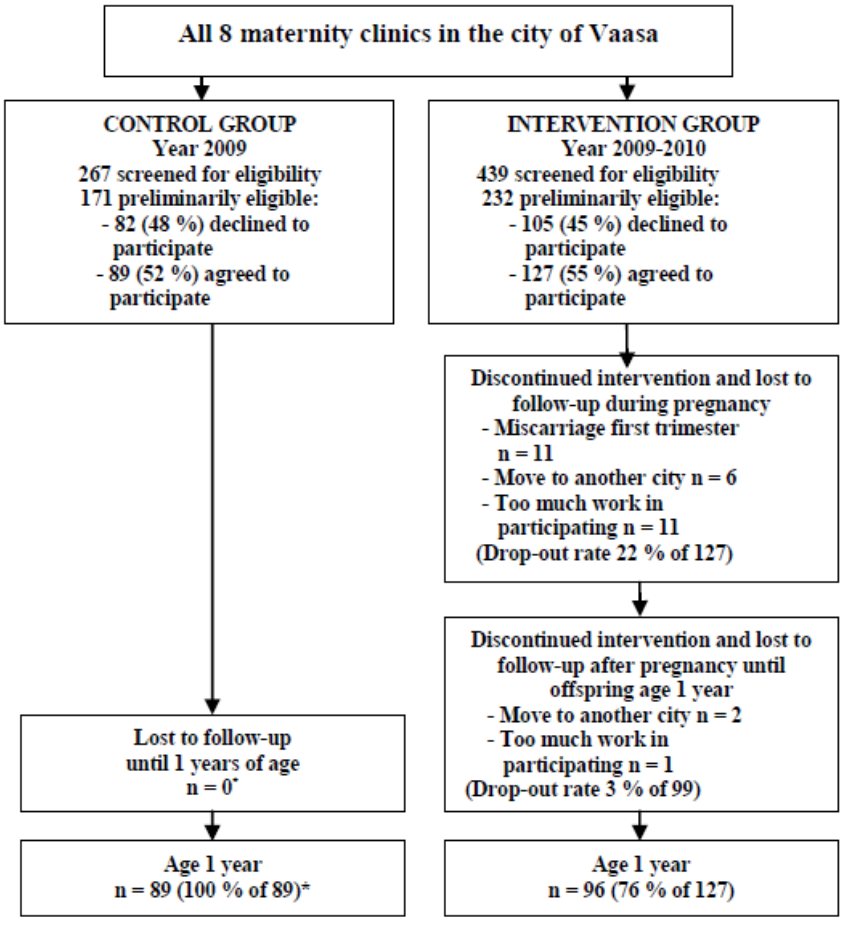
Figure 1. Flow chart of the study.



* Because of one year retrospective recruitment

Table 1. Baseline characteristics of the trial groups (mean or frequency and 95% CI).

	Intervention	Control	p-value	Missing (n in groups)
N	96	89		
Age of mother before pregnancy (years)	30.9 (29.7 to 32.0)	30.1 (29.0 to 31.2)	0.37 [a]	-
Mother's education			0.82 [c]	-
Low	32.3% (23.8% to 42.2%)	28.1% (19.8% to 38.2%)		
Medium	43.8% (34.3% to 53.8%)	46.1% (36.1% to 56.4%)		
High	24.0% (16.6% to 33.4%)	25.8% (17.8% to 35.8%)		
Father's education			0.27 [c]	1, 4
Low	34.7% (25.9% to 44.7%)	35.3% (26.0% to 45.9%)		
Medium	36.8% (27.8% to 46.8%)	45.9% (35.7% to 56.4%)		
High	28.4% (20.3% to 38.2%)	18.8% (11.9% to 28.4%)		
Mother's pre-pregnancy BMI (kg/m^2)	27.5 (26.6 to 28.5)	26.6 (25.7 to 27.4)	0.15 [a]	-
Proportion of obese mothers (BMI ≥ 30 kg/m^2)	26.0% (18.3% to 35.6%)	19.1% (12.3% to 28.5%)	0.26 [c]	-
Father's BMI (kg/m^2)	27.3 (26.5 to 28.1)	27.1 (26.2 to 28.0)	0.86 [b]	2, 6
Proportion of obese fathers (BMI ≥ 30 kg/m^2)	20.2% (13.3% to 29.4%)	16.9% (10.3% to 26.4%)	0.57 [c]	2, 6
Mother, Type 2 Diabetes	0.0% (0.0% to 3.9%)	1.1% (0.2% to 6.1%)	0.48 [d]	1, 0
Father, Type 2 Diabetes	1.1% (0.2% to 5.8%)	1.1% (0.2% to 6.2%)	1.00 [d]	2, 2
Proportion of obese grandparent (BMI ≥ 30 kg/m^2)	56.8% (46.4% to 66.7%)	63.1% (52.4% to 72.6%)	0.40 [c]	8, 5
Proportion of a grandparent having type 2 Diabetes	39.1% (29.8 % to 49.3%)	43.2% (33.0% to 54.1%)	0.59 [c]	4, 8
Parity			0.24 [c]	-
Primiparous	57.3% (47.3% to 66.7%)	43.8% (35.0% to 55.3%)		
Second pregnancy	26.0% (18.3% to 35.6%)	32.6% (23.7% to 42.9%)		
At least third pregnancy	16.7% (10.5% to 25.4%)	23.6% (15.0% to 32.2%)		
History of newborn >4500g	2.1% (0.6% to 7.4%)	3.4% (1.2% to 9.4%)	0.60 [c]	1, 0
Mother smoking during pregnancy	5.2% (2.2% to 11.6%)	11.2% (6.2% to 19.5%)	0.13 [c]	-
Mother's physical activity (hours/week) during first trimester of pregnancy (before intervention)	4.5 (3.9 to 5.1)	4.7 (3.8 to 5.6)	0.41 [b]	2, 5

[a] Independent Samples T-test, [b] Mann-Whitney U-test, [c] Chi-Square Test, [d] Fisher's Exact Test
BMI = body mass index; CI, confidence interval

Table 2. Secondary maternal and neonatal outcomes in the trial groups (mean or frequency and 95% CI).

	Intervention	Control	p-value	Missing (n in groups)
N	96	89		
Maternal				
First trimester				
Systolic blood pressure (mmHg)	119.1 (116.9 to 121.2)	116.5 (114.3 to 118.7)	0.10 [a]	4, 5
Diastolic blood pressure (mmHg)	73.9 (72.4 to 75.4)	72.1 (70.0 to 74.1)	0.14 [a]	4, 5
Second trimester				
Systolic blood pressure (mmHg)	116.8 (114.7 to 119.0)	117.7 (115.4 to 119.9)	0.59 [a]	2, 6
Diastolic blood pressure (mmHg)	71.7 (70.1 to 73.3)	70.5 (68.5 to 72.5)	0.33 [a]	2, 6
Physical exercise (h/week)	4.2 (3.6 to 4.7)	4.5 (3.6 to 5.4)	0.62 [b]	2, 5
OGTT (Gestational weeks 26-28)				
Fasting-0 h (mmol/l)	4.8 (4.7 to 4.8)	4.9 (4.8 to 5.0)	0.12 [b]	-
1 h (mmol/l)	8.7 (8.4 to 9.0)	9.0 (8.7 to 9.4)	0.21 [a]	-
2 h (mmol/l)	6.8 (6.6 to 7.1)	6.9 (6.6 to 7.1)	0.77 [a]	-
Pathological OGTT result (cP-gluk) (0 h ≥ 5.3 or 1 h ≥ 11.0 or 2 h ≥ 9.6 mmol/l)	14.6 % (8.9% to 23.0%)	29.2 % (20.8% to 39.4%)	0.016[c]	
Third trimester				
Systolic blood pressure (mmHG)	122.4 (120.1 to 124.6)	122.5 (120.0 to 125.0)	0.79[b]	3, 4
Diastolic blood pressure (mmHG)	77.8 (76.1 to 79.5)	75.2 (73.2 to 77.3)	0.052[a]	3, 4
Physical exercise (h/week)	3.4 (3.0 to 3.8)	3.2 (2.5 to 3.9)	0.11[b]	4, 4
Gestational weight gain until 37 gw (kg)	11.4 (10.4 to 12.5)	12.7 (11.5 to 14.0)	0.11[a]	2, 0
Min – Max	-4.9 to 27.2	-1.0 to 34.7		
Neonatal				
Non-complicated vaginal delivery	77.1 % (67.7% to 84.4%)	75.3 % (65.4% to 83.1%)	0.77[c]	-
Gestational age at birth	39.8 (39.4 to 40.1)	39.4 (39.2 to 39.7)	0.084[b]	-
Sex of the newborn (boy)	51.0% (41.2% to 60.8%)	50.6 % (40.4% to 60.7%)	0.95[c]	-
Birthweight (grams)	3509 (3404 to 3615)	3507 (3417 to 3596)	0.97[a]	-
Ponderal index (weight, kg/length, m^3)	27.4 (26.9 to 27.9)	27.5 (27.0 to 27.9)	0.89[a]	-
Large for gestational age	7.3 % (3.6% to 14.3%)	5.6 % (2.4% to 12.5%)	0.64[c]	-
Small for gestational age	13.5 % (8.1% to 21.8%)	6.7 % (3.1% to 13.9%)	0.13[c]	-
Exclusive breastfeeding (months)	3.0 (2.5 to 3.4)	2.8 (2.3 to 3.2)	0.52[b]	8, 0

[a]Independent Samples T-test, [b]Mann-Whitney U-test, [c]Chi-Square Test, [d]Fisher's Exact Test; OGTT, oral glucose tolerance test (75 g glucose load, 2-hour); cP-gluk, capillary plasma glucose; CI, confidence interval

Table 3. Anthropometric data in study groups during first year (mean ± sd or frequency and %).

	Intervention	Control	p-value	Missing (n/group)
N	96	89		
Weight-for-length SDS				
0 months	-0.08 ± 0.96	-0.07 ± 0.93	0.94[a]	
4 months	0.05 ± 0.99	0.17 ± 1.10	0.46[a]	
6 months	0.13 ± 1.02	0.20 ± 1.18	0.65[a]	
12 months	0.09 ± 1.06	0.06 ± 1.11	0.85[a]	3, 0
Change in weight-for-length SDS				
0 to 4 months	0.13 ± 1.17	0.24 ± 1.28	0.56[b]	
0 to 6 months	0.21 ± 1.14	0.27 ± 1.38	0.74[b]	
0 to 12 months	0.16 ± 1.20	0.14 ± 1.39	0.89[b]	3, 0
4 to 12 months	0.05 ± 0.90	-0.10 ± 0.74	0.21[b]	3, 0
6 to 12 months	-0.02 ± 0.74	-0.14 ± 0.66	0.28[b]	3, 0
Change in weight-for-length SDS ≥ 0.67				
0 to 4 months	32 (33.3 %)	31 (34.8 %)	0.83[c]	
0 to 6 months	33 (34.4 %)	36 (40.4 %)	0.39[c]	
0 to 12 months	32 (34.4 %)	31 (34.8 %)	0.95[c]	3, 0
4 to 12 months	20 (21.5 %)	13 (14.6 %)	0.23[c]	3, 0
6 to 12 months	13 (14.0 %)	11 (12.4 %)	0.75[c]	3, 0
Change in weight-for-length SDS ≤ - 0.67				
0 to 4 months	25 (26.0 %)	22 (24.7 %)	0.84[c]	
0 to 6 months	21 (21.9 %)	23 (25.8 %)	0.53[c]	
0 to 12 months	23 (24.7 %)	23 (25.8 %)	0.86[c]	3, 0
4 to 12 months	23 (24.7 %)	17 (19.1 %)	0.36[c]	3, 0
6 to 12 months	21 (22.6 %)	16 (18.0 %)	0.44[c]	3, 0
Weight-for-length ≥ +10% [e]				
0 months	9 (9.4 %)	10 (11.2 %)	0.68[c]	
4 months	15 (15.6 %)	18 (20.2 %)	0.41[c]	
6 months	15 (15.6 %)	22 (24.7 %)	0.12[c]	
12 months	16 (17.2 %)	18 (20.2 %)	0.60[c]	3, 0
Weight-for-length > +20% [f]				
0 months	1 (1.0 %)	1 (1.1 %)	1.00[d]	
4 months	0 (0.0 %)	4 (4.5 %)	0.052[d]	
6 months	4 (4.2 %)	5 (5.6 %)	0.74[d]	
12 months	3 (3.2 %)	1 (1.1 %)	0.62[d]	3, 0
Body mass index (kg/m2)				
0 months	13.8 ± 1.3	13.8 ± 1.1	0.93[a]	
4 months	17.0 ± 1.4	17.2 ± 1.6	0.32[a]	
6 months	17.4 ± 1.5	17.6 ± 1.7	0.58[a]	
12 months	17.2 ± 1.4	17.2 ± 1.6	0.89[a]	3, 0

[a]Independent Samples T-test , [b]Linear regression analysis, unadjusted, [c]Chi-Square Test, [d]Fisher's Exact Test
[e]assessed as overweight, [f]assessed as obese; SDS, standard deviation score

Table 4. Estimates and 95% confidence intervals for weight-for-length SDS from multilevel mixed-effects linear regression model.

Weight-for-length SDS from 0 to 12 months of age	**Coefficient**	**95% CI**	**p-value**
Group (intervention/control)	-0.71	-0.31 to 0.16	0.56
Age in months	-0.06	0.02 to 0.01	0.002
Age in months ^{2}	-0.004	-0.007 to -0.002	0.002
Group * Age	-0.006	-0.023 to 0.034	0.71

SDS, standard deviation score