Heli-Minttu Hyppänen

Early-life overweight and obesity in the FinnBrain Birth Cohort Study and Finland in 1- and 2-year-olds

M.D. Thesis

Spring 2020

Heli-Minttu Hyppänen

Early-life overweight and obesity in the FinnBrain Birth Cohort Study and Finland in 1- and 2-year-olds

Department of clinical medicine

Spring 2020

Supervisors: Minna Lukkarinen and Jetro Tuulari

TURUN YLIOPISTO

Lääketieteellinen tiedekunta

HYPPÄNEN, HELI-MINTTU: Varhaislapsuuden ylipaino ja lihavuus FinnBrain-syntymäkohortissa ja Suomessa 1- ja 2-vuotiailla.

Syventävien opintojen kirjallinen työ, 29 s.

Lastentautioppi

Helmikuu 2020

Lasten ylipaino ja lihavuus yleistyvät nopeasti, ja maailman terveysjärjestö (WHO) onkin listannut ne yhdeksi merkittävimmistä maailmanlaajuisista terveysriskeistä. Lapsuusiän lihavuudella on taipumus jatkua myös aikuisikään, ja lihavuus lisää riskiä sairastua moniin liitännäissairauksiin. Vaikka lapsuusajan ylipainoon tulisi puuttua mahdollisimman varhain, varhaislapsuuden ylipainoa ja lihavuutta on tutkittu hyvin vähän. Tästä tutkimuksesta saadaan uutta tietoa 1-vuotiaiden suomalaislasten ylipainon ja lihavuuden yleisyydestä, sekä lisätietoa 2-vuotiaiden suomalaislasten ylipainosta ja lihavuudesta. Tulokset saatiin vertailemalla FinnBrain syntymäkohorttia Suomen kansallisiin rekisteritietoihin.

FinnBrain-syntymäkohorttitutkimus on laaja monitieteellinen seurantatutkimus, jossa tutkitaan perimän ja ympäristön vaikutuksia lapsen kehitykseen ja terveyteen. Tutkimukseen rekrytoitiin 3808 odottavaa äitiä vuosina 2011–2015 Varsinais-Suomen ja Ahvenanmaan alueelta. Heitä ja heidän lapsiaan on seurattu kyselykaavakkeilla raskauden aikana, lapsen syntymähetkellä sekä lapsen ollessa 6 kuukautinen, 1-vuotias ja 2-vuotias. Tässä tutkimuksessa tutkittiin ylipainon ja lihavuuden yleisyyttä 1- ja 2-vuotiailla tytöillä ja pojilla. Mittatiedot olivat saatavilla 1586 1-vuotiaasta ja 1245 2-vuotiaasta lapsesta.

Molemmissa ikäryhmissä pojilla esiintyi merkittävästi enemmän ylipainoa ja lihavuutta kuin tytöillä. 17.7 % pojista ja 14.0 % tytöistä (yhteensä 16 %) oli ylipainoisia tai lihavia 1-vuotiaana. 2-vuotiaana 29.3 % pojista ja 16.1 % tytöistä (yhteensä 23.1 %) oli ylipainoisia tai lihavia. Tulokset olivat yhteneväisiä Terveyden ja hyvinvoinnin laitoksen koko Suomen sekä Varsinais-Suomen tilastotietojen kanssa.

Tässä tutkimuksessa saatua uutta tietoa varhaislapsuuden ylipainosta ja lihavuudesta voidaan käyttää tulevaisuudessa tutkimuksissa, joissa selvitetään varhaislapsuuden ylipainon ja lihavuuden syitä ja seurauksia, sekä suunnitellaan keinoja ehkäistä maailmanlaajuisesti lisääntyvää lapsuusajan ylipainoa ja lihavuutta.

Avainsanat: varhaislapsuus, ylipaino, lihavuus

UNIVERSITY OF TURKU

Faculty of Medicine

HYPPÄNEN, HELI-MINTTU: Early-life overweight and obesity in the FinnBrain Birth Cohort Study and Finland in 1- and 2-year-olds.

M.D. Thesis, 29 pp.

Paediatrics

February 2020

Childhood overweight and obesity are increasing rapidly, and World Health Organization has listed it as one of the major global health risks. Childhood overweight tends to persist into adulthood, and it increases the risk for later comorbidities. Although childhood overweight should be intervened as early as possible, there is still very little research about early childhood overweight. This study provided new information on the prevalence of overweight and obesity in 1-year-old Finnish children, and more information of overweight and obesity in 2-year-old Finnish children, by comparing FinnBrain Birth Cohort to Finnish national registries.

FinnBrain Birth Cohort Study is a prospective population-based study investigating the effects of genetic and environmental factors on children's health outcomes. 3808 pregnant mothers were recruited between 2011 and 2015 in Southwest Finland. The mothers and their children were followed up with questionnaires during gestation, at childbirth, and when the child reached the ages of 6 months, 1 year and 2 years. The prevalences of overweight and obesity in 1- and 2-year-old girls and boys were investigated in this study. Measurement data was available from 1586 1-year-old children and 1245 2-year-old children.

It was found out that boys were more overweight and obese compared to girls in both age groups. At child age of 1 year, 17.7 % of boys and 14.0 % of girls (16 % in total) were overweight or obese, and at 2 years 29.3 % of boys and 16.1 % of girls (23.1 % in total) were overweight or obese. The results were in line with Finnish national health statistics.

The information this study provided on early childhood overweight can be used in future research of underlying factors and future health outcomes of childhood overweight. Furthermore, this study can also be utilised for developing interventions to prevent the globally increasing health problem of childhood overweight.

Key words: Early childhood, overweight, obesity

Table of contents

1 Introduction

1.1 Definition of overweight and obesity

Overweight and obesity are defined as abnormally increased amount of body adiposity (Koponen et al. 2018, WHO 2018b). Being easy to assess, body mass index (BMI; kg/m^2) is used to define overweight and obesity, and it is the most commonly used measure of weight status. It is calculated by dividing body mass (kg) by the square of the person's height (m) (BMI=mass(kg)/height(m)^2). Although BMI correlates with high body fat percentage, it does not measure directly the amount of body adiposity (Romero-Corral et al. 2008). As BMI is calculated with total body mass, it does not separate adipose tissue and lean mass, and therefore is not a precise meter of obesity and should be considered only as a directional indicator of body measures. For adults, overweight is defined as BMI $\geq$ 25 kg/m^2 and obesity as BMI $\geq$ 30 kg/m^2. (Koponen et al. 2018, WHO 2018b.) In addition, the severity of obesity can be expressed in three classes. Class I, moderate obesity (BMI=30.00-34.99), class II, severe obesity (BMI= 35.00-39.99) and class III, very severe obesity (BMI $\geq$40.00). (WHO 2000.)

For children, healthy BMI depends both on the age and the sex of the child. Body dimensions and speed of growth, and therefore healthy BMI range, are variable throughout childhood, hence a single BMI value cannot define weight status for children of different ages. (Cole et al. 2000, WHO 2000, Saari et al. 2011.) In BMI-for-age curves, overweight and obesity are defined by percentiles. For instance, if the BMI of a child sets above the percentile curve defined for obesity, the individual is categorized as obese. There are two commonly used ways to define weight status of a child by using BMI; comparing individual BMI values between children of same age and sex (1) or linking the age- and sex-specific BMI percentile curves to widely used adult BMI cut-off points (2).

1. Standard deviation score (SDS) is used to compare individual BMI values between children of same age and sex. SDS represents how many standard deviation units the value in question is above or below the mean value of the reference population. SDS is a mathematically calculated value equivalent to percentiles. (Krebs et al. 2007, Vuorela 2011.) For instance, in a normally distributed population, SDS +1 represents the 84.13th percentile, and SDS +2 the 97.72nd percentile of the population. In other words, SDS is a simpler way to express percentiles. Whereupon an average sized individual is on BMI-SDS 0, heavier is above, and lighter below BMI-SDS 0. By how many SDS the BMI of the individual differs from the mean value of the reference group (children of same age and sex), the individual can be grouped to the appropriate weight category. According to WHO reference, childhood overweight is defined as BMI-for-age greater than SDS+1, and obesity greater than SDS+2 from the reference mean, for children older than 5-years. For 5-year-old and younger children, WHO cut-off points are SDS+2 and SDS+3, respectively. (Cole and Lobstein 2012, WHO 2018a.)

2. International (IOTF; International Obesity Task Force) childhood BMI, also known as ISO-BMI, makes it easier to classify children to weight categories by the same criteria regardless of age. Otherwise, understanding the definitions of overweight and obesity is quite difficult, when the healthy BMI changes constantly throughout childhood. According to IOTF criteria, the cut-off points for obesity and overweight in BMI-for-age percentile curves are set to the percentiles which meet the adult BMI cut-off points for overweight and obesity at the age of 18. Therefore, when using international (IOTF) childhood BMI, or ISO-BMI, cut-off points are the same regardless of the age, ≥25 kg/m^2 for overweight and ≥30 kg/m^2 for obesity, just as in adult BMI. (Cole et al. 2000, Vuorela et al. 2009, Saari et al. 2011.)

Using IOTF criteria, the classification does not change suddenly at a specific age, or when a child grows up to be adult. According to WHO criteria, a child who is normal weight at the age of 4 years 11 months (for example SDS+1.5) can be overweight at the age of 5 years 1 month, without gaining any weight. And an 18-year old “child” can be obese, whereas 18-year old “adult” with the exact same BMI is just overweight.

However, since the cut-off points are defined by percentile curves of the reference population, the classifications are more useful in clinical decision making when using reference curves of a population with the same genetic and ethnic background. As populations differ from each other by genetic factors, such as changes in growth speed, so do the cut-off points for overweight and obesity. (Saari et al. 2011, Vuorela 2011.) International (IOTF) childhood BMI reference is based on the average of six international datasets (Hong Kong, Britain, the Netherlands, Singapore, USA and Brazil), and cut-off points for overweight and obesity are the 89.3rd and the 98.6th percentile for girls, and the 90.5th and the 98.9th percentile for boys, respectively (Cole and Lobstein 2012). They correspond respectively to ISO-BMI 25 kg/m^2 and 30 kg/m^2. On the contrary, in the Finnish population, reference curves differ slightly from the international reference. According to the new Finnish reference of growth curves, corresponding cut-off points in BMI-for-age curves for girls are the 87.8th percentile for ISO-BMI 25 kg/m^2 and the 98.2nd percentile for ISO-BMI 30 kg/m^2, and respectively for boys, the 78.2nd percentile and the 95.6th percentile (Saari et al. 2011), corresponding to approximately SDS+1.2 and SDS+2.1 for girls, SDS+0.8 and SDS+1.7 for boys, respectively.

BMI defines overweight and obesity based on body ratios, and it is used for children between 2-18 years of age. It is not suitable for younger children, because during the first two years of life, body dimensions changes constantly and rapidly. For children under 2 years of age, we use weight-for-length/height percentile curves as a growth reference. (Saari et al. 2011.) Weight-for-length/height percentage represents the percentual deviation in a child’s weight compared to median weight of children of the same height and sex, but not necessarily the same age. BMI-for-age and weight-for-length/height are not interchangeable; BMI-for-age catches changes in weight-height relation better than weight-for-length/height, therefore children are more likely categorized as overweight or at risk of overweight, when using BMI-for age. (Flegal et al. 2002.) Until quite recently, weight status of Finnish children was determined by weight-for-length/height percentage in all ages (Saari et al. 2011). Hence, weight-for-length/height cut-off points still exist for children, separately for under 7-year-old children and for 7 years or older. Although, this classification is now preferred to be used only up to the age of 2 years, from where BMI-based classification can be applied. In Finland, the cut-off points in weight-for-length/height for children up to 7 years, which we still use for children up to 2 years, are $\geq$ 10 % for overweight and >20 % for obesity. (Vuorela 2011, Obesity (Children): Current Care Guidelines 2013.)

New-born infants are categorized by their birth size (birth weight and/or length), either as SGA (small for gestational age), AGA (appropriate for gestational age), or LGA (large for gestational age). SGA is defined as SDS -2 from the gestational age- and sex-specific reference mean value, and LGA as SDS +2. (Sankilampi et al. 2013.)

1.2 Epidemiology of childhood overweight and obesity

1.2.1 Worldwide epidemiology

Overweight and obesity is a rapidly increasing global health problem not only among adults, but even more drastically among children. Between the years of 1980 and 2013 the prevalence of overweight and obesity rose by 27.5 % for adults, and by 47.1 % for children. By the year 2013, there were 2.1 billion overweight or obese people globally. (Ng et al. 2014.) World Health Organization has listed overweight and obesity as one of the major global health risks (WHO 2009). Childhood overweight and obesity prevention is one of the targets of WHO Sustainable Development Goals (WHO 2018a). The trend of increasing prevalence of obesity is seen all around the world (Figure 1).

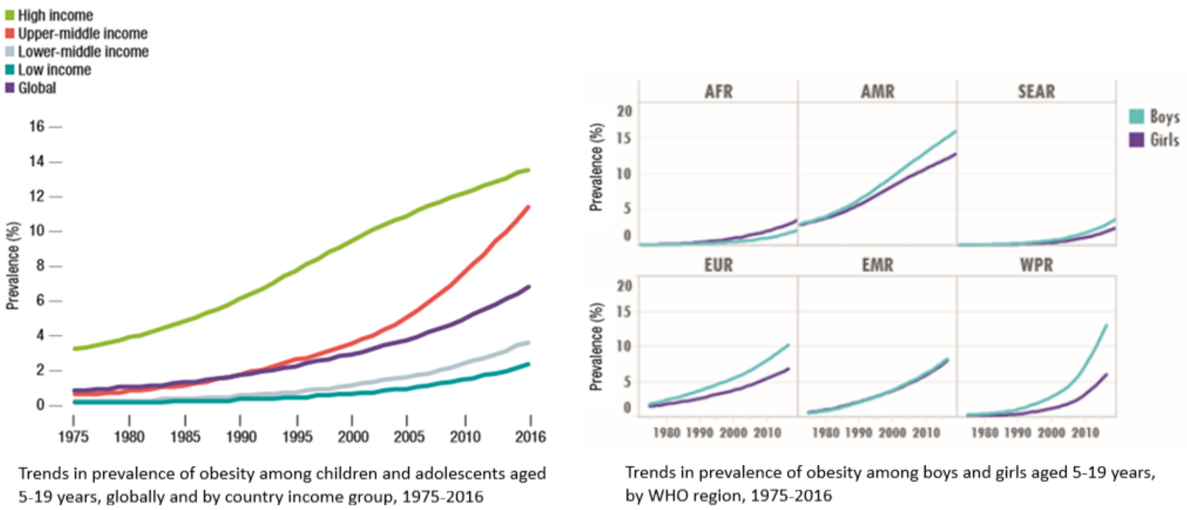

Figure 1: Trends in prevalence of obesity among children and adolescents. Modified from: (WHO 2018a). AFR: WHO African Region, AMR: WHO Region of the Americas, SEAR: WHO South-East Asia Region, EUR: WHO European Region, EMR: WHO Eastern Mediterranean Region, WPR: WHO Western Pacific Region

Even though most overweight adults were not overweight as children, childhood obesity has a tendency of persisting into adulthood (Singh et al. 2008, Juonala et al. 2011, Simmonds et al. 2016).

In 2016, there were almost 340 million overweight or obese children and adolescents aged 5-19 years globally, and in 2017, there is an estimate of 38,3 million overweight children under the age of 5 (UNICEF/WHO/World Bank Group 2018). Additionally, childhood obesity increases the risk for later comorbidities, such as type II diabetes mellitus, cardio-vascular diseases, orthopaedic problems, malignancies and psychological problems (Reilly and Kelly 2011, Butler et al. 2018, Lee and Yoon 2018, Weihrauch-Blüher and Wiegand 2018). Obesity and overweight in adolescence may increase the risk for later cardiovascular diseases even independently from weight status later in adulthood (Must and Strauss 1999, Stettler et al. 2002). Although, later studies present that non-obese adults who were overweight or obese as children have no greater risks compared to those who have been normal weight throughout their whole life (Juonala et al. 2011). Regardless, preventing childhood overweight and obesity as early in life as possible should be a priority, as some risk factors could still be modified in early life (Butler et al. 2018). And as mentioned earlier, high BMI easily persists into adulthood, and the persistence increases with age (Singh et al. 2008).

1.2.2 Epidemiology in Finland

The global trend of increasing childhood overweight is expectedly seen in the Finnish population as well. Between the years 1974 and 1995, defined by IOTF criteria, the prevalence of overweight and obesity combined rose significantly in 12-year-old Finnish children, from 13.4 % to 24.8 % in boys, and from 13.8 % to 19.5 % in girls (Figure 2). Interestingly, the trend seems to be opposite in younger children, according to Vuorela et al. (2011). In 2-year-old Finnish children, the prevalence of overweight and obesity combined has decreased from 13.3 % to 6.3 % in boys, and from 17.7 % to 11.3 % in girls between 1974-2001 (Figure 2, Vuorela et al. 2011).

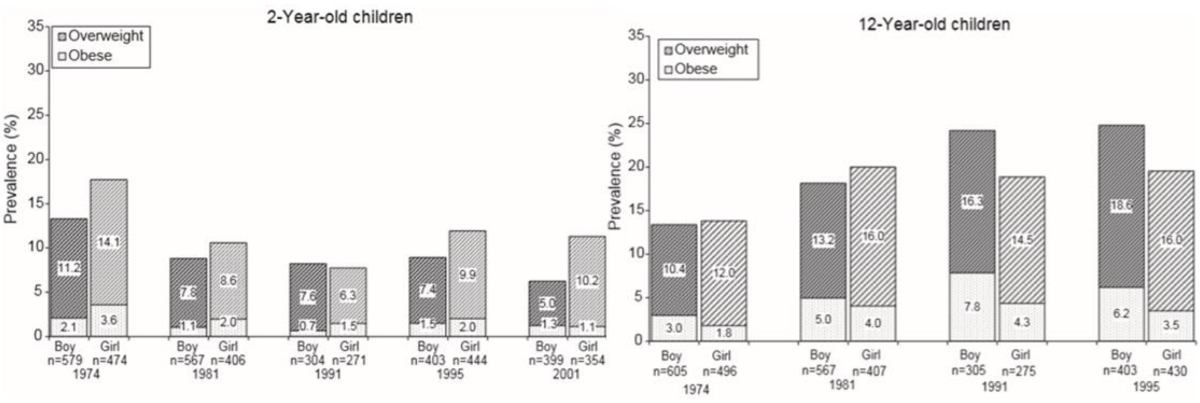

Figure 2: Change in prevalence of overweight and obesity in Finnish 2- and 12-year-old boys and girls by birth cohort. (Vuorela et al. 2011)

In 2018, 27 % of 2–16-year-old boys were overweight and 8 % were obese in Finland, and in girls of the same age group, 18 % were overweight and 4 % obese (Figure 3, Lundqvist et al. 2019).

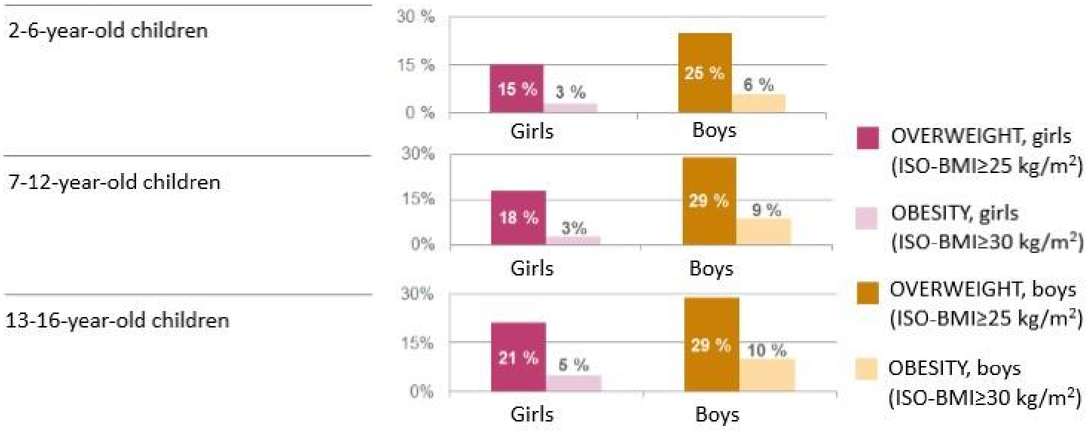

Figure 3; Prevalence of overweight and obesity in Finnish girls and boys by age categories in 2018. Modified from: Lundqvist et al. (2019). *Lasten ja nuorten ylipaino ja lihavuus 2018 - Tilastoraportti 9/2019.* THL. Retrieved from http://urn.fi/URN:NBN:fi-fe2019042413181 (Lundqvist et al. 2019)

There has been a limited amount of studies and data gathered about overweight and obesity in younger children. In a study that took place in 2007-2008 (LATE-study, published by National Institute for Health and Welfare), 6.4 % of study cohort of Finnish 1-year-old children were overweight or obese, defined by weight-for-length/height percentage (Figure 4, Mäki et al. 2010).

Weight-for-height/length (%)	6 months			1 year		
	Boys	Gils	Total	Boys	Gils	Total
Overweight 10-20%	13,5	13,8	13,6	8,2	0,9	4,6
Obesity >20%	1,8	2,8	2,3	1,8	1,8	1,8
N	111	109	220	110	109	219

Figure 4: Prevalence of overweight and obesity in Finnish ½- and 1-year-old children, defined by weight-for-height/length. Modified from: Mäki et al. (2010). *Child Health – Results of the LATE-study on growth, development, health, health behavior and growth environment.* Helsinki: National Institute for Health and Welfare (THL).

1.3 Risk factors for childhood overweight and obesity

Existing childhood obesity prediction models are still very limited. Therefore, tracking back to the very beginning of the problem is not an easy task, which again makes the problem of childhood overweight and obesity a complex target to intervene. (Ziauddeen et al. 2018.) Furthermore, there are very few guidelines for even determining obesity in infancy and early childhood (Butler et al. 2018). Additionally, there are numerous risk factors associated to childhood overweight (Lee and Yoon 2018).

1.3.1 Energy balance

Excess weight gaining is a consequence of an imbalance in energy intake and energy consumption (WHO 2000). In all its simplicity, when energy intake outweighs energy consumption, the excess energy accumulates to the body as adipose tissue. The intake of the energy, appetite, is controlled by the central nervous system. The complicated regulation mechanism consists of several brain systems working together: cognitive control, emotion and memory systems, homeostatic systems, reward network, and attention systems. (Farr et al. 2016.) When functioning optimally, the central nervous system receives signals from peripheral tissues and sends back regulatory signals to maintain stable body weight despite of significant changes in daily energy intake and consumption (Wynne et al. 2005). When there occurs an unfavourable genetic or environmental change, it can lead to dysfunction of the regulatory system and therefore excess energy intake and weight gaining (Wynne et al. 2005, Farr et al. 2016). For instance, if pleasure and reward signals overrule the inhibitory signals.

Dopaminergic and opioidergic systems are involved in reward and pleasure signalling in the brain, and alteration in them are associated with overeating (Karlsson et al. 2016, Tuulari et al. 2017). Contribution of opioidergic systems is present in both development and maintenance of obesity, as the μ-opioid receptor (MORs) system is strongly linked to pleasure response, but also to energy homeostasis. By activating MORs, μ-opioid receptor agonists increase pleasure responses and intake of food. Correspondingly, μ-opioid receptor antagonists decrease the pleasure responses and intake of food. On the other hand, eating food releases endogenous opioids in the brain even independently of subjective feeling of pleasure, suggesting that changes in energy homeostasis releases endogenous opioids regardless of pleasure. (Tuulari et al. 2017.)

Overeating causes this opioid release to happen repeatedly, which can lead to MOR downregulating, which in turn, in order to pursue the desired pleasure response, leads to overeating. Therefore, altered opioidergic system in the brain can maintain the cycle of overweight and overeating. (Karlsson et al. 2016, Tuulari et al. 2017.) In addition, weight loss can reverse this change in MOR system (Karlsson et al. 2016). Therefore, changes in the brain affect eating habits and appetite.

The neural and endocrine appetite regulating system that evolved in a drastically different environment in which food was a limited resource, hasn't adapted to the never-ending supply of energy-dense food and changed demands of physical activity. Therefore, it drives us easily towards a positive energy balance and weight gaining. (Wynne et al. 2005, Lenard and Berthoud 2008.) An apparent reason for increased overweight and obesity is changes in dietary habits and physical activity, so called obesogenic environment of modern times (Lee and Yoon 2018). For children, the base for these habits is built by their parents as they determine the dietary choices and eating times for their children (Mihrshahi and Baur 2018). In addition, some other factors that influence the risk of childhood overweight and obesity are psychological stress, sleep quality and duration as well as cultural environment (Lee and Yoon 2018). However, factors leading to developing overweight and obesity are fewer in very young children, when conscious decision-based lifestyles and habits are yet to develop, and habits have not yet been remarkably affected by cultural environment. Moreover, the consistency of diet is more converging amongst young children, and differences in diets increase with age.

In Finland, the parents of all children are provided with nutritional counselling for their children in a national program of regular, free-of-charge health-check-ups and counselling appointments in welfare clinics. The check-ups and counselling are very frequent, taking place at least 10 times during the first year of life. (Handbooks of the Ministry of Social Affairs and Health 2004.) Therefore, young children in Finland mainly follow the same national guidelines for nutrition, until they start to eat the same food, and at same times, with rest of the family, gradually starting from age of 1 year. (Handbooks of the Ministry of Social Affairs and Health 2004, THL 2019.) Close to 100 % of Finnish 1-year-old children's diet include potato, root vegetables, vegetables, fruit, grains and meat. As most common of the aforementioned, 99 % have potato and carrots, and/or berries and fruit included in their diet and, as least common but still vast majority, 93 % have vegetables included in their diet. (Mäki et al. 2010.)

Thereby, as consistency of diet follows the same guidelines, some other factors play a more essential role for Finnish children in the development of overweight and obesity during the first years of life compared to older children. Growing older, children's diets start to differ from each other. Only about half of 3–5-year old Finnish children include vegetables in their lunch or dinner, and about half snack between the meals (Mäki et al. 2010).

As overweight tends to persist from infancy to childhood and so on (Butler et al. 2018), the very earliest risk factors should be taken into focus. Early in life, there might be few critical periods considering the development of the weight management mechanisms that affect the weight status later in life. Studies suggest that rapid weight gain as early as the first months of one's life associates with childhood overweight. (Stettler et al. 2002.) Risk factors for developing overweight go back even further, beyond birth, to prenatal and preconception risk factors (Ziauddeen et al. 2018).

1.3.2 Prenatal factors

During sensitive periods of development in the beginning of one's life, their features are modified by certain programming to meet the requirements of the environment where the individual is most likely to live in. It is an important mechanism for plants and animals for adapting to the environment. (Bateson et al. 2004.) However, when the programming fails to match the environmental circumstances, it can lead to adverse health outcomes (Calkins and Devaskar 2011). At first, it was noticed that poor nutrition in early life increases the susceptibility to the effects of a distorted metabolic profile and heavy dietary habits, such as likelihood for ischaemic heart disease (Barker and Osmond 1986).

Beginning as Barker's hypothesis of early childhood nutrition affecting later health risks (Barker and Osmond 1986), the theory has since expanded to study widely perinatal factors that modify the phenotype of a child, thus affecting the susceptibility to later environmental influences (Eriksson 2016, Hoffman et al. 2017). The theory is known as Developmental Origins of Health and Disease (DOHaD-theory) and it explains how influences during sensitive windows of development alter the features of the developing individual (Eriksson 2016). For example, when a pregnant mother is suffering from undernutrition and the developing foetus does not receive an appropriate amount of glucose, the foetus adapts to harsh circumstances by increasing its insulin resistance, thereby reinsuring the brain gets enough glucose.

Hence, the developing child is programmed to survive in an environment where appropriate nutrition is hard to get. Consequently, if the child then lives in a modern obesogenic environment where it is easy to get excessive amounts of energy and sugars, chances of developing high blood sugar and type II diabetes increase. (Bateson et al. 2004.)

Additionally, developmental origins are associated to numerous other health outcomes beside ischaemic heart disease and diabetes mellitus mentioned above, such as later psychopathology (O´Donnell and Meaney 2017), cancer, hypertension, Alzheimer's disease, obesity, and so on (Calkins and Devaskar 2011). Birthweight is a commonly used indicator of foetal developmental processes (Risnes et al. 2011, O´Donnell and Meaney 2017), thus it is a predictor of risk for developing overweight as well (Ziauddeen et al. 2018). Not alone the birth size, but primarily being born small and gaining weight rapidly after birth as "catch-up growth", is strongly associated to childhood overweight and other adverse health outcomes (Stettler et al. 2002, Hoffman et al. 2017). Some of the most known factors affecting birthweight are maternal nutrition during pregnancy, maternal age and chronic diseases, gestational hypertension, diabetes and weight gain, socio-economic level, as well as cigarette, alcohol and drug consumption of the mother (de Bernabé et al. 2004). Contribution of psychological factors, however, still remain inconclusive. In several studies some sort of prenatal stress is associated to decreased birthweight (Graignic-Philippe et al. 2014, Lima et al. 2018). Furthermore, there are many potential mechanisms explaining DOHaD-theory of how the developmental environment programs later health risks; epigenetic mechanisms, altered HPA-axis, and metabolic adaptation for instance (Eriksson 2016, Hoffman et al. 2017).

1.4 Prevention of childhood overweight and obesity

Childhood overweight and obesity prevention should be focused widely to all the fields of risk factors; environment, diet, physical activity, psychological wellbeing, and at the earliest possible age (Lee and Yoon 2018, Mihrshahi and Baur 2018). Determining and identifying individuals at risk is crucial. Studies have shown the efficiency of targeted prevention and interventions compared to wide, population-based prevention (Butler et al. 2018).

Keeping in mind that most of the overweight or obese adults were not overweight or obese in childhood, and therefore could not have been individually targeted, population-based prevention shouldn´t be underrated either (Singh et al. 2008). Currently, we have knowledge of childhood risk factors leading to overweight and obesity, like environmental and behavioural factors (Lee and Yoon 2018, Weihrauch-Blüher and Wiegand 2018) but, what we distinctly need more information about, is early childhood and prenatal factors. Regardless, we are still lacking effective interventions, guidelines for determining and preventing early life obesity, and comprehensive and reliable childhood obesity prediction models (Butler et al. 2018, Weihrauch-Blüher and Wiegand 2018, Ziauddeen et al. 2018).

1.5 Aims

There is very little data and research on overweight and obesity in children under 2-years of age. It has been proposed that overweight should be prevented as early in age as possible, but to further assess this and early obesity risk factors normative assessment is warranted. The aims of this study are:

1. To provide new information of the prevalence of early-life overweight and obesity in 1-year-old Finnish children, and to compare the FinnBrain Birth cohort to another Finnish study cohort (LATE-study) in 1-year-old children's overweight and obesity frequencies (Mäki et al. 2010).
2. To find out whether the FinnBrain Birth Cohort (Karlsson et al. 2017) represents the Finnish population in prevalence of children´s overweight and obesity in the age group of 2-year-old children, by comparing the weight data of the children in the FinnBrain Birth Cohort Study to prevalence of overweight and obesity in other Finnish study cohorts (Vuorela et al. 2011) and Finnish national Health Statistics (Lundqvist et al. 2019, personal information from Lundqvist A. 2019).

1.6 Hypothesis

The FinnBrain Birth Cohort Study data represents the 1- and 2-year-old children´s overweight and obesity frequencies of the populations in Finland and in Southwestern Finland.

1.7 Implications

Having nationally representative weight data of young children will benefit future research by (hopefully) enabling the possible findings to be generalized nationally. This research is crucial for preventing childhood overweight and obesity, and managing the drastic concomitant health risks, as early as possible. Additionally, having data of early childhood overweight enables future research to study more precisely and draw conclusions from the associations between early weight development and future health outcomes, for example from the intriguing aspect of DOHaD-theory. On the basis of Barker and Osmond (1986) stating that early life undernutrition and underweight increase the risk for certain diseases and adverse health outcomes, having proper data of early childhood overweight enables future research to study whether early life overweight is a risk or protective factor considering later health.

2 Methods

2.1 Study design and subjects

Data from the FinnBrain Birth Cohort Study (Karlsson et al. 2017) was used to perform this study. It is a population-based pregnancy cohort, of which recruitment was carried out between December 2011 and April 2015 by nurses at gestational week (gwk) 12 at maternal welfare clinics in Southwest Finland. All over Finland these clinics offer free-of-charge pregnancy follow-up, ultrasound screenings and maternal- and child health counselling. The coverage of this service is close to 100 % of the Finnish population. Originally, out of 5790 newly pregnant mothers who were informed about FinnBrain study, N=3808 mothers (65.7 %) decided to participate. Total amount of recruited children was N=3837 at the time of birth. At 12 months N=1703 and at 24 months N=1454 Participants were followed up with questionnaires at gestational weeks 12, 24 and 34, at delivery and at 6, 12 and 24 months after birth. The FinnBrain Birth Cohort Study is planned to continue for decades with follow-up intervals of 12-36 months, the current measurements are ongoing.

The FinnBrain Birth Cohort Study data includes follow-up questionnaires, data from national registries and biological samples, brain imaging and neuropsychological testing (Karlsson et al. 2017). The data used in this study consists of weight and length measurements of the children at the time points of 0, 12 and 24 months from birth, along with some background factors, such as mother's age, pre-pregnancy BMI, maternal socio-economic status, long-term diagnoses, pregnancy duration and complications, and birth weight SDS. Time points for questionnaires during pregnancy were at gestational weeks 12, 24 and 34. Additionally, to compare the FinnBrain cohort to the Finnish population, data of children at same age points from Finnish national health statistics and other Finnish study populations is used (Mäki et al. 2010, Vuorela et al. 2011, Lundqvist et al. 2019, Personal information from Lundqvist A. 2019).

2.1.1 Inclusion and exclusion criteria

Children with available weight and length data at 12 and/or 24 months were included in this study. One child was excluded from both age groups due to extreme outlier values, presuming some disease or other medical condition interfering with growth of the child (Saari et al. 2011).

2.1.2 Sampling the data

Part of the execution of this thesis was inspecting and unifying the weight and length data of 1- and 2-year-old children from the FinnBrain Birth Cohort Study, as well as calculating weight-for-length/height percentages for 1-year-old children in the cohort. Each child's age, gender, weight and height were enrolled in an online counter (kasvuseula.fi), which calculates the weight-for-length/height percentage using the new Finnish growth reference (Saari et al. 2011).

2.2 Definitions

Main response variables of this study are weight-for-length/height percentage at the child age of 12 months and its cut-offs for overweight and obesity (≥10 % for overweight and ≥20 % for obesity) (Obesity (Children): Current Care Guidelines 2013) and BMI-SDS at the child age of 24 months and its cut-offs for overweight (ISO-BMI≥25kg/m^2) and obesity (ISO-BMI≥30kg/m^2) (SDS+1.2 and SDS+2.1 for girls, and SDS+0.8 and SDS+1.7 for boys, respectively), with regard to the new Finnish reference values (Saari et al. 2011).

2.3 Statistics

The statistical analyses were performed using IBM SPSS 26 (SPSS Inc., Chicago, Ill, USA). The population characteristics and subgroup comparisons were carried out using the Pearson chi-square test for dichotomous variables and the T-test or Mann-Whitney's u-test for continuous variables (Tables 1 and 2). The p-values <0.05 were considered statistically significant. Extremely outlying values were excluded due to suspected medical condition affecting child's growth.

2.4 Ethical issues

The FinnBrain Birth Cohort Study is performed in accordance with current legislation and ethical principles (e.g. Helsinki Declaration). The study was approved by the Ethics Committee of the Hospital District of Southwest Finland (ETMK: 57/180/2011). The parents have given their written informed consent on behalf of themselves and their child. The participation is voluntary, and the families receive no monetary compensation for their participation.

3 Results

3.1 Overweight and obesity in 1-year-old children

Questionnaire at 12 months was returned from 1703/3837 (44.4 %) children. Some questionnaires lacked the reply to questions of child's weight and/or height at 12 months. Weight data was available from 1602/3837 (41.8 %) children and height data from 1591/3837 (41.5 %) children. To be able to calculate weight-for-height percentage for defining overweight and obesity, only children with both weight and height data available were included in this study. Originally, height and weight data were available from 1583/3837 (41.3 %) children. Later, these measurements were gathered from three more children, resulting the total number of 1-year-old children with weight and height data available to be N=1586/3837 (41.3 %). However, one child was excluded from the analysis based on an extremely outlying value of weight. Weight of the excluded child was reportedly 17400g at the age of 1 year, next biggest value in the population being 14500g. One child being excluded, the total number of children included in this study at the age of 1 year was N=1585, n=840 (53 %) boys and n=745 (47 %) girls. (Table 1.)

At the age of 1 year, 253/1585 (16.0 %) children were overweight or obese (Table 1). Boys were significantly more overweight or obese (17.7 %) compared to girls (14.0 %) (p=0.04). In obesity alone, there was no significant difference between boys (2.0 %) and girls (3.2 %). (Table 1.) Prevalence of overweight and obesity in boys, girls and in total, are presented separately in figure 5. 15.7 % of boys were overweight and 2.0 % were obese. In girls, the corresponding percentages were 10.8 % and 3.2 %, respectively. (Figure 5.)

TABLE 1, Population characteristics, 1-year-old children

	Whole sample	Boys	Girls	P value*
	N=1585	n=840 (53.0)	n=745 (47.0)	
During gestation				
	n=1559	n=828	n=731	
Maternal pre-gestational BMI, (IQR)	23.45 (21.22;26.45)	23.38 (21.23;26.48)	23.53 (21.22;26.45)	0.752
Maternal overweight, pre-gestational BMI ≥25 kg/m^2 (%)	531 (34.1)	278 (33.6)	253 (34.6)	0.667
Maternal obesity, pre-gestational BMI ≥30 kg/m^2 (%)	179 (11.5)	92 (11.1)	87 (11.9)	0.625
Maternal smoking during gestation (%)	n=1584	n=839	n=754	0.752**
During the first trimester	105 (6.6)	51 (6.1)	54 (7.2)	0.274***
Throughout gestation	61(3.9)	35 (4.2)	26 (3.5)	
Older siblings (%)	678/1511 (44.9)	371/800 (46.4)	307/711 (43.2)	0.212
Maternal education (%)	n=1515	n=802	n=713	
Low, (up to 12 years)	470 (31.0)	256 (31.9)	214 (30.0)	0.423
Middle, (13-15 years)	447 (29.5)	231 (28.8)	216 (30.3)	0.525
High, (over 15 years)	598 (39.5)	315 (39.3)	283 (39.7)	0.869
Residential area (%)	n=1510	n=801	n=709	0.100
Urban	1068 (70.7)	552 (68.9)	516 (72.8)	
Rural	442 (29.3)	249 (31.1)	193 (27.2)	
At delivery				
	n=1585	n=840	n=745	
Duration of gestation, gwks (IQR)	40.0 (39.0;40.9)	39.86 (38.86;40.86)	40.14 (39.14;40.86)	0.085
	n=1563	n=829	n=734	
Age of the mother, years (SD)	30.83 (4.36)	30.94(4.34)	30.70(4.39)	0.285
Delivery method (%)	n=1561	n=828	n=733	0.645
Vaginal delivery	1302 (83.4)	694 (83.8)	608 (82.9)	
Caesarian section	259 (16.6)	134 (16.2)	125 (17.1)	
	n=1563	n=829	n=734	
Birth weight, kg (IQR)	3.54 (3.23;3.88)	3.59 (3.76;3.98)	3.48 (3.17;3.80)	<0.001
	n=1554	n=826	n=728	
Birth length, cm (IQR)	51.00 (49.00;52.00)	51.00 (50.00;53.00)	50.00 (49.00;51.00)	<0.001
Size for gestational age[#] (%)	n=1561	n=828	n=733	
SGA	49 (3.1)	30 (3.6)	19 (2.6)	0.244
AGA	1473 (94.4)	781 (94.3)	692 (94.4)	0.944
LGA	39 (2.5)	17 (2.1)	22 (3.0)	0.231
At 1 year				
Height, cm (SD)	75.9 (2.98)	76.80 (2.84)	74.96 (2.83)	<0.001
Weight, kg (SD)	9.90 (1.23)	10.26 (1.18)	9.51 (1.16)	<0.001
Weight-for-height-%, (IQR)	0.0 (-6.00-6.00)	0.00 (-5.00-7.00)	-1.00 (-7.00-5.00)	0.009
Overweight or obesity, WFH≥10% (%)	253/1585 (16.0)	149/840 (17.7)	104/745 (14.0)	0.040
Obesity, WFH >20% (%)	41/1585 (2.6)	17/840 (2.0)	24/745 (3.2)	0.123

AGA=appropriate for gestational age*; BMI*=body mass index*; gwks*=gestational weeks*; IQR*=interquartile range*; LGA*=large for gestational age*; SD*=standard deviation*; SGA*=small for gestational age*; WFH*=Weight-for-height.

Presented as numbers (percentages), means (standard deviations), or medians (interquartile ranges).

[#] Defined by standard deviation from the gestational age- and sex-specific reference mean value. SGA= SDS-2, LGA= SDS+2.
*The comparison between boys and girls
**groups compared: “no smoking” and “smoking at any point of gestation”
***groups compared: “smoking during the first trimester” and “smoking throughout gestation”

3.2 Overweight and obesity in 2-year-old children

Questionnaire at 24 months was returned from 1454/3837 (37.9 %) children. Some returned questionnaires lacked the information of weight and/or height at the age of 2 years. Weight data was available from 1266/3837 (33.0 %) children and height data from 1258/3837 (32.8 %) children. Both weight and height data were available from 1234/3837 (32.2 %) children at 24 months, and as in 1-year-olds, only children with both height and weight information available were included in this study. Measurement data at 24 months was gathered later from 11 more children, resulting the total number of 2-year-olds included in this study to be N=1245/3837 (32.4 %). One child was excluded from this age group too, due to a severely outlying height measurement. Reportedly, height of the excluded child was 68.5 cm, the next lowest value in the population being 74.5 cm. With one child excluded, at the age of 2-years N=1244 children were included in this study, n=659 (53 %) boys and n=585 (47 %) girls. (Table 2.)

From 2-year-old children, 287/1244 (23.1 %) were overweight or obese. 29.3 % of boys and 16.1 % of girls were overweight or obese ($p<0.001$). Significant difference between boys and girls is seen in obesity alone as well. 6.9 % of 2-year-old boys were obese, whereas only 2.7 % of girls of the same age were obese ($p=0.001$). (Table 2.) Percentages representing the prevalence of overweight and obesity separately, in boys and girls and in total, are presented in figure 5.

In the study population of 2-year-olds, there was notably more boys who were born small for gestational age compared to girls. 22/652 (3.4 %) boys were categorized as small for gestational age when only 6/578 (1.0 %) girls were in same category ($p=0.006$). (Table 2.) There was no such difference in 1-year-olds (Table 1).

TABLE 2, Population characteristics, 2-year-old children

	Whole sample	Boys	Girls	P value*
	N=1244	n=659 (53.0)	n=585 (47.0)	
During gestation				
	n=1230	n=652	n=578	
Maternal pre-gestational BMI, (IQR)	23.44 (21.16;26.72)	23.24 (21.09;26.70)	23.67 (21.20;26.72)	0.497
Maternal overweight, pre-gestational BMI ≥25 kg/m^2 (%)	424 (34.5)	222 (34.0)	202 (34.9)	0.741
Maternal obesity, pre-gestational BMI ≥30 kg/m^2 (%)	154 (12.5)	82 (12.6)	72 (12.5)	0.949
Maternal smoking during gestation (%)	n=1244	n=659	n=585	0.980**
During the first trimester	82 (6.6)	43 (6.5)	39 (6.7)	0.849***
Throughout gestation	48 (3.9)	26 (3.9)	22 (3.8)	
Older siblings (%)	514/1184 (43.4)	271/630 (43.0)	243/554 (44.9)	0.769
Maternal education (%)	n=1188	n=633	n=555	
Low, (up to 12 years)	342 (28.8)	191 (30.2)	151 (27.2)	0.260
Middle, (13-15 years)	339 (28.5)	176 (27.8)	163 (29.4)	0.551
High, (over 15 years)	507 (42.7)	266 (42.0)	241 (43.4)	0.626
Residential area (%)	n=1186	n=632	n=554	0.385
Urban	857 (72.3)	450 (71.2)	407 (73.5)	
Rural	329 (27.7)	182 (28.8)	147 (26.5)	
At delivery				
	n=1244	n=659	n=585	
Duration of gestation, gwks (IQR)	40.0(39.0;40.86)	39.86(38.86;40.86)	40.00(39.14;40.86)	0.186
	n=1231	n=653	n=578	
Age of the mother, years (SD)	31.21 (4.36)	31.19 (4.39)	31.22 (4.34)	0.914
Delivery method (%)	n=1230	n=652	n=578	0.580
Vaginal delivery	1006 (81.8)	537 (82.4)	469 (81.1)	
Caesarean section	224 (18.2)	115 (17.6)	109 (18.9)	
	n=1231	n=653	n=578	
Birth weight, kg (IQR)	3.55 (3.23;3.90)	3.59 (3.26;3.96)	3.49 (3.19;3.80)	<0.001
	n=1223	n=652	n=571	
Birth length, cm (IQR)	51.00 (49.00;52.00)	51.00 (50.00;52.00)	50.00 (49.00;51.00)	<0.001
Size for gestational age# (%)	n=1230	n=652	n=578	
SGA	28 (2.3)	22 (3.4)	6 (1.0)	0.006
AGA	1172 (95.3)	618 (94.8)	554 (95.8)	0.380
LGA	30 (2.4)	12 (1.8)	18 (3.1)	0.148
At 2 years				
Height, cm (SD)	87.84 (3.49)	88.60 (3.42)	87.00 (3.37)	<0.001
Weight, kg (SD)	12.68 (1.47)	13.03 (1.40)	12.28 (1.44)	<0.001
BMISDS (SD)	0.10 (1.11)	0.17 (1.06)	0.03 (1.16)	0.029
Overweight or obesity, ISO-BMI ≥25 (%)	287/1244 (23.1)	193/659 (29.3)	94/585 (16.1)	<0.001
Obesity, ISO-BMI ≥30 (%)	61/1244 (4.9)	45/659(6.9)	16/585(2.7)	0.001

AGA=appropriate for gestational age*; BMI*=body mass index*; gwks*=gestational weeks*; ISO-BMI*=Age and Sex adjusted BMI at the age of 18*; IQR*=interquartile range*; LGA*=large for gestational age*; SD*=standard deviation*; SGA*=small for gestational age.

Presented as numbers (percentages), means (standard deviations), or medians (interquartile ranges).

Defined by standard deviation from the gestational age- and sex-specific reference mean value. SGA= SDS-2, LGA= SDS+2.
*The comparison between boys and girls
**groups compared: "no smoking" and "smoking at any point of gestation"
***groups compared: "smoking during the first trimester" and "smoking throughout gestation"

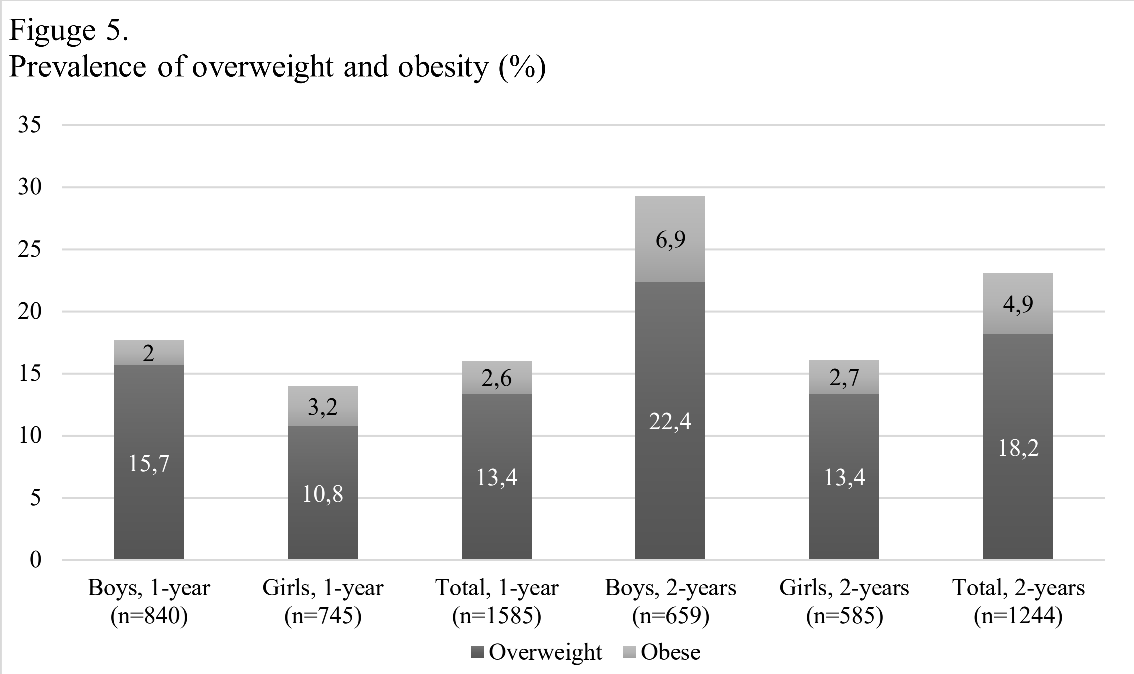

Figure 5: Prevalence of overweight and obesity in 1- and 2-years old boys and girls in the FinnBrain Birth Cohort Study.

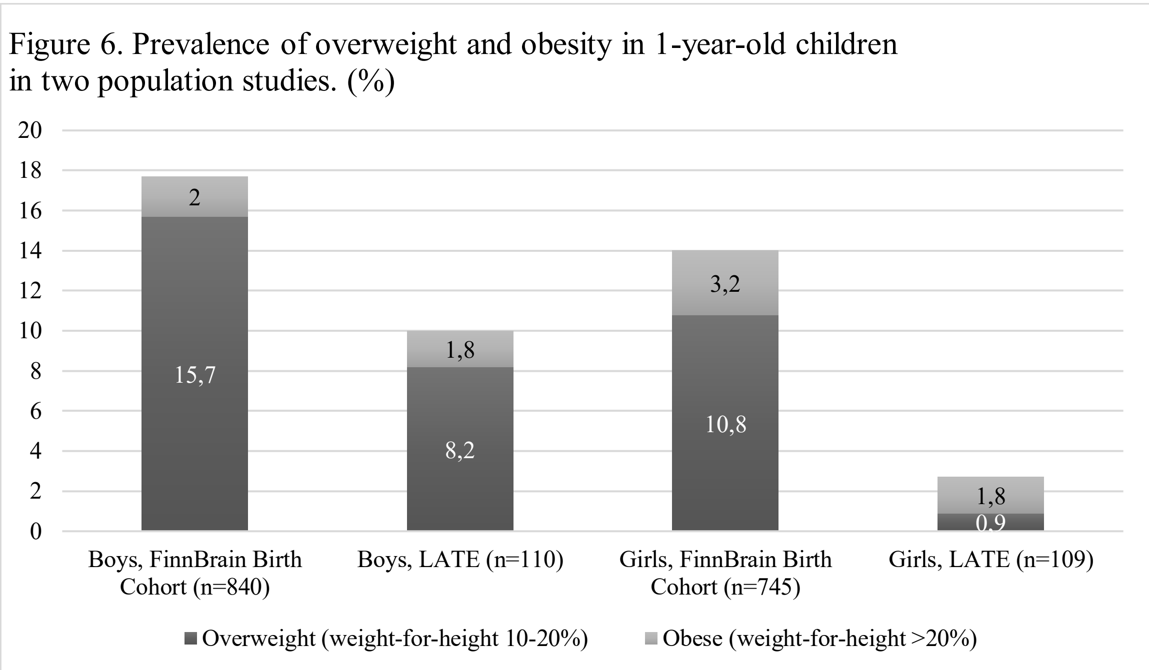

Figure 6: Prevalence of overweight and obesity in 1-year-old boys and girls in the FinnBrain Birth Cohort Study and LATE- study (Mäki et al. 2010)

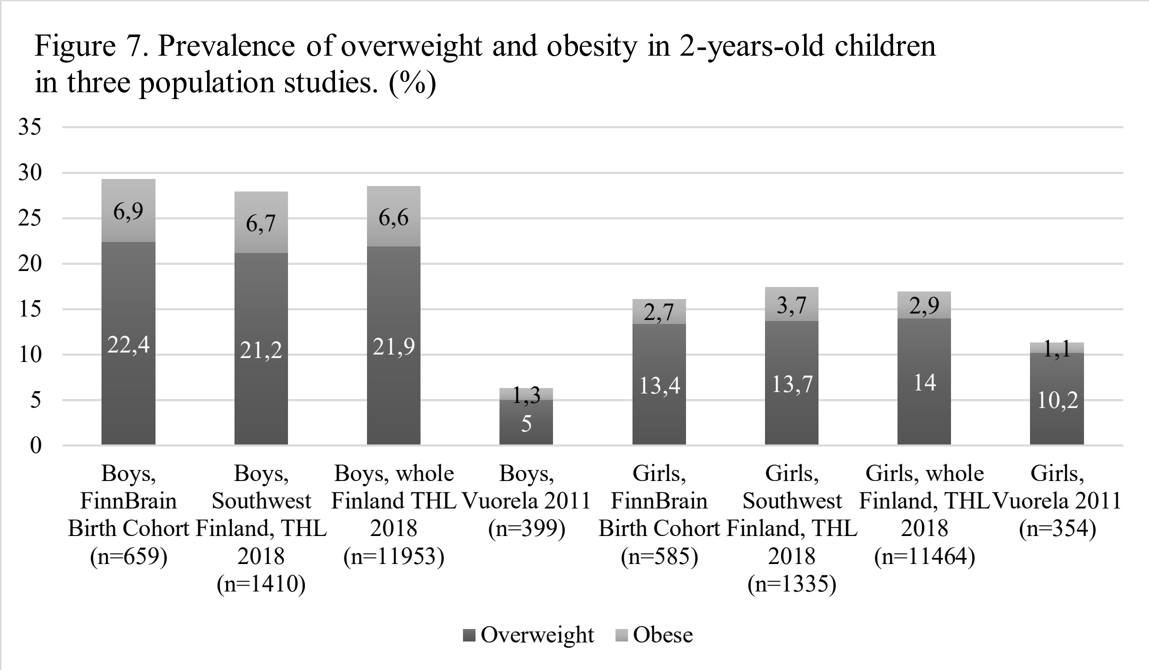

Figure 7: Prevalence of overweight and obesity in 2-years-old boys and girls in the FinnBrain Birth Cohort Study, Childhood overweight and obesity study by N. Vuorela et al. (Vuorela et al. 2011) and THL statistics report: *Lasten ja nuorten ylipaino ja lihavuus 2018 - Tilastoraportti 9/2019.* THL. Retrieved from http://urn.fi/URN:NBN:fi-fe2019042413181 (Lundqvist et al. 2019, Personal information from Lundqvist A. 2019).

4 Discussion

4.1 Main findings

This study provided new information on the prevalence of overweight and obesity in 1-year-old Finnish children as well as additional information on the prevalence of overweight and obesity in 2-year-old children in Finland. The findings suggest that 1- and 2-year-old boys have significantly higher prevalence in overweight compared to girls of the same age. Additionally, 2-year-old boys have significantly higher prevalence in obesity, compared to 2-year-old girls. The findings in prevalence of overweight and obesity in 2-year-old children are very similar to data from Finnish national institute for health and welfare (THL) in the populations of Southwest Finland and whole Finland. (Figure 7, Lundqvist et al. 2019, Personal information from Lundqvist A. 2019.)

1-year-old children

In this study, 1-year-old boys were taller and heavier than girls, as expected, and had higher prevalence in overweight and obesity (Table 1). There are very little studies of overweight and obesity in children this young. However, this study suggests substantially higher prevalence in 1-year-old children's overweight and obesity than previously presumed by LATE-study of Finnish children's overweight and obesity (Figure 6, Mäki et al. 2010).

In both studies, overweight and obesity were defined by weight-for height/length percentage and using the same cut-off points; ≥10 % for overweight and ≥20 % for obesity. However, as weight-for-height/length percentage is calculated as percentual deviation from the population mean, there might be a slight difference in the results of these two studies due to different reference curves. The old Finnish growth reference was used in the LATE-study, whereas in this study weight-for-height/length percentage was calculated by an online counter that uses the new Finnish growth reference. Additionally, LATE-study had weight and length data from N=219 1-year-old children, whereas this study had the data from N=1585, denoting our sample size is larger.

As overweight and obesity in early childhood has rarely been studied, important new information is provided with this study and its notable sample size.

2-year-old children

Boys were taller and heavier than girls also in the age of 2 years, as expected. In this study cohort, 2-year-old boys had significantly higher prevalence in both overweight and obesity, compared to girls (Table 2). This finding is contrary to findings from a previous study which suggested that 2-year-old girls were more overweight and obese than boys (Vuorela et al. 2011) but very similar to findings in a statistics report from Finnish national institute for health and welfare (THL) (Figure 7, Lundqvist et al. 2019, Personal information from Lundqvist A. 2019).

Part of the difference between this study and the study by Vuorela et al. is explained by the growth reference used in defining overweight and obesity. In both studies overweight and obesity were defined by BMI percentile curve passing through BMI 25 kg/m^2 and BMI 30 kg/m^2 at the age of 18. Whereas Finnish growth reference was used in this study, Vuorela et al. used international growth reference. In International reference, BMI 25 kg/m^2 represents the 89.3rd percentile for girls and the 90.5th percentile for boys, and BMI 30 kg/m^2 represents the 98.6th percentile for girls and the 98.9th percentile for boys. Correspondingly, in the Finnish reference, percentiles representing BMI 25 kg/m^2 and 30 kg/m^2 are the 87.8th and the 98.2nd for girls, and the 78.2nd and the 95.6th for boys in the same order. Therefore, this study is more accurate due to using the new Finnish growth reference when studying the Finnish population. Additionally, in the study by Vuorela et al., population size of 2-year-old children in 2001 was N=753, whereas in this study there were N=1244 2-year-olds included.

The findings of this study correspond relatively well to data in the statistics report from Finnish national institute for health and welfare (THL) in the population of Southwest Finland and whole Finland (Figure 7). The same growth reference and same cut-offs were used in both studies. Therefore, the FinnBrain Birth Cohort represents the Finnish population in 2-year-old children's overweight and obesity in Southwest Finland and whole Finland.

4.2 Clinical implications

Findings in this study are very important for future research of early overweight. There is a commendable sample size of overweight children in our cohort, n=253 overweight or obese 1-year-olds and n=287 overweight or obese 2-year-olds, and wide background information for studying the causes and outcomes of early childhood overweight. As it is already known that early undernutrition and underweight lead to adverse health outcomes, it is interesting and important to investigate whether early overweight, in turn, is an increasing or decreasing factor for some later health risks. This study provides applicable resources for that research.

There is very little data and research on very early childhood overweight and obesity. As there are no national records in Finnish 1-year-old children's overweight and obesity yet, the prevalence or overweight and obesity in 1-year-old children in the FinnBrain Birth Cohort could not be compared to the Finnish population. However, this study and findings lay the groundwork for future research. This study enables future studies to compare their findings to another, notably large Finnish cohort, and to draw conclusions about the congruence of findings in their studies and this study.

The FinnBrain Birth Cohort represents the population of Finland and Southwest Finland in 2-year-old children's overweight and obesity in good accuracy. Future findings from overweight and obesity studies from the FinnBrain Birth Cohort can be generalized and applied to the whole Finnish population. This study lays a great base for further investigating childhood overweight in order to provide additional information for fighting the constantly growing global health problem of childhood overweight.

4.3 Strengths and limitations

The strengths of this study consist a large sample size of prospective birth cohort of non-selected 1585 1-year-old children and 1244 2-year-old children in addition to reliable measurements taken by professionals in child health centres during regular check-ups.

Nearly all Finnish children attend the regular child health visits regardless of social status or income level. The nurses are specially trained for child health care and use standardized height and weight measurement techniques and calibrated equipment. Moreover, all measurement values were checked, uniformed, and possible typing errors were corrected. An important strength of this study is that the new Finnish growth reference was used in it, making sure that the study population is compared to a reference population with similar, nationally varying growth patterns.

Limitations of this study include loss in the returned questionnaires and therefore cohort size over the years. As there might be some factors leading to dropping out of the study that might also affect the weight status of the child, the loss could cause some bias to the results. In addition, the questionnaires of background factors are based on self-report, which might cause bias regarding some questions, for example questions about smoking during the gestation.

4.4 Conclusions

In conclusion, it was found that boys are more overweight than girls in 1- and 2-year-old children. In addition, 2-year-old boys are more obese compared to girls. This study provided new information on overweight and obesity frequencies in 1-year-old Finnish children, and more information on overweight and obesity in 2-year-old Finnish children. The FinnBrain Birth Cohort Study data represents the 2-year-old children's overweight and obesity frequencies of the populations in Finland and in Southwest Finland considerably well.

The information this study provided of early childhood overweight can be used in future research of underlying factors, future health outcomes, and for developing interventions to prevent the globally increasing health problem of childhood overweight.

References

Barker D., Osmond. C., 1986. Infant mortality, childhood nutrition, and ischaemic heart disease in England and Whales. *The Lancet.*

Bateson P., et al., 2004. Developmental plasticity and human health. *Nature,* p. 430; 419–421.

Butler E., et al., 2018. Childhood obesity: how long should we wait to predict weight?. *Journal of Pediatric Endocrinology and Metabolism,* p. 31(5): 497–501.

Calkins K., Devaskar S., 2011. Fetal Origins of Adult Disease. *Curr Probl Pediatr Adolesc Health Care,* pp. 41: 158-176.

Cole T., et al., 2000. Establishing a standard definition for child overweight and obesity worldwide: international survey. *BMJ,* p. 320: 1240–3. .

Cole TJ., Lobstein T., 2012. Extended international (IOTF) body mass index cut-offs for thinness, overweight and obesity. *Pediatric Obesity,* pp. 7, 284–294.

de Bernabé JV., et al., 2004. Risk factors for low birth weight: a review. *European Journal of Obstetrics & Gynecology and Reproductive Biology,* pp. 116; 3-15.

Eriksson J., 2016. Developmental Origins of Health and Disease-from a small body size at birth to epigenetics. *Annals of medicine,* pp. 46:6 456-467.

Farr O., et al., 2016. Central nervous system regulation of eating: Insights from human brain imaging. *Metabolism clinical and experimental,* pp. 65; 699-713.

Flegal KM., et al., 2002. Weight-for-stature compared with body mass index–for-age growth charts for the United States from the Centers for Disease Control and Prevention. *American Journal of Clinical Nutrition,* p. 75:761–6.

Graignic-Philippe R., et al., 2014. Effects of prenatal stress on fetal and child development: A critical literature review. *Neuroscience and Biobehavioral Reviews,* pp. 43: 137-162.

Handbooks of the Ministry of Social Affairs and Health, .., 2004. *Child health clinics in support of families with children. A guide for staff..* Helsinki: Sosiaali- ja terveysministeriö.

Hoffman D., et al., 2017. Developmental Origins of Health and Disease: Current Knowledge and Potential Mechanisms. *Nutrition Reviews,* pp. 75(12): 951-970.

Juonala M., et al., 2011. Childhood Adiposity, Adult Adiposity, and Cardiovascular Risk Factors. *The New England Journal of Medicine,* pp. 365:1876-85.

Karlsson HK., et al., 2016. Weight loss after bariatric surgery normalizes brain opioid receptors in morbid obesity. *Molecular Psychiatry ,* pp. 21, 1057–1062 .

Karlsson L., et al., 2017. Cohort Profile: The FinnBrain Birth Cohort Study (FinnBrain). *International Journal of Epidemiology,* pp. 1-12.

Koponen P., et al., 2018. *Terveys, toimintakyky ja hyvinvointi Suomessa FinTerveys 2017 -tutkimus,* Helsinki: Terveyden ja Hyvinvoinnin laitos.

Krebs NF., et al., 2007. Assessment of Child and Adolescent Overweight and Obesity. *Pediatrics,* p. 120: S193–228.

Lee EY., Yoon K.-H., 2018. Epidemic obesity in children and adolescents: risk factors and prevention. *Frontiers of medicine.*

Lenard N., Berthoud H., 2008. Central and Peripheral Regulation of Food Intake and Physical Activity: Pathways and Genes. *Obesity,* p. 16;3.

Lima S., et al., 2018. Is the risk of low birth weight or preterm labor greater when maternal stress is experienced during pregnancy? A systematic review and meta-analysis of cohort studies. *PLoS ONE,* p. 13(7): e0200594.

Lundqvist A., et al., 2019. *Lasten ja nuorten ylipaino ja lihavuus 2018 - Tilastoraportti 9/2019,* s.l.: THL.

Mäki P., et al., 2010. *Child Health – Results of the LATE-study on growth, development, health, health behavior and growth environment,* Helsinki: National Institute for Health and Welfare (THL).

Mihrshahi S., Baur L., 2018. What exposures in early life are risk factors for childhood obesity?. *Journal of Paediatrics and Child Health,* p. 1294–1298.

Must A., Strauss R., 1999. Risks and consequences of childhood and adolescent obesity. *International Journal of Obesity,* pp. 23;2, 2-11.

Ng M., et al., 2014. Global, regional, and national prevalence of overweight and obesity in children and adults during 1980–2013: A systematic analysis for the Global Burden of Disease Study 2013. *Lancet,* p. 384: 766–81.

Obesity (Children)*:* Current Care Guidelines. Working group set up by the Finnish Medical Society Duodecim and the Finnish Paediatric society. Helsinki: The Finnish Medical Society Duodecim, 2013, *cited 07.05.2019. Available online at www.kaypahoito.fi*.

O´Donnell K., Meaney M., 2017. Fetal Origins of Mental Health: The Developmental Origins of Health and Disease Hypothesis. *American Journal of Psychiatry.*

Reilly JJ., Kelly J., 2011. Long-term impact of overweight and obesity in childhood and adolescence on morbidity and premature mortality in adulthood: systematic review. *International Journal of Obesity,* p. 35; 891–898 .

Risnes K., et al., 2011. Birthweight and mortality in adulthood: a systematic review and meta-analysis. *International Journal Of Epidemiology.*

Romero-Corral A., et al., 2008. Accuracy of body mass index in diagnosing obesity in the adult general population. *International Journal of Obesity,* pp. 32, 959–966.

Saari A., et al., 2011. New Finnish growth references for children and adolescents aged 0 to 20 years: Length/height for-age, weight-for-length/height, and body mass index-for-age. *Annals of Medicine,* pp. 43:3, 235-248.

Sankilampi U., et al., 2013. New population-based references for birth weight, lenght, and head circumference in sigletons and twins from 23 to 43 gestation weeks. *Annals of Medicine,* pp. 45:5-6, 446-454.

Simmonds M., et al., 2016. Predicting adult obesity from childhood obesity: a systematic review and meta-analysis.. *Obesity Reviews,* p. 17:95–107..

Singh A., et al., 2008. Tracking of childhood overweight into adulthood: a systematic review of the literature. *Obesity reviews ,* p. 9; 474–488.

Stettler N., et al., 2002. Infant weight gain and childhood overweight status in a multicenter, cohort study. *Pediatrics,* p. 109; 194.

THL, et al., 2019. *Eating together - food recommendations for families with children.* Helsinki: THL Kide 26.

Tuulari JJ., et al., 2017. Feeding Releases Endogenous Opioids in Humans. *The Journal of Neuroscience,* p. 37(34):8284–8291.

UNICEF/WHO/World Bank Group., 2018. *Joint Child Malnutrition Estimates 2018 edition.* [Online]
Available at: https://www.who.int/nutgrowthdb/estimates2017/en/

Vuorela N., 2011. *Body Mass Index, Overweight and Obesity Among Children in Finland.* Tampere: Tampere University Press.

Vuorela N., et al., 2009. Prevalence of overweight and obesity in 5- and 12-year-old Finnish children in 1986 and 2006. *Acta Pædiatrica ,* pp. 98; 507-512.

Vuorela N., et al., 2011. Change in prevalence of overweight and obesity in Finnish children – comparison between 1974 and 2001. *Acta Pædiatrica,* pp. 100, pp. 109–115.

Weihrauch-Blüher S., Wiegand S., 2018. Risk Factors and Implications of Childhood Obesity. *Current Obesity Reports,* p. 7:254–259.

WHO., 2009. *Global health risks: mortality and burden of disease attributable to selected major risks.,* s.l.: World Health Organization.

WHO., 2018a. *World health statistics 2018: monitoring health for the SDGs, sustainable development goals.,* Geneva: World Health Organization.

WHO, 2018b. *Obesity and overweight: Key Facts.* [Online]
Available at: https://www.who.int/en/news-room/fact-sheets/detail/obesity-and-overweight

WHO, 2000. *Obesity: preventing and managing the global epidemic, Report of a WHO Consultation (WHO Technical Report Series 894),* Geneva: WHO Technical Report Series.

Wynne K., et al., 2005. Appetite control. *Journal of Endocrinology ,* pp. 184, 291–318 .

Ziauddeen N., et al., 2018. Predicting childhood overweight and obesity using maternal and early life risk factors: a systematic review. *Obesity Reviews ,* p. 19; 302–312.