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CURRENT GROWTH PATTERNS OF
FINNISH CHILDREN AGED 0 TO 4 YEARS

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Growth monitoring by anthropometry is used worldwide to assess health and nutritional status of individual children and populations. Prerequisite for successful appraisal is the utilization of a reliable growth reference against which to compare the growth. The Finnish national growth reference was introduced in 1986 but studies on its adequacy for assessment of contemporary linear growth patterns of Finnish children have not been published since. WHO launched a prescriptive growth standard in 2006 promoting its universal use worldwide but its applicability for Finland has not been evaluated.

The aim of this study was to describe the current growth patterns of Finnish children by assessing it against the Finnish reference and the WHO 2006 standard and compare the prevalence of growth faltering identified by the references. Mixed longitudinal sample of 2809 children (17780 measurements from boys and 17346 from girls) aged 0-4 years and born between October 2003 and September 2004 were obtained from Tampere Municipality child health clinic register. Growth curves were constructed from the data using LMS method and plotted against the reference curves. Percentages of measurements that exceeded the screening limits for growth faltering were also calculated and compared.

Height-for-age (HFA) of the sample children exceeded the Finnish reference values at each assessed centile (5th, 50th and 95th) at 12 months and the difference had a slowly increasing pattern so that boys were 1.5 cm taller and girls 1.0 cm taller at 48 months. The relative weight-for-height (WFH) mean was slightly lower than the reference mean after 6 months and at 48 months it was even. In comparison with the WHO standard, the sample children were 1.0 cm longer and 0.3 kg heavier at birth. All assessed centile curves were above the standard curves at each age and at 48 months the difference in height was 1.4 cm in boys and 0.8 cm in girls and in weight 0.9 kg and 0.6 kg respectively. The WHO reference identified fewer children as wasted, slightly more as obese or stunted and considerably more as very tall compared to the Finnish reference.

Average height of Finnish children has increased but relative weight has decreased or remained constant in most ages between 0 to 4 years since construction of the Finnish national growth reference. Compared to the WHO reference, Finnish children were slightly taller and heavier at each assessed age. Discussion is needed whether 1.5 cm increase in boys' height and 1cm increase in girls' height at 48 months justifies the updating of the Finnish growth reference. Since the WHO standard values for weights are lower and it shows higher levels of obesity, its adoption in Finland should be considered and the public health implications of the adoption evaluated. However, further study is needed to assess if the same growth pattern as was seen in 0-4 year old children applies also to older children and adolescents.

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ABBREVIATIONS

BMI	Body mass index
GH	Growth hormone
HAZ	Height-for-age z-score
HFA	Height-for-age
MGRS	World Health Organization (WHO) Multicentre Growth Reference Study
SD	Standard deviation
UNISEF	United Nations Children's Fund
WHO	World Health Organization
WAZ	Weight-for-age z-score
WFA	Weight-for-age
WFH	Weight-for-height
WHZ	Weight-for-height z-score

1. INTRODUCTION

Anthropometric measurements are used worldwide to assess growth of children and health status of populations. Child growth, especially height growth, is an effective and sensitive indicator of child general health and nutritional status. Anthropometric indices, e.g. height and weight, are measured regularly and so formed growth curves are used to monitor growth. A healthy and well nourished child that lives in an optimal environment grows linearly in his/her genetically determined growth channel. Deviations from normal growth may underline chronic illnesses, inadequate nutrition or other problems in child well being. At population level, growth of different populations can be compared and information on nutritional status or general well being of populations can be obtained (de Onis et al., 2006a; Pere, 2006; Asworth et al., 2008).

An important requirement for assessment of child growth is the availability of a reliable growth reference or standard against which to compare the growth of a child (Cole, 1990). If a standard is inadequate, it may lead to false conclusions on child or population well being and even to missed or wrong treatments or interventions (Garza and de Onis, 1999). Reliability of a growth standard should be assessed regularly and growth charts updated since secular changes in growth lead to changes in average size and shape of children (Cole, 2006). Also recent studies on child growth and its consequences for health in later life have increased knowledge on optimal growth of children (Must and Strauss, 1999; Bruining, 2000; Laitinen et al., 2001; Nuutinen and Nuutinen, 2001; Singhal and Lucas, 2004; Knip et al., 2008).

The reference that is currently utilized in Finland uses data collected from two sets of Finnish children born in 1954-1962 and in 1968-1972. The reference was published first in 1986 and it was revised in 1994 (Pere, 2000; Ignatius¹, personal communication). Studies on average linear growth of Finnish children have not been published since the construction of the reference and thus adequacy of the reference for assessment of contemporary growth of Finnish children has not been judged.

WHO published a new international growth standard in April 2006. According to WHO, this standard describes how children should optimally grow disregarding their

¹ Anneli Ignatius (former Pere) is a medical doctor and one of the main architects of the Finnish national growth reference

ethnic background or country of living, since genetic differences between populations have minor effect on growth of children compared to the effects of health status and environmental influences. According to WHO, this standard could be used anywhere in the world instead of national references and the standard is already widely adopted (Garza and de Onis, 2004; de Onis et al., 2004a; Garza, 2006; WHO, 2006b; Onyango et al., 2007). However, some previous studies suggest that the standard does not adequately reflect the optimal growth of all ethnic groups in all ages due to variation in growth in height and weight as well as tempo and timing of maturation across populations (van Buuren and Wouwe, 2008; Hui et al., 2008; Wright et al., 2008). Studies on comparison of growth of Finnish children and the WHO standard or the standard's adequacy for use in Finland have not been published.

This study described how Finnish children are currently growing and compared the growth with the Finnish reference and the WHO standard. It assessed if Finnish reference still adequately reflects the contemporary growth of Finnish children or if Finnish children grow more like the WHO standard population. Implications of adopting the WHO standard in place of the Finnish reference and its likely impacts on the assessment of infant and childhood growth are also discussed. Growth curves were constructed from anthropometric data of 0-4 year's old Finnish children born during one calendar year between October 2003 and September 2004. The curves were smoothed with the LMS method and plotted against the reference curves. Percentages of children who exceed the upper and lower screening limits of the references were also calculated and compared.

2. LITERATURE REVIEW: HUMAN GROWTH AND GROWTH MONITORING

Fundamental for beneficial growth assessment is comprehension of the patterns of normal human growth and the mechanisms and influencing factors behind it. This literature review first describes the normal growth with the special emphasis on infancy and childhood. Adequate nutrition is naturally essential and nutritional disorders are often diagnosed by growth monitoring thus effects of nutrition are discussed more in details. Some adverse factors affecting growth are then briefly introduced.

Growth anomalies can be detected with rigorous growth monitoring. Prerequisites and methods of beneficial monitoring are summarized in the next chapters. Differences of growth references and standards are described and the importance of the selection of a reference, indicators and cut-off points for assessment of growth faltering is explained. After that, construction methods and smoothing procedure of growth curves, which are also used in this study, are briefly explained.

The construction and the characters of the Finnish national growth reference and the WHO 2006 growth standard are then introduced in the next chapters although detailed sampling- and statistical methods used for construction of the references was left out due to lack of space. Finally, the scarce knowledge on current growth of Finnish children is reviewed and justification of this study explained.

The literature review was conducted unsystematically, using Medline, PubMed and Google Scholar search engines and key words related to human growth, growth monitoring and growth chart construction. References of searched articles were used for expanding the reference literature and some WHO reports were also included. Emphasis was given to recent literature although some older books and articles were also reviewed.

2.1. Human growth

Human growth is a complex, sensitive and continuous process. It is regulated by genes and endocrines but it is also dependent on nutrition and affected by environmental factors and diseases (de Onis et al., 2006a; Pere, 2006; Asworth et al., 2008). Several

hormones control growth; thyroxine from the thyroid gland, cortisol and adrenalin, testosterone, oestrogen, insulin, melatonin, growth hormone (GH), thyroid stimulating hormone (TSH), adrenocorticotropin and the gonadotrophic hormones (Tanner, 1990). Environmental factors like nutrition, infections, poverty, stress, lack of affection, high altitude and pollutants have significant effects on growth, possibly also through interaction with genes (Schell and Knutson, 2006; Towne et al., 2006). Even seasons have considerable influence on velocity of growth, even if varying availability of nutrients and rates of disease in different seasons are excluded, especially in countries where different seasons vary distinctively from each others. In western European countries, children gain more length in spring and in summer than in autumn and in winter (Tanner, 1990).

The shape of human growth curve is typical only for primates (Tanner, 1990). Human growth has at least three distinct phases: infancy, childhood and puberty (Hindmarch, 2006). These phases can be seen as components that are additive and partly superimposed (Karlberg, 1989). The genetic, hormonal, environmental/nutritional factors that regulate the growth have different influences at different phases (Hindmarch, 2006; Rosenboom, 2007).

Growth process is relatively easily disturbed by adverse factors. That makes child growth, especially height growth, an effective and sensitive indicator of child's general health and nutritional status. A healthy and well nourished child that lives in an optimal environment grows linearly in his/her genetically determined "growth channel" and deviations from normal growth may underline chronic illnesses, inadequate nutrition or other problems in child's well being (de Onis, 2006a; Pere, 2006; Asworth et al, 2008). A child inherits from the parents the genes that determine the "growth channel", the pace and timing of growth events and the potential for adult height (Pere, 2006). Growth has tendency to return to its own channel after periods of growth restriction due to e.g. diseases or malnutrition. That can be seen as rapid growth period known as "catch up growth" (Tanner, 1990). Height growth velocity follows the same pattern in each normally growing child so that growth velocity curves have the same shape. The absolute height might differ and the growth spurts may be experienced in different times but the shape is still the same (Lejarraga, 2006).

An average girl is slightly shorter than an average boy at all ages before adolescence. The difference is small at birth but at 5 years of age boys are on average 1.0 cm taller than girls. Then adult difference of 12.5-13.0 cm between sexes develops gradually prior to and during the pubertal growth spurt (Lejarraga, 2006). Girls mature earlier than boys, they reach 50% of their adult height earlier, enter puberty earlier and their growth ceases earlier. An average girl stops growing at 15,5 years and boy at 17,5 years (Tanner, 1990).

It is estimated that 85 to 90% of total genetic variability of humans resides within populations (i.e. between individuals) and only 10% to 15% between populations (Ulijaszek, 1998; Jorde et al., 2000; Jorde and Wooding, 2004). Growth of shape and size of stature is determined by multigenic factors and it is unlikely that large, nonisolated population groups would differ significantly on the basis of genetics alone (Cooper et al., 2003). Because of that, few differences in growth would remain between populations if all children lived in a similar environment and had optimal nutrition and care (WHO, 1995b).

2.1.1. Growth in infancy and childhood

Infancy is the time for the most rapid growth in human life after prenatal period. At the same time cognitive and motor skills develop rapidly due to the fast growth of brains (Bogin, 2006). However, growth velocity changes fast in infancy. During the first few months, growth velocity is approximately 20 cm/year and at the end of the first year it has declined to 10-12 cm/year. At this stage, most of children change their percentile position in a growth chart (Rosenboom, 2007). Children with genes for large size but born to small mothers move upwards through the centiles and children born large but with genes making for small size move downwards (Tanner, 1990). During the second year, growth rate averages 10-13 cm/year, during the third year 7.5-10 cm/year and thereafter is stable at 5-6 cm/year until the growth spurt in puberty (Rosenboom, 2007).

Maternal size and nutritional status have the strongest effects on size of a foetus during prenatal period with little influence from genes. Insulin-like growth factors (IGFs) and insulin influence the growth, but thyroid hormone and growth hormone do not affect at this state (Rosenboom, 2007). In addition, many sociodemographic, behavioural and environmental factors influence intrauterine growth, like maternal size, maternal smoking, socioeconomic status and parity (Wang et al., 1995; Aber et al., 1997).

Size at birth depends on uterine conditions much more than on child's genotype. Growth during the first 6 months is continuum of foetal growth and is greatly dependent on nutrition (Hindmarch, 2006). This infant component of growth starts affecting during the foetal period, has decelerating trend and diminishes by 3 to 4 years. Childhood component starts influencing growth sometimes between 6 months and 2 years during which growth process switches from nutritionally dependent phase to growth hormone regulated phase (Lejarraga, 2006). Childhood phase is dependent not only on normal thyroid- and growth hormone secretion but also on genetic factors (Hindmarch, 2006). By the end of the second year, the size that is determined by the size of the womb and nutritional conditions changes to the size that is genetically determined. This very often results to "growth channel" or "centile crossing" i.e. the percentile position of a child's weight and height measurements changes on a growth chart (Perheentupa and Pere, 1997). The mid-childhood spurt occurs between 6 to 8 years in many children during which the growth velocity increases slightly. So called mini-spurts, short term fluctuations in growth velocity, may occur even monthly. These spurts are not easy to pick up in total body height changes but can be seen in changes in length of the lower limb from knee to heel and measured by a knemometer (Tanner, 1990).

2.1.2. Nutrition and growth

Adequate nutrition is fundamental to growth. One of the first responses of body to food scarcity is growth restriction and growth evaluation by anthropometry is probably the most commonly used way to assess nutritional status of children. Although growth is highly nutrition sensitive, only less than 10% of total energy intake is required for growth of stature and very wide range of diets can satisfy nutritional needs and promote optimal growth. However, deficiency of even one nutrient, like zinc or iron, may cause growth retardation (Norgan, 2006; Walker et al., 2007).

Breast feeding is recognised as optimal method of feeding an infant during the first months of life. Exclusively or predominantly breastfed infants have shown to have different growth patterns than formula fed infants. Breast fed infants typically grow faster than their formula fed counterparts during the first two months but slower from 3 to 12 months changing their percentile position downwards in growth charts. In the second year, breast fed infants tend to gain weight more rapidly and at 24 months the difference between breast fed and formula fed infants has diminished. This difference in growth patterns is more evident in weight growth than in height growth (Dewey et al., 1995; Dewey, 2001).

In a comprehensive international comparison conducted by WHO, growth was found not being sensitive for different timing of introduction of complementary food if it was introduced between 4 and 6 months when weaning should begin. Nor it was sensitive to different types of complementary food or differing frequencies in feeding in healthy infants (WHO, 2002).

Obesity, not only in adulthood but also in childhood, is a fast growing problem globally. Chronic diseases, earlier seen only in obese adults, are now affecting also children. The “obesity epidemic” started in 1960’s in adults and 1980’s in adolescents and in children (WHO, 2000). Obesity is caused by positive energy balance when more energy is taken in than consumed. It is associated with risk factors of many chronic diseases, including hyperlipidemia, hypertension, early atherosclerosis and diabetes (Mahoney et al., 1996; Berenson et al., 1998) increasing morbidity and mortality. When weight increases above 20% of average, the extra mortality rises 20% for men and 10% for women mostly due to increased death rate for heart diseases, diabetes mellitus, digestive diseases and cancer (Bray, 1987). Heart disease risk factors, dyslipidemia, hypertension and insulin resistance are nowadays common also in children and obese children are very often also obese in adulthood (Must and Strauss, 1999; Laitinen et al., 2001; Nuutinen and Nuutinen, 2001). Early detection and interventions in childhood may prevent the diseases from inducing and reduce the prevalence of obesity also in adulthood remarkably since it is easier to reduce weight gain in childhood than trying to control the weight of adults (WHO, 2000). Breast feeding may also have a significant protective effect against obesity in later childhood (von Kries et al., 1999).

Malnutrition delays growth and tempo of growth is affected first. Protein-energy malnutrition is a common form of malnutrition which leads to marasmus or kwashiorkor if severe and to stunting and wasting if less severe (Norgan, 2006). Weight-for-height growth faltering due to chronic malnutrition starts usually at 3 months and is pronounced between 6 and 15 months of age during the transition from infant to childhood growth phase, when the nutritional needs are high and when weaning takes place. Stunting process begins in birth and continues during the first 3 years of life (Shrimpton et al., 2001). Stunting has been estimated to affect about 30% of children in developing countries. Malnutrition makes children more prone to infections and constant, severe infections affect growth even more than malnutrition itself whereas effects of infections in well nourished children are minimal.

Malnourishment in childhood causes huge loss of development potential in children due to vulnerability to infections, micronutrient deficiencies causing development failures and lack of energy making children less enthusiastic for playing and learning.

Chronically undernourished children with linear growth retardation (stunting) are also found to be having poorer cognitive abilities and more socio-emotional problems than normally growing children. Early detection of malnourishment is important for timely interventions to prevent the loss of development potential and excess morbidity and mortality. However, often in the case of malnourishment the underlying cause is poverty with its multiple consequences and not the parent's willingness to do the things right (Grantham-Mc Gregor et al., 2007; Walker et al., 2007).

Some recent studies suggest that delayed transition from infancy to childhood growth phase, which is evident in many malnourished children, has a lifelong impact on growth causing idiopathic short stature. This is explained by adaptive strategy in the timing of the transition from infancy to childhood during low energy supply decreasing body size and it is not followed by catch up growth. When the transition is delayed beyond 12 months of age, it has permanent effect on final adult height. This delay may affect growth over several generations even if later generations get sufficient amount of nutrients since this adaptation process is regulated by "nutrient-gene interaction" causing epigenetic changes. It is suggested to be an "evolutionary strategy" for survival during energy crisis. (Waterland and Jirtle, 2004; Hochberg and Albertsson-Wikland, 2008).

2.1.3. Growth disorders and other pathological conditions affecting growth

In addition to nutritional disorders, wide variety of other chronic conditions, disorders and diseases affect growth; chromosomal disorders, endocrine gland disorders, cartilage and bone disorders, disorders of absorption of food, general diseases of lungs, heart and kidney, steroid treatment and radiation, intrauterine growth restriction and psychological stress. Rigorous growth monitoring is fundamental in detection of varying disorders and diseases since growth failure is often their early symptom and apparently normal child can be diagnosed as having a treatable disorder if growth is followed regularly (Tanner, 1990). Treatment should be started as early as possible, and if the condition is not treatable, early detection allow for counselling for the parents to minimize psychological consequences (Fayter et al., 2008).

Children with pathological conditions of growth can have short or tall stature and reduced or increased growth rate. Many chromosomal abnormalities produce short stature, e.g. Down syndrome and Turner syndrome. Achondroplasia is the best known disorder leading to dwarfism. It is caused by single gene mutation and it is inherited as a dominant. Short stature may also be consequence of normal genetic shortness (Bramswig, 2007). Examples of syndromes that produce tall stature are Klinefelter syndrome and Marfan syndrome (Fayter et al., 2008).

The main endocrine disorders affecting growth are growth hormone insufficiency and thyroid hormone insufficiency. A child with growth hormone deficiency becomes stunted and obese. Children who lack growth hormone grow to about 130 cm height. Also psychological stress may restrict growth hormone secretion and cause stunting (Tanner, 1990).

Prolonged malabsorption of food causes growth failure just like undernutrition. The most common cause for malabsorption is celiac disease. It is caused by abnormal reaction of cells of the gut to glutens which exists in many flours. Gluten-free diet allows the gut to heal and normal growth occurs (Tanner, 1990).

Low birth weight is probably the most important single factor affecting neonatal mortality globally. Low birth weight can be caused by short gestation or intrauterine growth restriction (Mc Cormic, 1985). Growth restriction in utero may be due to many reasons; fault in the ovum, placental malfunction limiting the supply of nutrients and oxygen to the foetus or disease, malnutrition, smoking or excessive alcohol consumption of the mother (Kramer, 1987). Mother's short stature and low weight before pregnancy has been shown to be associated with newborn's low birth weight. These mechanisms are not well known and these factors may have influence over several generations (Wang et al., 1995; Aber et al., 1997). Maternal smoking affects intrauterine growth significantly and maternal smoking during pregnancy is associated with small birth weight, shorter length and reduced head circumference. It is also associated with smaller organ size and poorer organ function (Pringle et al., 2005). There is no catch up growth in length after maternal smoking during pregnancy although there is compensatory growth in weight and head circumference. Also social class has been demonstrated to have an effect on babies' size at 6 months independent on parental smoking or different feeding practises (Hindmarch et al, 2007).

Velocity of growth can also be too fast. Rapid linear growth and weight gain in childhood has been found to be associated with risks for cardiovascular diseases, diabetes and endocrine malignancy (Bruining, 2000; Singhal and Lucas, 2004; Knip et al., 2008). Especially children who have low birth weight and who are thin at 2 years and who then gain weight rapidly are found to be having increased risk of coronary events in adulthood. This growth pattern is associated with insulin resistance in later life (Barker et al., 2005; Kajantie et al., 2008).

2.1.4. Secular changes in growth

The patterns of growth at population level are not static but changing with time. Such changes are called secular growth changes. The average length, weight and velocity of growth of healthy people living in favourable environments have been increasing and the age of menarche declining all over the world as long as this positive secular trend was first observed in the mid 19th century (van Wieringen, 1978). The average height of people has increased from 1900 to present by about 1-4 cm in a decade. Women's trend has been less than men's increasing sex difference. In Northern European countries the secular trend in height appears now close to plateau but the trend in weight continues due to increasing levels of obesity (Larnkjaer et al., 2006). It seems to be taking 150 years or 6 generations to reach full height growth potential (Cole, 2003). The increase that has been observed in adult height seems to be present already at the age of two years (Cole, 2000a) although birth lengths have not increased (Cole, 2000b). Previous studies have suggested that the positive secular trend in height results from increase in leg length only (Cole, 2003). Improved nutrition, better socio-economic conditions and decline in infectious diseases are thought to be the factors responsible for the positive secular trend (Cole, 2000b; Larnkjaer et al., 2006).

2.2. Growth monitoring

Growth monitoring has long history. The oldest known longitudinal growth record was made by Count Philibert Guéneau de Montbeillard during the years 1759 -77 on the growth of his own son from birth to 18 years of age (Tanner, 1990). Regular child growth monitoring was used first time in 1850s by Guillot in order to assess milk intake of newborn babies. The first growth reference was introduced in England in 1906 (Tanner, 1981). Nowadays child growth monitoring is recognized worldwide as an

important part of primary health care. In a study by de Onis et al (2004c), 178 Ministries of Health reported monitoring child growth.

Growth monitoring can be used in different ways; for assessment and comparison of health and/or nutritional status of individual children or different populations or sub-populations, for screening and identifying children with health problems that cause growth faltering and might need treatment, for identifying undernourished children who should be included in supplementary feeding programmes, for following the effect of interventions such as medication or supplementary feeding, for demonstrating the parents the effects of appropriate nutrition and child care practices and to motivate parents to improve their performance. In addition, growth monitoring provides regular contact with primary health care workers and helps detecting also other problems (Asworth et al., 2008). Growth monitoring in developing countries aims mostly at identification of malnutrition and in developed countries the main aim is to retrieve growth disorders, such as Turner Syndrome, growth hormone deficiency and celiac disease (van Buuren et al., 2004; Grote et al., 2008).

Detecting pathological growth from normal but unusual growth is a demanding task due to the wide variation of normal growth (Sorva et al., 1990). Proper growth monitoring consists of serial measurements of at least weight and height over time so that growth velocity can also be assessed. Accurate measurements with standardized measurement technique, good quality equipment and trained, reliable measurers who can adequately interpret the results and also explain the caregivers the actions needed are fundamental for beneficial growth assessment. This requires well functioning health system as a whole allowing also referral to further investigation, adequate treatment and follow up (Dietitians of Canada et al., 2004). Growth monitoring increases the utilization of health care facilities but can reduce the overall costs due to fewer referrals to curative care. However, growth monitoring itself hasn't been found to improve child-care practises but it should always be combined with education of the parents (Wright et al., 1998; Asworth et al, 2008).

Although growth monitoring is widely used all over the world, relatively little research has been conducted on its potential benefits and harms. Evidence on its sensitiveness and specificity as a tool in identification of anomalies is limited especially during the first years when "growth canal crossing" is common even in normal children (Garner et

al., 2000; Grote et al., 2008). However, this is probably due to lack of research rather than evidence against the benefits (Dietitians of Canada et al., 2004).

2.2.1 Growth references and standards

An important requirement for proper assessment of child's growth is a reliable growth reference or standard against which to compare the growth. A reference or a standard is a database defining the statistical distribution of anthropometric measurements of a population it is derived from. It is usually presented as a chart plotted against age (Cole, 2007). Deviances from reference values may indicate problems in growth and need for further investigations (Cole, 1990). If a reference is inadequate, it may lead to false conclusions on child or population well being and even to missed or wrong treatments or interventions (Garza and de Onis, 1999). Updating of a growth reference should be considered regularly since secular changes in growth lead to changes in average size and shape of children. Typical time interval for growth reference updating is 15 years (Cole, 2006).

Construction of a growth reference is a complex task. Data can be collected cross-sectionally using different children at different ages, longitudinally using the same children at each age point or using both methods as a mixed longitudinal study (Cole, 2006). To achieve reliable data, the sample size should be at least 200 individuals in each age and sex group, the sample should be representative of the population using the reference, sampling procedure clearly defined and measurement procedure standardized. For the curve construction, state-of-art statistical methods should be used and the procedure meticulously recorded and reported. Finally the health workers using the growth charts should be adequately trained (Waterlow et al., 1977).

There is a significant difference between growth references and standards. A growth reference has a descriptive approach. It describes how children of a certain population grow in certain time and is not universally applicable in other populations. A representative sample of children from certain population is chosen for construction of a reference. A growth standard has a prescriptive approach describing how children should grow. Well nourished children who grow in optimal environments and under optimal conditions are chosen for development of a standard (Garza, 2006; Mei et al., 2008).

A problem in growth reference construction and use is that the information is already old when the reference is published since data collection is a time consuming task. In

addition, the secular trend in a reference population may also be towards less desired direction and this has to be taken into consideration when a reference is being updated. This is especially true with BMI charts due to fast increasing obesity levels. It may actually be beneficial not to update those references at all since updating would “normalize” obesity (Cole, 2007).

Standards do not change over time (unless knowledge on optimal growth changes) and they also promote healthier weight gain (Cole, 2007). Nevertheless, standards also have disadvantages. If a growth standard that is made according to the growth of the most affluent children is used for screening of children from a standard population, there is a risk that large amounts of totally normal children are ascertained as pathological. This may cause unnecessary anxiety in parents and neglect of those children who are truly pathological and also cause pressure for health care systems (Tanner, 1990).

The selection of a growth reference or a standard that is utilized is very important in defining the nutritional status of individual children and populations. Average nutrition status of the reference population determines also the status of monitored individuals since it is assessed against the reference. Different references may flag significantly differing amounts of growth faltering and this has to be considered carefully when a reference or standard is selected for use (WHO, 1995a).

2.2.2 Indicators and cut-off points

A body measurement itself has no value unless it is related to age or another measurement e.g. weight related to height. These combinations of measurements are called anthropometric indices. The term “indicator” relates to the use of indices e.g. weight for height is an indicator of body composition. Cut-off points are the limits that determine growth faltering when different indicators are used. Selection of indicators used for growth assessment and definition of cut-off points are crucial for the amount of growth faltering detected by a reference (WHO, 1995a; WHO, 1995b).

Indicators that are used commonly in growth monitoring are length/height-for-age, weight-for-age, weight-for-length/height, body mass index-for-age, head circumference-for-age and mid upper arm circumference (WHO, 1995a; WHO, 2006b). Weight-for-height (wasting or obesity) indicates present or recent state of health and nutrition and height-for-age (stunting) past or long term nutrition. They are considered as primary indicators of nutritional status. Weight-for-age (under- or overweight) is an indicator for

acute and chronic conditions and it is useful when serial measurements are taken in child health clinics, particularly in children under 1 year old and if height measurements can not be taken accurately (Waterlow et al., 1977; Fenn and Penny, 2008).

Cut-off points should be sensitive enough to identify as many pathological cases as possible but also specific enough to identify only few false positives. Cut-off points of 3rd and 97th centile or -2 or +2 standard deviations (SD) are commonly used as conventional limits of normal growth and provide feasible limit for referral. 3% of children lie under or above these limits and are considered as potentially pathological although most of them are in fact normal. Children who have truly pathological growth usually lie closer to 1st centile (Dietitians of Canada et al., 2004; Tanner, 1990). If a child is short (below 3rd centile) or tall (above 97th centile) the child should be examined more thoroughly and the heights of child's parents should be measured. If the child is within the normal limits of the parents, then the height is most probably normal unless the parents' have a growth disorder or have grown in unfavourable conditions (Tanner 1990). WHO recommendation for management of severe acute malnutrition is -3 SD for weight-for-height which is equivalent to 0.13th centile (WHO, 2009).

More important than the child's position in the relation to the 3rd and 97th centile are the velocity of growth and the direction of series of measurements. Most children with growth failure have slow growth velocity and measurements of velocity identify the abnormal growth better and faster than measurements of distance (i.e. height-for-age). If the direction of measurements is continuously away from the median of the reference, i.e. the growth is "crossing centiles", it often indicates pathological condition (Tanner, 1990; WHO, 1995a; WHO 1995b). A general rule is that crossing more than one percentile line or failure to gain weight between two consecutive measurements is alerting (WHO, 1995a). However, change towards the mean of the reference is less alarming than changes away from it (Pere, 2006). All percentile positions of different anthropometric measurements of an individual child should be close to each others. If one measurement is different, it may also indicate problems (Dietitians of Canada et al., 2004).

2.2.3 Growth charts

Growth chart is a graphic presentation in which growth curves are constructed according to the anthropometric measurements of a child and plotted against reference curves. Reference curves are drawn on the chart representing the distribution of

reference measurements at each age. A child's measurement's position related to the population he represents and the trend of his growth performance can be visualised in a chart (Cole, 1990).

The frequency distribution of anthropometric indices can be expressed in growth charts with three different systems; as Z-scores (standard deviation scores), percentiles or percent of median. Z-score expresses the measurement's position in a reference population as a standard deviation from the median of a reference population. Its advantage is that means and standard deviations can be calculated for groups of z-scores and interpreted under normality (WHO, 1995a; Pere, 2000).

Percentiles or centiles tell how many percentages of reference children are above the individual children's measurement. 50th centile represents median so that 50% of children are shorter and 50% taller than the 50th centile. Height is often distributed normally, but weight is not. Centiles are easy to understand and interpret but means and standard deviations can not be calculated since change in percentiles in different parts of the distribution corresponds to different amounts of absolute height or weight. In addition, centiles don't accurately classify children who are at extremes of the distribution (WHO, 1995a; Waterlow et al., 1977).

Percent of median expresses how many percentages the individual's measurement is from reference population's median. It is easy to understand but it lacks exact correspondence with a fixed point of the distribution across ages and cut-offs for different indices are not the same (WHO, 1995a).

A growth curve is a curve joining the values of specified z-scores or centiles at different ages. A common practice is to draw seven reference curves on a chart representing the mean, and one, two and three SDs above and below the mean or seven centile curves for 3rd, 10th, 25th, 50th, 75th, 90th and 97th centiles. Individual child's curves are then drawn on the reference curves and his size or growth can then be assessed comparing the values (Cole, 2006).

Velocity curves can be often more informative than linear growth curves. Three distinct phases of growth can be seen in the velocity curves. First is the phase of rapid decelerating growth from birth up to 2-3 years. A small spurt in growth velocity can often be seen related to the change from infant growth phase to the childhood phase

(Karlberg et al., 1994). Second phase is the slowly decelerating phase from 3 years to the beginning of the adolescent growth spurt and the third phase is the adolescent growth spurt phase (Lejarraga, 2006).

2.2.4 Growth curve smoothing

In order to attain smooth growth curves from data that always have sampling and measurement variability and remaining outliers, growth curves have to be smoothed. Even with large samples, lack of smoothing leads to very irregular growth curves. However, over-smoothing flattens the biological growth pattern's peaks and valleys and leads to biased curves (Borghini et al., 2006). Smoothing normalizes skewed distribution of anthropometric measurements using power transformation which stretches one tail of the distribution and shrinks the other (Cole, 1990). Smoothed centile values can be converted to z-scores which allows more precise assessment of growth of children who are at the extremes of the distribution (Fenton and Sauve, 2007).

There are several methods for curve smoothing and no single method is best for all purposes. Estimates of growth faltering may be sensitive to the method chosen (Flegal, 1999). Cole's LMS method is often used method to fit smooth centile curves to reference data. The LMS method uses Box-Cox power transformation to normalize the distribution and cubic spline¹ technique is used for fitting the curves. Rescaled time axis can be used to stretch the periods of rapid growth, e.g. infancy, and compress the periods of lower growth velocity. That usually gives better fitting when the data is monotonous but complex like height or weight growth data often is (Cole et al., 1998). LMS method produces three different curves, L representing skewness, M the median and S the coefficient of variation². Extend of smoothing required is expressed as equivalent degrees of freedom (edf values)³. The fitting of the parameters can be assessed by detrended Q-Q plots⁴ and Q tests⁵ for fit (Pan and Cole, 1997-2005). Percentile curves can then be generated from the smoothed LMS parameters and they allow the calculation of z-scores (Borghini et al, 2006).

Edge or boundary effect in growth curve construction means that the precision of the estimated values is smaller at the extremes of the age range than close to the mean. The

¹ A polynomial function that passes through a set of control points

² The ratio of the standard deviation to the mean

³ The number of control points used to fit the cubic splines

⁴ Plots that compare the distribution of a given set of observations to the normal distribution

⁵ A statistical test which combines overall and local tests assessing departures from the normal distribution with respect to median, variance, skewness and kurtosis

effect can be minimized by over-sampling at birth (four fold) and by extending the age range during the smoothing by one year over the target age. (Borghi et al., 2006; Ignatius, personal communication).

2.3. The Finnish national growth reference

The reference that is currently utilized in every child health clinic in Finland was published in 1986 and it was reviewed 1994 so that some errors were corrected and screening rules were revised (Ignatius, personal communication; Pere, 2000). The 1986 reference replaced the older Finnish reference published in 1964. The current reference uses data from two sets of healthy Finnish children born in 1954-1962 (94% in 1959-1961) and in 1968-1972 (99% in 1969-1971). Mixed longitudinal data for construction of the reference was collected retrospectively from schools and health centres in Helsinki and in Eastern Finland. The data consists of measurements of 1143 boys and 1162 girls and over 45 000 recordings (Pere, 2000).

Premature children, infants with low (<2.5kg) or unknown birth weight, twins and unhealthy children were excluded from the reference population. Finnish reference curves were smoothed using LMS method. The downward change in children's measurements, when length measurement changes into height measurement at 24 months, was dealt by smoothing the curves over the age point so that the gap diminishes (Ignatius, personal communication). Detailed description of the methodology of the growth reference construction has not been published.

In the Finnish reference, growth is assessed using height-for-age (HFA) and weight-for-height (WFH) indices. Height in the charts is presented as standard deviation scores (SDS). Weight is presented as deviation in percentages from the median weight-for-height of the reference. Median weight-for-age (WFA) is also given but it has been estimated from the HFA and WFH values and is relatively reliable only for children whose weight and height is close to the median. Standard deviation for weight is not given since it was believed that weight data can not be well normalised in the tail areas of the distribution. In the growth charts, horizontal line represents normal growth thus deviations or changes in individual "growth channel" can easily be detected by eye (Ignatius, personal communication; Pere, 2006). In addition to the growth curves, Finnish reference gives screening tables for the change of relative size and for the

relative size itself to allow screening of growth faltering by “centile crossing” (Perheentupa and Pere, 1997).

2.4. The WHO 2006 growth standard

WHO published a new international growth standard for infants and children up to age of 5 years in April 2006. For the first time, an international growth standard was constructed to describe how children should grow disregarding of their ethnic background, place of living or time of assessment instead of describing how children are growing in a certain population and in a particular time. The standard was made to replace the 1977 National Centre for Health Statistics (NCHC) growth reference which was used internationally but which had several weaknesses, e.g. it was derived only from cohorts of US children who did not necessarily follow the feeding practises that are considered optimal. The observation that healthy breast fed infants have different growth patterns than the references which were used was the main reason to develop a new standard that used breast feeding as a norm (Garza and de Onis, 2004). The aim was to provide a tool for more accurate estimation of adequate feeding and improve the ability to detect children who are in process of becoming under- or over nourished (Garza, 2006). WHO Multicentre Growth Reference Study (MGRS) was conducted between 1997 and 2003 to develop the standard (de Onis et al., 2006a; WHO, 2006 b).

For the study, anthropometric data was collected from widely differing ethnic backgrounds and cultural settings from six sites around the world: Pelotas, Brazil; Accra, Ghana; New Delhi, India; Muscat, Oman; Oslo, Norway; and Davis, CA, The United States. The MGRS collected data on the growth of 8500 healthy, breastfed infants living under conditions likely to enable the achievement of their full genetic growth potential, combining a longitudinal component of children aged 0-24 months and a cross-sectional component of children aged 18-71 months (Garza, 2006; WHO, 2006a; WHO, 2006b). The data was collected and managed using rigorously standardized methods that lead to high quality data. Standard values for length/height-for age, weight-for-age, weight-for-length/height and body mass index-for-height were developed and presented as z-scores and percentiles. Data collection and management methods, inclusion and exclusion criteria and methods for construction of the standards

are explained fully elsewhere (de Onis et al., 2004a; de Onis et al., 2004b; Onyango et al., 2004; Borghi et al., 2006; WHO, 2006a; WHO, 2006b; WHO, 2006c)

Several studies have been conducted on comparison of the WHO standard with different references or growth of children in different countries and the WHO standard is already widely utilized. However, there are studies reporting remarkable variation in length/height between the different sites e.g. in countries like China that has not been included in the study, questioning the universal applicability of the standard (van Buuren and Wouwe, 2008; Hui et al., 2008; Wright et al., 2008). For this reason, more comparative studies are needed on assessment of individual children in different populations. However, if the WHO standard is used, it certainly shows how much local populations differ from global standards (van Buuren and Wouwe, 2008).

The switch to WHO standards has had significant impacts on the numbers of children diagnosed of having growth faltering. Because of different cut-off values of the WHO standard, remarkably more children are identified as being severely malnourished than when the old WHO/NCHS 1977 reference was used in nutrition programmes. This has led to shorter treatment periods, better recovery rates and less deaths (Seal and Kerac, 2007; Isanaka et al., 2009; WHO and UNICEF, 2009). The WHO standard has also shown to be better than some national references in identifying excess weight gain at its early stages when interventions are also more effective (van Dijk and Innis, 2009). In addition, because breast feeding is a norm in the WHO standard, it has also shown to be reflecting growth of predominantly breast fed infants better than national references (de Onis et al, 2006b).

2.5 Justification for the present study

Studies on average linear growth of Finnish children has not been published since the currently utilized Finnish national growth reference was constructed thus it has not been assessed if the reference still reflects adequately contemporary growth of Finnish children. In addition, WHO claims that their 2006 published standard could and should be used worldwide since it promotes optimal growth. Overweight and obesity prevalence has reported to be increasing worldwide (Ekblom et al., 2004; Lobstein et al., 2004; Wang et al., 2007) and also among Finnish children (Kautiainen et al., 2002; Hakanen et al., 2006; Vuorela et al., 2008). Studies on comparison of the growth of

Finnish children and the WHO standard has never been published and the WHO standard's applicability for Finland has never been assessed although the standard is already widely adopted elsewhere.

Previous studies have shown that predominantly breastfed infants have different growth patterns than formula fed infants (Dewey et al., 1995; Dewey, 2001) and that predominantly breastfed infants grow slower than reference infants in many countries (Dewey et al., 1995), including Finland (Salmenperä et al., 1985). In 1960's and 1970's, when most of the Finnish growth reference children were born, breast feeding levels were lower than in any other time, years 1970-1972 having the lowest levels of all times. After that, breast feeding levels have increased rapidly mostly due to longer maternity leaves and active breast feeding promotion programmes. This change has been exceptionally fast in Finland, assumable faster than in any other western country (Verkasalo, 1980; Verronen, 1988; Hänninen-Nousiainen et al., 2004). In 1962 48% of 3 months old infants and 14% of 6 months old infants were at least partially breastfed and in 1970 the proportions were 30% and 9% respectively (Verkasalo, 1980). By 2005 the levels had increased remarkably so that 76% (51% exclusively) of 3 months old and 60% (1%) of 6 months old infants were at least partially breastfed (Hasunen and Ryytänen, 2006). In 1996-1999, children in Tampere region were breastfed on average 7 months (Erkkola et al., 2005). Also recommendations and patterns of complementary feeding have changed remarkably in Finland from the 1960's and 1970's and that has also influenced growth of children (Siimes et al., 1985; Hasunen and Ryytänen, 2006). In conclusion, feeding recommendations and feeding patterns of the Finnish reference children were different than feeding patterns today. It is important to ensure that the growth reference utilized adequately reflects the growth of infants that are fed according to the current recommendations (WHO and UNISEF, 2003; Sosiaali- ja Terveysministeriö, 2004).

Because the average anthropometric measurements of a population can change considerably over a time due to secular changes, the standard values of the used growth reference should be determined regularly (Cole, 2006). Scanty evidence suggests that secular trend has stopped in some Northern European countries (Larnkjaer et al., 2006; Schmidt et al., 1995), including Finland (Dahlström et al., 1984) although in a study by Sorva et al. (1985) some secular changes were still detected. Studies on continuity of positive secular trend in Finland have not been published since these studies.

3. OBJECTIVES

The objectives of the study were to describe the contemporary growth of Finnish children and to assess the prevalence of growth faltering according to the references.

The specific objectives were:

1. To compare the lengths/heights and weights of the study children to the Finnish national growth reference
2. To compare the lengths/heights and weights of the study children to the WHO 2006 growth standard
3. To compare the proportions of stunted, very tall, underweight, overweight, obese and wasted children identified by the Finnish national growth reference or the WHO growth standard

4. METHODS

4.1. Study design

Anthropometric data of 0 to 4 years old children born during one calendar year were collected retrospectively from Tampere municipality child welfare clinic register in order to assess their growth patterns. The data were semi longitudinal but were handled cross-sectionally. Permission for the study was obtained from Tampere Municipality Institutional Review Board but the participants were not contacted since the data were handled anonymously.

4.2. Study site

The study was carried out in Tampere, Finland. Finland itself is a high-income country in northern Europe with a population of 5.3 million inhabitants. Tampere is a city situated in southern Finland. Its population of 210 000 inhabitants makes it Finland's 3rd biggest city. Tampere area has net migration and mixed population originated from different parts of Finland. Tampere municipality has a health centre with almost 60 child welfare clinics scattered around the area and more than 200 public health nurses monitoring the health of pre-school aged children. The Finnish public health nurses are specially educated in child health and prevention and their core duty is to assess the health and development of infants and pre-school aged children, including standardized anthropometric measurements. This screening system is well developed and monitors nearly all pre-school aged children living in Finland. All visits are free of cost for all of the inhabitants who belong to the Finnish social security system.

4.3. Study subjects

The target population for enrolment included children who were born over period of one year between 1st of October 2003 and 30th of September 2004 and who had visited Tampere Municipality child welfare clinics between 1st of October 2003 and 4th of November 2008. Eligible participants were identified from Tampere municipality child welfare clinic register (Pegasos program). The study population consisted of children from all social groups and from families with high, moderate and low income.

Inclusion criteria for the study subjects were: born between 1st of October 2003 and 30th of September 2004, at least one anthropometric measurement taken in Tampere municipality child welfare clinics and recorded with the Pegasos computer program. There were no exclusion criteria at the data collection phase.

4.4. Data collection

The children living in Tampere were scheduled to have regular visits in the child welfare clinics where their health and development was followed and anthropometric measurements were taken. Each child was scheduled to visit a clinic at the age of 1-2 weeks, 3-4 weeks, 6-8 weeks, 2 months, 3 months, 4 months, 5 months, 6 months, 8 months, 10 months, 12 months, 18 months, 24 months, 36 months and 48 months. Children may have had also extra visits if their health or development had been of special concern. Children who had moved to or from Tampere Municipality area during the period that the data was collected from had had fewer visits. At each scheduled visit weight and length/height was supposed to be measured and head circumference was supposed to be measured up to two years of age. The birth measurements were taken in a hospital where the child was born and recorded in the register afterwards according to the information sent from the hospitals.

Standardized and calibrated measurement equipment was used in each clinic and in principal, same public health nurse assessed the same children at each visit using same measurement equipment. Weight was measured with an electronic scale in principle to the nearest 5 g (some to the nearest 1g) while child was naked or in light clothes. Length was measured to the nearest millimetre in supine position up to 24 months using length boards and in standing position thereafter using tape measurement with vertical plane and measurement attached on the wall. Public health nurses recorded the measurements in the municipality electric records (Pegasos program). Pediator program (Markkula,2005), that uses the Finnish reference database for drawing the growth curves, works as part of the Pegasos program.

4.5. Methods used for data extraction

This cross-sectional study was a secondary analysis of child health and anthropometric data recorded and stored electronically in to the Tampere municipality health registries

as part of child welfare clinic activity. The data was collected retrospectively from the registry by Tampere Information Technology Centre at the end of October 2008 and formed three Excel files. One to sixteen measurement events were obtained from each child.

4.6. Variables

Lists of all children born in predefined period, consisting of their identification codes, birthdays, measuring days, sex, weight, height and head circumference, were collected from the register and formed an Excel file. Another Excel file, consisting of the social security numbers and identification codes of the same children, was also formed. Two files were formed so that they can be combined later in case additional information on these children needs to be collected for later studies. In addition, other baseline data of the participants were also collected for needs of later analysis (see Appendix 1.). These data formed another Excel file.

4.7. Outcome measures

The primary outcome measures were:

- a. Attained length/height in centimetres between 0 and 48 months of age
- b. Attained weight in grams between 0 and 48 months of age

The secondary outcome measures were:

- a. Proportion of children in different age categories classified as stunted (<-2.7 SD) according to the Finnish growth reference or moderately ($HAZ < -2$) or severely ($HAZ < -3$) stunted according to the WHO growth standard
- b. Proportion of children classified as tall ($>+2.7$ SD) according to the Finnish growth reference or tall ($HAZ > +2$) or very tall ($HAZ > +3$) according to the WHO growth standard
- c. Proportion of children classified as wasted (weight for height $<-15\%$ from reference median) according to the Finnish reference or moderately ($WAZ < -2$) or severely ($WAZ < -3$) underweight or moderately ($WHZ < -2$) or severely ($WHZ < -3$) wasted according to the WHO standard
- d. Proportions of children classified as obese (weight for height $> +20\%$ from reference median) according to the Finnish reference or moderately ($WAZ > +2$)

or severely (WAZ >+3) overweight or moderately (WHZ >+2) or severely (WHZ > +3) obese according to the WHO standard

4.8. Data management

Analysis was done mainly using STATA 9.0 statistical software (StataCorp, College Station, TX, USA). The comparison of growth of the study population to the WHO standard and calculation of the anthropometric indices: weight-for-height z-score (WHZ), weight-for-age z-score (WAZ) and height-for-age s-score (HAZ) were done with WHO Anthro STATA macro that uses the 2006 published WHO standard data as reference. For comparison of the study population and the Finnish reference, anthropometric indices were calculated with MS Office Excel 9.0 computer program using currently utilized Finnish reference population data base. Cole's LMS method and LMS ChartMarker Pro version 2.3 (Harlow Printing Limited, UK) software was used for smoothing the growth curves. Growth curves were drawn with MS Office Excel 9.0 computer program and the growth curves attained from the study data were plotted against the reference curves with MS Office Power Point program.

4.9. Data cleaning

The check for data errors included the following variables: birth date, date of measurement, age at visit, weight, length/height and head circumference. The data was cleaned using STATA 9.0 software. WHO Anthro STATA macro was used in calculating anthropometric indices WAZ, HAZ and WHZ for the anthropometric data. Children who did not have sex or permanent id code recorded were excluded from the study.

Duplicate entries (observations that were recorded more than once) were identified and excluded. Recordings of children who had negative age were checked. The date of the measurement was corrected if possible and otherwise the measurement was excluded. All very low (<-5) and high (> +5) values for WAZ and HAZ were checked. Children who had high or low HAZ or WAZ measurements were identified and all of their measurements were checked for consistency. If measurements were found not to be consistent with the child's other measurements, errors were corrected if possible and otherwise measurements were excluded. Scatter plots were drawn from height and

weight measurements of boys and girls separately. All possible outliers were checked by identifying the individuals and checking all of their measurements. If those measurements were found to be consistent with child's other measurements, they were considered valid. Otherwise they were excluded. At the end, new anthropometric indices WHZ, WAZ and HAZ were calculated for the corrected and cleaned data.

Only one observation per child per target age was included in the study in order to avoid over presentation of children who had extra visits outside of the target ages and assumable growth faltering. Age windows were created and only the measurements closest to the target age were included. Then children with very low birth weight (<1.5 kg) were identified and excluded.

4.10. Addressing potential sources of bias

Inhabitants from the whole Tampere municipality area were included to avoid selection bias regarding different living areas and social groups since some of the areas have more affluent inhabitants than the others. Data of children born during one calendar year was collected to avoid bias caused by seasonality of growth. All extra visits outside of the target ages were excluded. It was assumed that those children who had extra measurements taken had had some growth faltering and over presentation of their measurements would probably have depressed the growth curves.

4.11. Sample size and its justification

This sample from the population based cohort yielded in sufficient number of observations at each age group. The required amount of measurements was predefined earlier as being 200 at each age group or 800 measurements per year for both sexes in this kind of a study in order to estimate the mean and the standard deviation well, to provide adequate information about the distribution of the data and to attain adequate results when fitting the curves with LMS method (WHO, 1995b; van Buuren and Fredriks, 2001; de Onis et al., 2004a; Cameron, 2006). The measurements were not grouped at exact ages but distributed along the whole age ranges (Cameron, 2006). Age groups that were used for the sample size calculation were: 0 to 12 (0 - 12.500) months, 13 to 24 (12.501 - 24.500) months, 25 to 36 (24.501 - 36.500) months, 37 to 48 (36.501 -

48.500) months and 49 to 61 (48.501 – 61.000) months. Age group of 49 to 61 months was used only for data smoothing purpose but not in other analysis.

4.12. Construction of the growth curves

Age groups of 0, 0.5, 1, 1.5, 2, 3, 4, 5, 6, 8, 10, 12, 18, 24, 36 and 48 months were created for checking the data. The distributions of weight and height were examined for normality by checking normality plots (histograms), comparing median and mean values and calculating skewness and kurtosis for the distribution at each age group.

Cole's LMS method and LMS ChartMarker Pro program version 2.3. (Harlow Printing Limited) were used for smoothing the growth curves. To reduce the "right edge effect", i.e. to make the precision of the estimated values good also at the end of the target age range, the age range was extended over the target age 48 months, up to 60 months during the smoothing process. The "left edge effect" was assumed to be quite small, i.e. the precision of the estimated values were good also at the beginning of the age range. Curve smoothing was done using all of the attained measurements and exact ages in days (i.e. not age groups).

Optimal degree of freedom values (edf) for the L curve (Box-Cox power to reduce skewness), M curve (median) and S curve (coefficient of variation¹) were determined. Rescaled age² was used to improve the fitting of the L, M and S curves. Distribution of the constructed growth curves were assessed with Q-tests. Edf values were chosen so that the L, M and S curves were in or as close as possible to the range of -2 to +2 in the Q-test, indicating normal distribution. Deviance change was followed and values were chosen so that deviance between consecutive edf values was less than 10 or close to it. Distribution was also assessed by detrended Q-Q test. Level of kurtosis was noted although LMS method does not model kurtosis (Cole, personal communication³). Level of kurtosis was considered not to be very important in this analysis since it mostly affects the extremes of the distribution and in this study, 5th, 50th and 95th curves were

¹ A ratio to the standard deviation to the mean

² An empirical transformation based on the fitted M curve. Rescaled time axis can be used to stretch the periods of rapid growth, e.g. infancy, and compress the periods of lower growth velocity. This process can greatly improve the fit of complex monotonic data (Pan and Cole, 1997-2005).

³ Dr Tim Cole is a Professor of medical statistics at the University College London, Institute of Child Health. He was a member of the WHO Multicentre Growth Reference Advisory Group and participated the construction of the WHO 2006 growth standard. He has also developed the LMS method.

drawn and compared, not the extremes. At the end, attained median values were compared with the empirical medians of the study data and assured that the smoothed medians were close to the empirical medians. Large difference from the observed medians would have indicated over smoothing of the curves which is not desirable since it flattens the natural variation in growth patterns.

To make the growth curves as comparable as possible, the same methods that were used for construction of the reference curves were followed as closely as possible when constructing growth curves from the study data.

4.12.1 Construction of the velocity curves

Growth velocity of the study population was assessed by constructing growth velocity curves for height and weight separately for girls and boys. This was done mainly for data checking purposes and to give a general idea of the growth velocity of the children. Velocity was not assessed at individual level but LMS smoothed median values for the study population were used for velocity curve construction so that attained growth in centimetres or in kilograms were calculated for each month. For height curves, LMS values that were used for comparison with the Finnish reference were used to avoid the 7 mm drop at 24 months that results from measurement position change when WHO method is used.

4.12.2. Construction of the HFA curves for comparison of the Finnish reference and the study population

Finnish reference values for height were taken from the Finnish reference database (Markkula, 2005). Since only mean and standard deviation values for height were given in the database, 5th and 95th centile values were calculated from the reference values with a formula:

$$95^{th} \text{ centile: } M + (SD * 1.645)$$

$$5^{th} \text{ centile: } M - (SD * 1.645)$$

where M is the mean value and SD is the standard deviation value.

Reference curves for 5th, 50th and 95th centiles were then constructed.

Growth curves were smoothed with LMS method as explained earlier. Edf values for L, M and S were chosen so that they gave the best fit for all of the curves. The gap between the measurements, when the measurement position was changed from supine

to standing position, was handled by smoothing the curves well over the age where the position change happens (at 24 months) to follow the Finnish reference construction methods as close as possible (Ingnatius, personal communication). Since the curves were smoothed using age range up to 60 months, the gap at 24 months smoothed and also the “right edge effect” was handled.

Growth curves were drawn from 5th, 50th and 95th centile values at 0 to 48 months of age. Then growth curves of the study population, boys and girls separately, were plotted against the growth curves of the Finnish reference to make the comparison.

4.12.3. Construction of the HFA curves for comparison of the WHO standard and the study population

The WHO standard values for height were adopted from the WHO standard technical report (WHO Department of Nutrition for Health and Development, 2006) and 5th, 50th and 95th centile curves were constructed from the values.

To fit a single model for the whole age range and to follow the WHO method as closely as possible (WHO, 2006b), height of the sample children were first adjusted so that 7mm was added to all measurements after 23 months. Then LMS program was used to smooth the growth curves of the sample children using method described in earlier chapter.

After the model was fitted, 5th, 50th and 95th centile values were calculated for height-for-age. Then the curves were shifted back downwards for 7mm in ages 23 months upwards and the coefficient of variation curve was adjusted to the new median values to construct the growth curves. The adjusted coefficient of variation (S^*) was calculated with a formula:

$$S^* = StDev/M^* = M \times S/M^*$$

where S and M were, respectively, the fitted median and coefficient of variation values, M^* were the shifted-down median values and $StDev$ was the standard deviation calculated as the median times of the coefficient of variation.

New values for 5th, 50th and 95th centiles were counted from attained values and separate growth curves were drawn from 0 to 24 and 24 to 48 months of age accordingly to

allow the 7mm gap to be seen in the curves. At the end, separate curves were put into one figure. Then growth curves of the study children, boys and girls separately, were plotted against the growth curves of the WHO standard to make the comparison.

4.12.4. Construction of the WFA curves

The same method was used for construction of the weight-for-age curves for comparison of the study population data with the Finnish reference and for comparison of the study population data with the WHO standard. LMS method was again used to smooth the study population growth curves with the method explained in earlier chapters.

For comparison with the Finnish reference, 5th, 50th and 95th centile curves of the study population data were plotted only against 50th centile (median) curve attained from the Finnish reference measurements. Other centiles for the Finnish reference were not possible to calculate since only median weight and no standard deviation was given in the reference database¹. For comparison with the WHO standard values, growth curves for 5th, 50th and 95th centile values of the study population data were constructed and plotted against same centile curves constructed from the WHO reference values.

4.12.5 Construction of the relative height and weight curves for comparison of the Finnish reference and the study population

To compare the relative growth of the study population and the Finnish reference population, curves for median HFA, percentages of median weights from reference median weights and weight as percentages from height specific target weights were constructed for the study population data and plotted against the reference medians (0 z-score or 100%). Median values were calculated in age categories for boys and girls separately. Age categories that were used for calculating the median values were 0 (0-0.129), 1 (0.50-1.49), 2(1.50-2.49), 3(2.50-3.49), 4(3.50-4.49), 5(4.50-5.49), 6(5.50-6.49), 8(7.50-8.49), 10(9.50-10.49), 12(11.50-12.49), 18(17.50-18.49), 24(23.00-25.00), 36(35.00-37.00) and 48(47.00-49.00) months. Measurements between the age categories were discarded. Histograms for each age category and for each variable were constructed for boys and girls separately to assess the distribution. In most of the age groups, the distribution was found to be slightly skewed. For curve construction purposes, values for ages between target ages were extrapolated from the target age values.

¹ Weight-for-height reference values were estimated from the weight-for-height reference values and only the median values are reasonably accurate (Ignatius, personal communication)

In construction of the HAZ curves, difference between individual lengths and reference lengths at that age was first calculated for each individual child. This difference was divided by reference length's standard deviation at that age to get standard deviation scores (z-scores) for each individual measurement. Then median values of these height-for-age z-scores were calculated in age categories. HFA curves for study population data were constructed from these median values and plotted against the reference median.

Since the Finnish reference does not have standard deviations for reference weights, z-scores for weight-for-age comparison with the Finnish reference could not be calculated. WFA values in the Finnish reference were estimated from the WFH values and thus weight-for-age comparisons are only indicative. Comparison of the study population data with the Finnish reference was made by comparing smoothed median weights that were attained from the LMS program, with the reference medians. This was done for boys and girls separately. Percentages of the study population's median weights from the Finnish reference weights were calculated in age categories. Curves were constructed according to the results and plotted against reference median. For comparison of different methods, percentages of weights of individual study sample boys from the reference weights were also calculated and medians values in age categories were calculated from these results.

When WFH curves were constructed, all lengths that were under 47 cm were excluded due to lack of reference weights for lengths less than 47cm in the Finnish reference. That lead to exclusion of 53 boys' and 77 girls' measurements. Only those measurement events that had both height and weight measurements recorded were included. At first, reference weights were identified for each individual height. Then percentages from reference weight of each individual weight measurement were calculated. After that, medians of these percentages were calculated in age categories. Finally, curves were constructed according to the results and plotted against the reference median.

4.12.6 Construction of the relative weight and height curves for comparison of the WHO standard and the study population

To describe relative growth of 0-48 month old study children and to compare it with the WHO standard population growth, curves for median HAZ, median WAZ and median WHZ were constructed for the study children's data and plotted against the reference

medians (0 z-score). Median values were calculated in each age group for boys and girls separately using WHO Anthro STATA macro that calculates the z-scores using WHO 2006 standard population as reference. Then Z-score curves from the attained values were constructed. For curve construction purposes, values for ages between the calculated age categories were extrapolated from the calculated values.

4.13. Sensitivity analysis for assessing influence of incomplete follow-up

Analysis of the whole data included all children who had at least one measurement recorded in the registry. In order to assess if growth patterns of children who had measurements recorded at each assessed age differs from the whole data, data of those children were extracted from the whole data. Only children who had both weight and height measurements taken at each age category from 0 to 12 months (0-0.129, 0.50-1.49, 1.50-2.49, 2.50-3.49, 3.50-4.49, 4.50-5.49, 5.50-6.49, 7.50-8.49, 9.50-10.49, 11.50-12.49 months) were included. Data was smoothed, growth curves constructed and curves plotted against the Finnish reference curves and the WHO standard curves using the same methods as was used for the analysis of the whole data. Also z-score curves were constructed using the same methods as with the whole data.

4.14. Identifying measurements that exceed the screening limits of the Finnish reference or the WHO standard

Numbers of measurements that indicate obesity, overweight, wasting, underweight, tallness and stunting were calculated following the screening rules of the Finnish reference and the WHO standard. Cut-off points for the Finnish reference height comparison and the WHO standard comparison were defined by using z-scores. For Finnish reference weight-for-height comparison, percentages from reference median were used.

For Finnish reference comparison, numbers of measurements that exceed the screening limits in six months age categories, 0-6 (0.00-6.50) months, 7-12 (6.51-12.50) months, 13-18 (12.51-18.50) months, 19-24 (18.51-24.50) months, 25-30 (24.51-30.50) months, 31-36 (30.51-36.50) months, 37-42 (36.51-42.50) months and 43-48 (42.51-48.50) months, were calculated. At first it was calculated, how many standard deviations each individual length/height measurement is from the reference mean or how many

percentages each weight-for-height measurement is from the reference median. For weight-for-length analysis, those measurements where height was under 47 cm were excluded (53 for boys and 77 for girls) since the Finnish reference does not have reference measurements for lengths under 47 cm. Then numbers of measurements that exceed the screening limits in each age category were calculated.

Screening limits for the Finnish reference were:

Length/height < -2.7 SD from the reference mean = stunted

Length/height $> +2.7$ SD from the reference mean = very tall

Weight for height $\leq -15\%$ from the reference median = underweight

Weight for height $\geq +20\%$ from the reference median = overweight

For WHO standard comparison, numbers of measurements that exceed the screening limits at the same age categories were calculated using WHO Anthro STATA macro.

Screening limits for the WHO standard were:

HAZ < -2 = moderately stunted, < -3 = severely stunted, $> +2$ = tall, $> +3$ = very tall

WAZ < -2 = moderately underweight, < -3 = severely underweight, $> +2$ = moderately overweight, $> +3$ = severely overweight

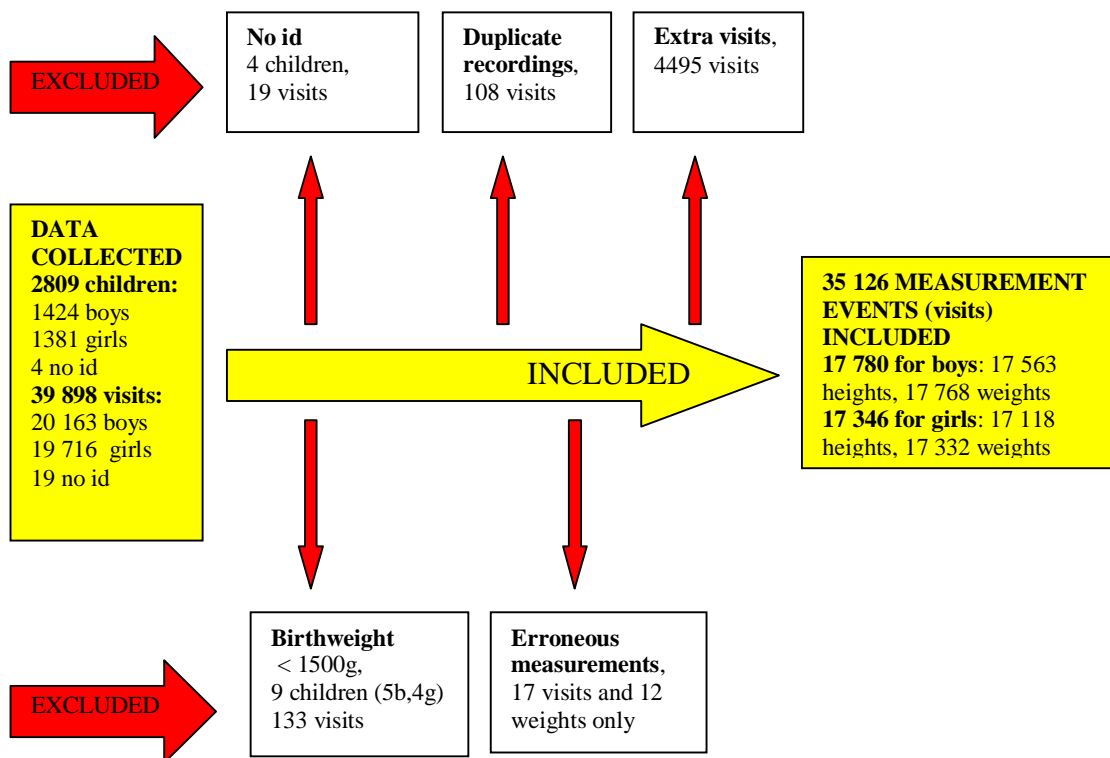
WHZ < -2 = moderately wasted, < -3 = severely wasted, $> +2$ = moderately obese, $> +3$ = severely obese

5. RESULTS

5.1. Study subjects

Extraction of data from Tampere municipality health records yielded measurements from 2809 children and 39 898 measurement events (visits). After exclusions, there were 35 126 measurement events left with 17 780 events from boys and 17 346 from girls (Figure 1.) thus 88% of the collected measurements were included in both boys and girls. There were all together 58 measurement sites (clinics) where the measurements had been recorded and 239 different measurers for weights and 234 measurers for heights when birth measurements were excluded. It was not possible to evaluate the amounts of measurement sites and measurers for the birth measurements since they were taken in hospitals but recorded into the municipality health records by other people.

Figure 1. Flow of subjects during the study



5.2 Sample size

There were 799 to 12 726 measurements for height and weight in each 12 months age group up to 48 months fulfilling all the criteria of adequate sample size. Age group of 49-61 months was used only for data smoothening purposes. The amount of measurements in the first age group was remarkably larger than in the other age groups reducing the “left hand effect” (Table 1.).

Table 1. Number of observations in age groups

Age (mo)	BOYS		GIRLS	
	Height (n)	Weight (n)	Height (n)	Weight (n)
0-12	12 518	12 726	12 132	12 346
13-24	2 912	2 909	2 867	2 869
25-36	930	930	896	895
37-48	799	800	812	812
49-61	404	403	411	410
Total	17 563	17 768	17 118	17 402

5.3 Growth velocity

Velocity curves constructed for height growth are presented in Figure 2. and velocity curves for weight growth are presented in Figure 3. Growth velocity of the sample children was found to be following the normal growth patterns of 1 to 48 months old children indicating valid data. Rapidly decelerating growth velocity was seen during the first and second year. At around 12 months growth velocity levelled indicating the shift from infant to childhood phase of growth. After that the velocity slightly decreased again up to around 24 months and then almost levelled reflecting the slowly decelerating phase of growth.

Figure 2. Sample children's growth velocity for height, boys and girls separately

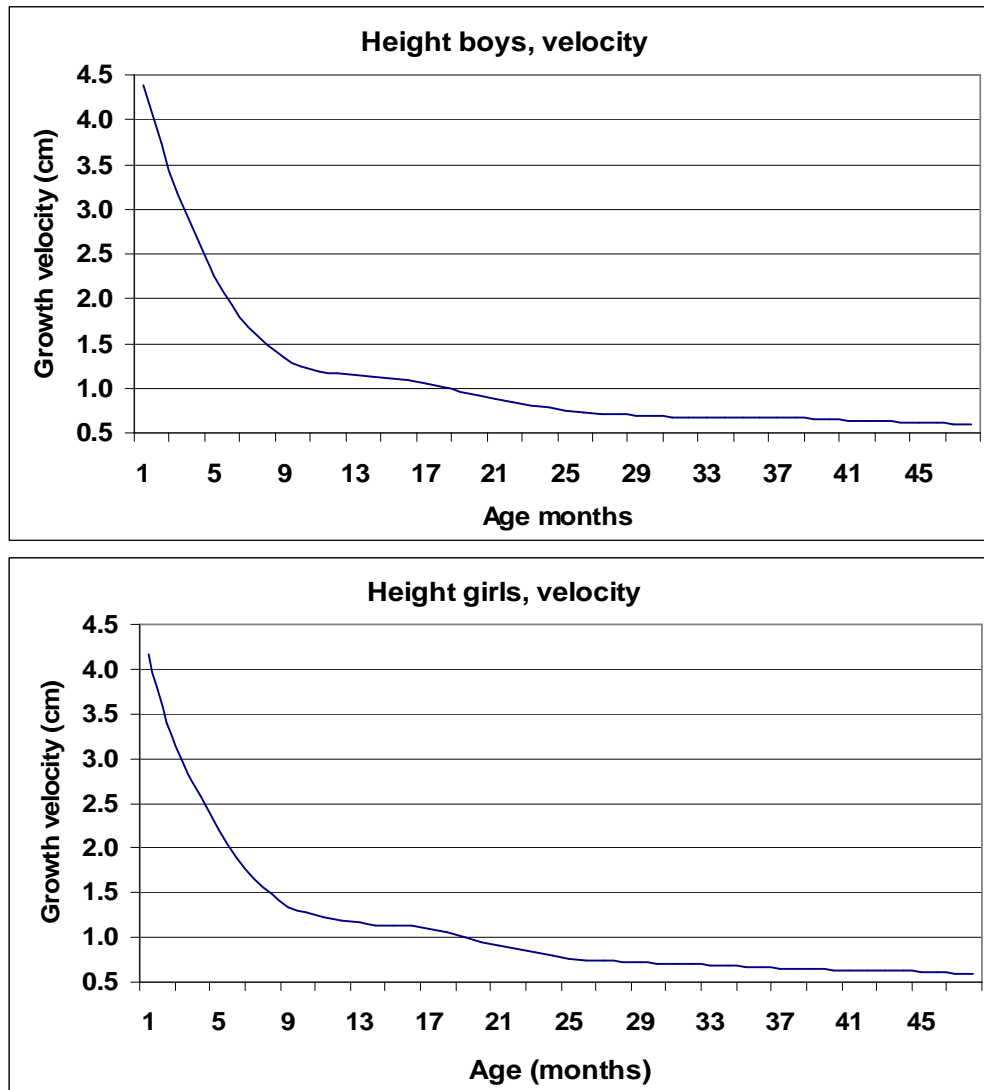
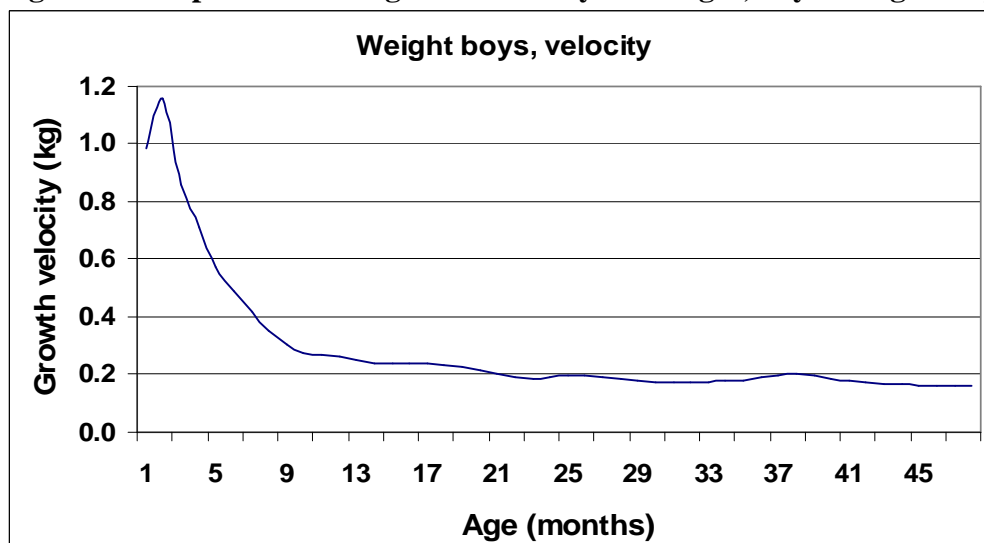
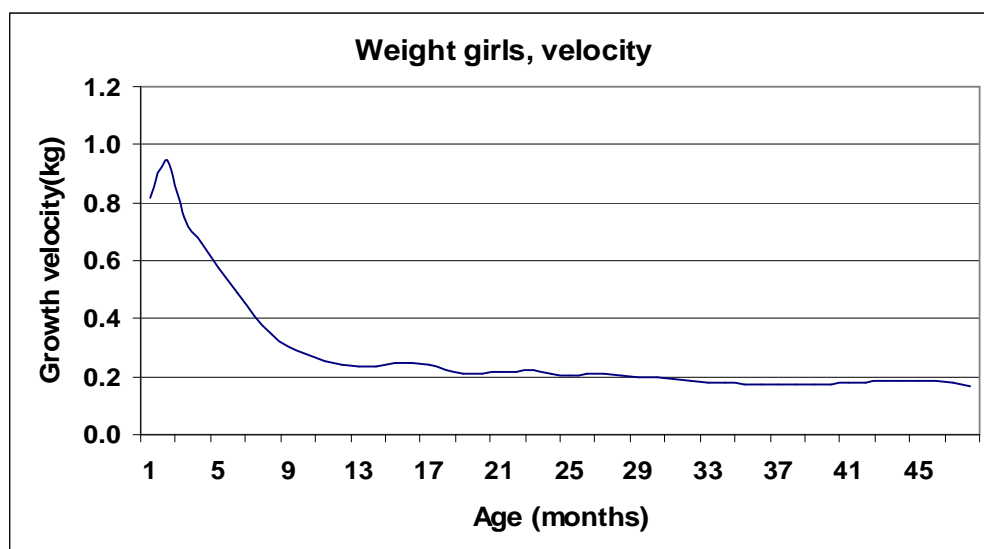


Figure 3. Sample children's growth velocity for weight, boys and girls separately





5.4. Comparison of the Finnish reference and the study population

5.4.1 LMS values

When smoothing the growth curves with the LMS method, edf values $L=5$, $M=9$, $S=4$ for boys and $L=4$, $M=10$, $S=4$ for girls were found to be optimal for heights and edf values $L=6$, $M=12$, $S=4$ for boys and $L=5$, $M=12$, $S=5$ for girls were found to be optimal for weights when using rescaled age. With these values, smoothed medians were close to the empirical medians; difference varied from 0 to few millimetres or grams in all ages and for both sexes. All curves were between -2 and +2 in the Q test and deviance was less than 10 indicating normal distribution.

5th, 50th and 95th centile values for height and weight attained by LMS method and compared with the reference centiles are shown in Appendix 2.

5.4.2. Attained height at various ages in comparison with the Finnish reference

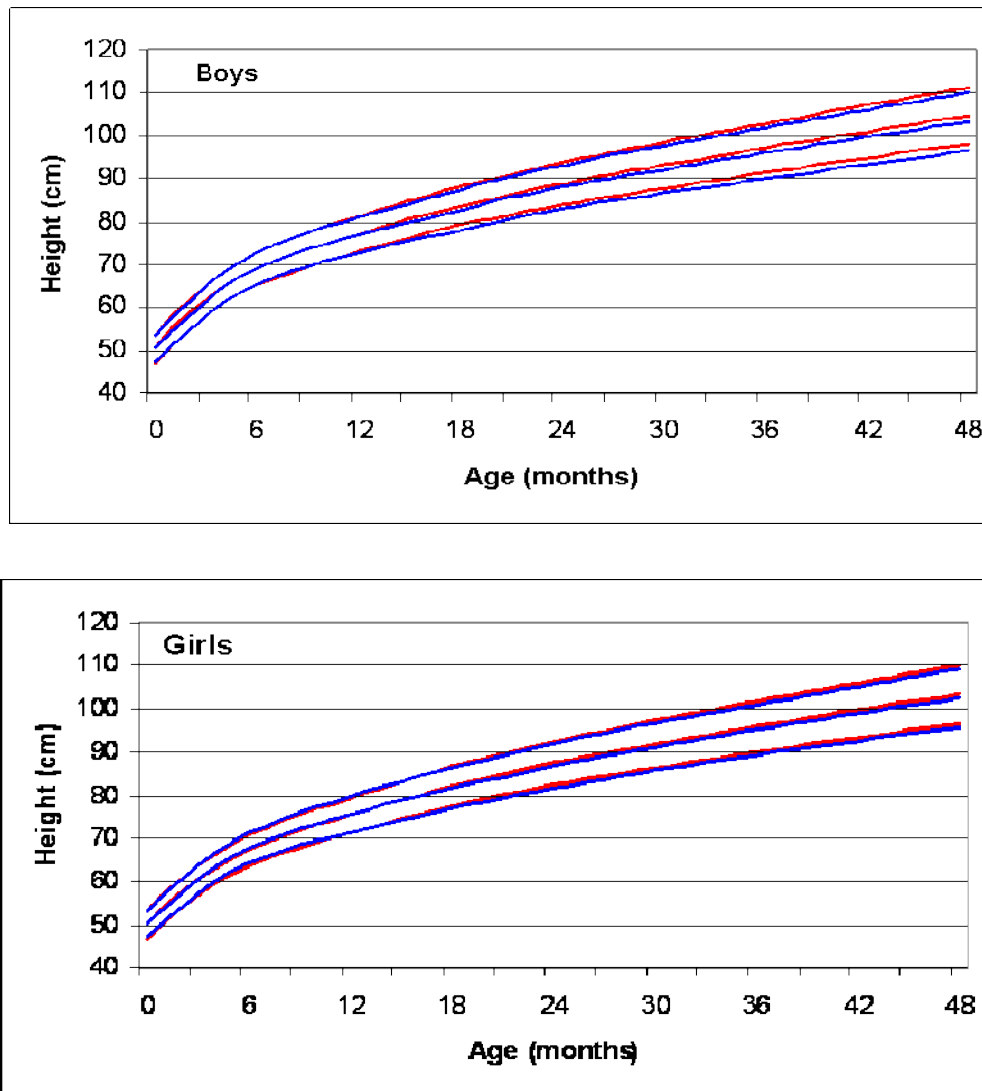
Boys' height was found to be following the Finnish reference growth pattern quite closely up to 12 months, excluding a peak at 1 to 3 months, but from 12 months onwards height of sample boys increased slightly faster than height of the Finnish reference children. At birth, sample boys were on average 0.18 cm taller than the reference children and at 48 months the difference was 1.42 cm.

Sample girls were found to be slightly shorter than the Finnish reference girls up to 14 months, excluding a peak at 1 to 3 months, and after 14 months, slightly taller than the reference children. At birth, the sample girls were on average 0.12 cm shorter than the

reference children but at 48 months the sample girls were already 0.97 cm taller. Similar, slightly increasing pattern in differences was seen in each assessed centile in both sexes.

Height growth patterns of the sample children compared to the Finnish reference are presented in Figure 3. The exact numbers are presented in Appendices 2.1. and 2.2.

Figure 3. Attained height centiles (5th, 50th and 95th) of the study children (red line) compared to the Finnish reference centiles (blue line) for boys and girls separately



5.4.3. Attained weight at various ages in comparison with the Finnish reference

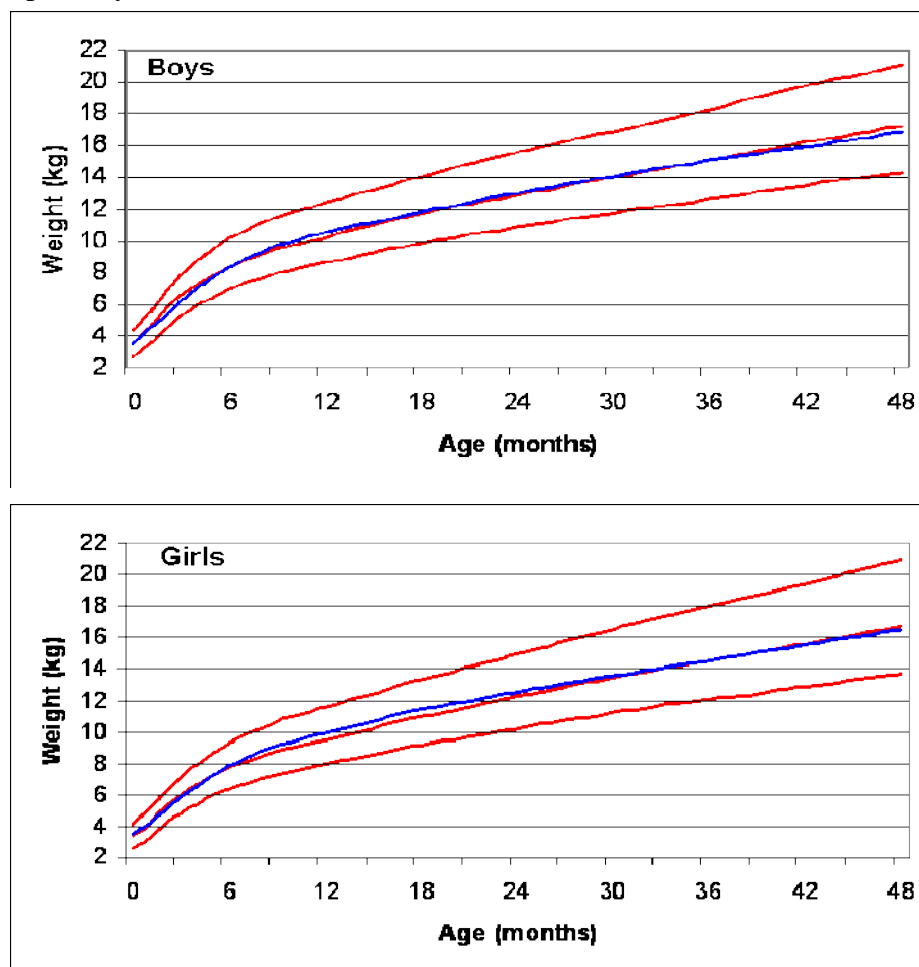
Study population boys and girls were found to be having quite similar weight growth patterns with each others and with the Finnish reference population. The study children were slightly lighter up to three years excluding a brief peak at first months, and slightly heavier from 3 years onwards.

There were no differences between the birth weights of the study children and the reference children. At two to three months, the study boys were on average 0.4 kg heavier than the reference boys but at 6 months the weights were again even. After that, up to 36 months the study boys were slightly lighter than the reference boys. Then the pattern showed slight increase so that at 48 months the study boys were 0.4 kg heavier than the Finnish reference boys.

At two to three months, study girls were on average 0.2 kg heavier than the reference girls but between 5 and 36 months they were lighter. At 18 months the study girls started to slowly catch up and were 0.2 kg heavier at 48 months.

Weight growth patterns of the study children compared to the Finnish reference are presented in Figure 4. The exact numbers are presented in Appendices 2.3. and 2.4.

Figure 4. Attained weight centiles (5th, 50th and 95th) of the study children (red line) compared to the 50th centile of the Finnish reference (blue line), for boys and girls separately

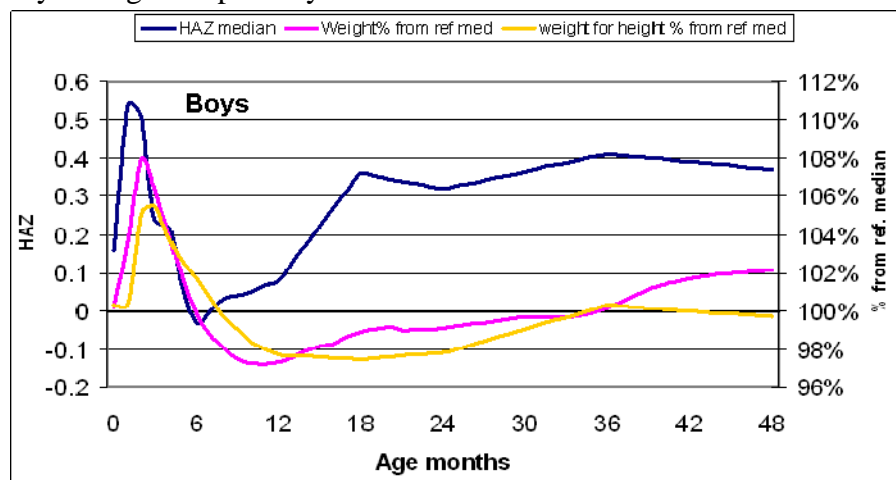


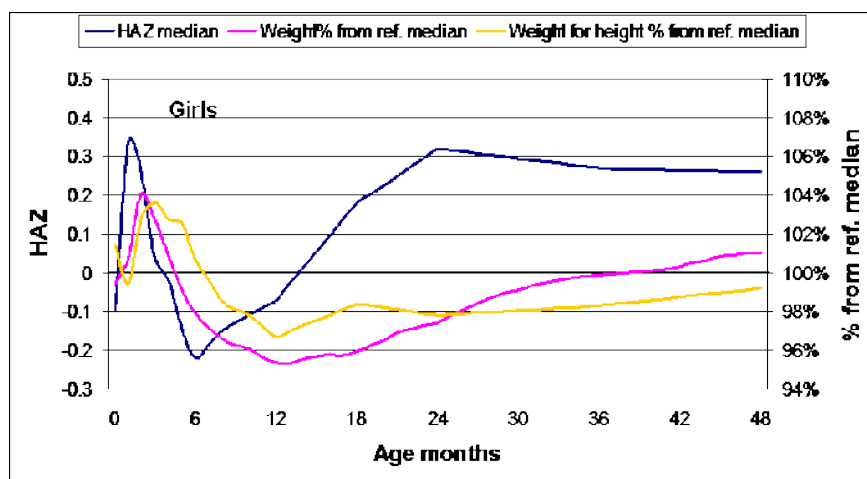
5.4.4 Relative height and weight of the study population compared to the Finnish reference

Figure 5. shows the relative height and weight of the study population compared to the Finnish reference population with the differences in height given in z-scores (HAZ), weight presented as how many percentages the study children's median weights are from the reference medians and WFH presented as how many percentages the study children's median WFH are from the reference median. The horizontal zero-line in the figures represents the reference median. It was noted that there were not much differences when smoothed median values were used for WFA comparison than when raw median values of individual children were used. The median (range) number of measurements included in the analysis at each age category was 1025 (642-2033).

At birth study children's WFA and WFH were on average the same as the reference populations but HAZ was almost continuously higher than the reference values. The curves peaked at two to three months when compared to the reference. Then again height increased steeply up to 18 months in boys and up to 24 months in girls when paralleled with the reference. Weight-for-age gain increased slowly after 12 months and study children's weight exceeded the reference weight at 36 months in boys and at 30 months in girls and then the difference increased continuously. Boys' weight-for-height was lower than the reference population's between 6 to 36 months and then equal with the reference. Girls' weight-for-height was lower than the reference population's after 6 months and almost even at 48 months.

Figure 5. Relative growth of the study children compared to the Finnish reference, for boys and girls separately





Height-for-age (HAZ) for study children presented in z-scores (blue line), scale presented in the left y-axis
 Weight-for-age presented as percentages from reference median (pink line), scale presented in the right y-axis

Weight-for-height presented as percentages from reference median (yellow line), scale presented in the right y-axis

5.5. Comparison of the WHO standard and the study population

5.5.1. LMS values

When smoothing the growth curves with the LMS method, edf values $L=5$, $M=9$, $S=4$ for boys and $L=4$, $M=9$, $S=4$ for girls were found to be optimal for heights and edf values $L=6$, $M=12$, $S=4$ for boys and $L=5$, $M=12$, $S=5$ for girls were found to be optimal for weights when using rescaled age and the same methods as were used for WHO standard construction. With these values, smoothed medians were close to the empirical medians; difference varied from 0 to few millimetres or grams in all ages and for both sexes. All curves were between -2 and +2 in the Q test and deviation was less than 10 indicating normal distribution. Kurtosis curve was again quite high in Q test and Q-Q test showed light tails in the distribution.

5th, 50th and 95th centile values for height and weight attained by LMS method and compared with the reference centiles are shown in Appendix 2.

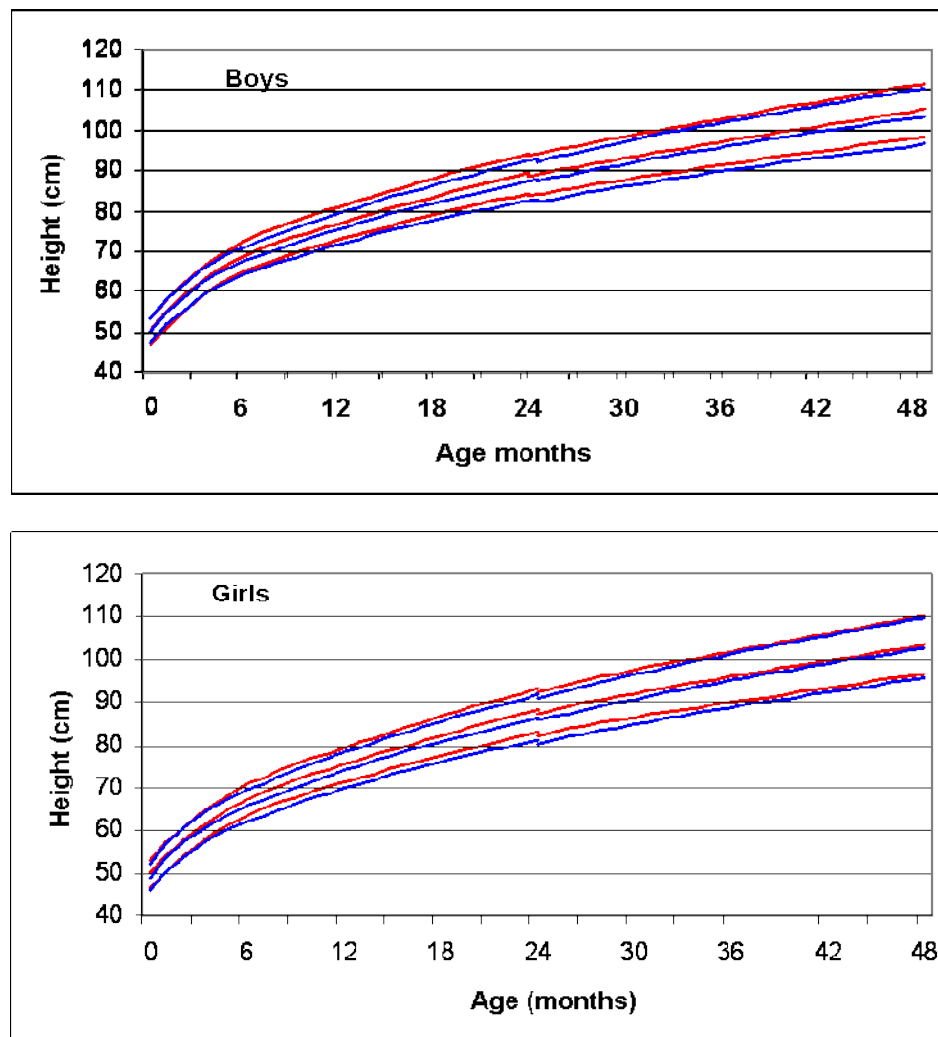
5.5.2. Attained height at various ages in comparison with the WHO standard

Study children, both boys and girls, were found to be taller at each age compared to the WHO standard although there was only a minor difference until six months. At birth, the study children were on average 1.0 cm taller than the standard children. The difference reduced to about 0.5 cm at one to two months but then again increased and varied between 0.8 cm and 1.7 cm ending to 1.4 cm in boys and 0.8 cm in girls at 48

months. The difference between the standard centiles and the study population's centiles remained relative constant after 6 months at 5th and 50th centiles but had slightly decreasing pattern at 95th centiles in both sexes.

Height growth patterns of the study children compared to the WHO standard are presented in Figure 6. The exact numbers are presented in Appendices 2.1. and 2.2.

Figure 6. Attained height centiles (5th, 50th and 95th) of the study children (red) compared to the WHO standard centiles (blue), for boys and girls separately



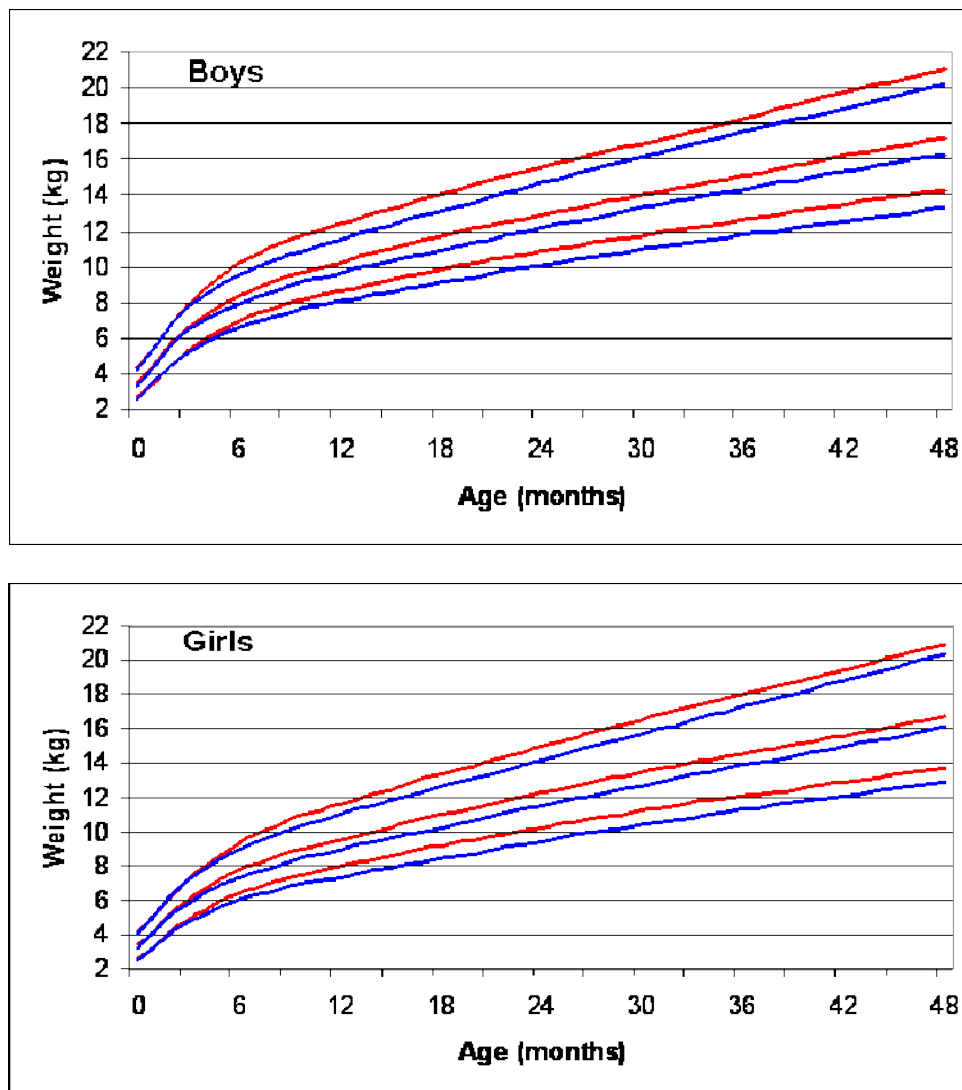
5.5.3 Attained weight at various ages in comparison with the WHO standard

The study children, both boys and girls, were found to be heavier at each age compared to the WHO standard children although the difference was small until four months. At birth, sample boys and girls were on average 0.3 kg heavier than the WHO reference children. At one to two months, difference was only 0.1 kg but it soon increased so that at 6 months sample boys were 0.5 kg heavier and girls 0.4 kg heavier than the standard

population. Then the difference increased being 0.9 kg and 0.6 at 48 months retrospectively. Boys' weight gain showed slightly increasing pattern compared to the standard but the same phenomenon was not seen in girls. Similar trend in the differences between the standard centiles and study population centiles were seen in each assessed centile curve in both sexes.

Weight growth patterns of sample children compared to the WHO standard are presented in Figure 7. The exact numbers are presented in Appendices 2.3. and 2.4.

Figure 7. Attained weight centiles (5th, 50th and 95th) of the study children (red line) compared to the WHO standard centiles (blue line), for boys and girls separately



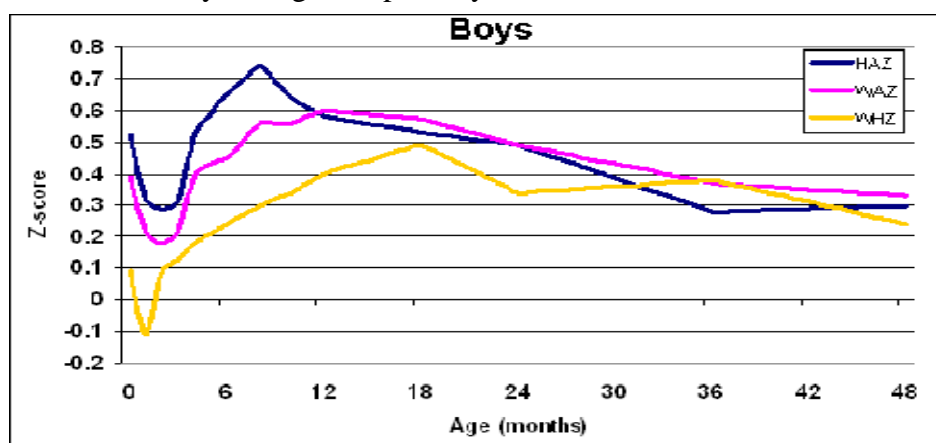
5.5.4. Relative height and weight of the study population compared to the WHO standard

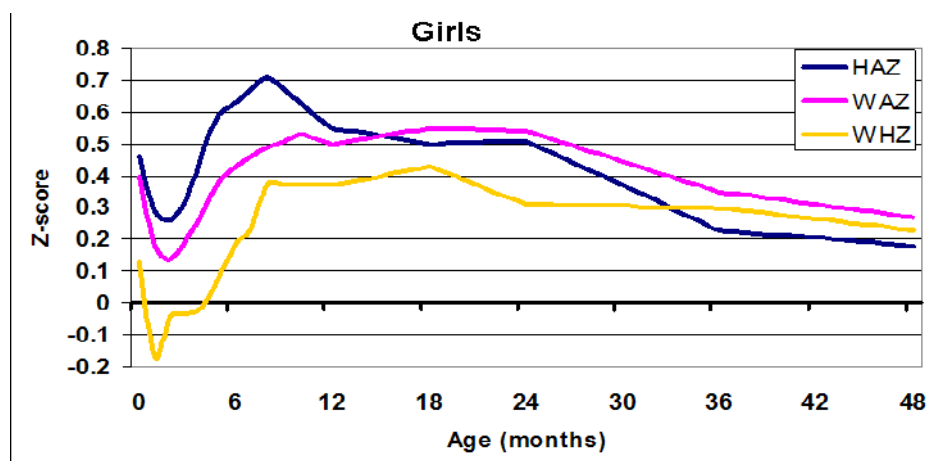
Figure 8. shows the growth pattern of the sample children compared to the WHO reference population with the differences given in z-scores. The curves indicate the median WAZ, HAZ and WHZ for the sample children and the horizontal zero line in the figures represents the reference median (0 z-score). The median (range) number of measurements included in the analysis at each age category for HAZ, WAZ and WHZ was 1025 (642-2033).

Growth of boys and girls showed very similar pattern with each others and between indicators. Both boys and girls were heavier and taller at birth than the standard population. There was a deep dip in the growth velocity at two to three months but then the height and weight gain increased again steeply. The differences between heights of the populations were largest at eight months being then about 0.7 units for the study children but after that the study children gained height relatively slower than the reference children. At 36 months the difference in heights levelled in boys at 0.3 units and in girls at 0.2 units.

The differences between weights were largest at 12 months in boys being then 0.6 units and at 18 to 24 months in girls being then 0.55 units. Then the study children's weight gain slowed down compared to the reference children's weight gain. The difference between the study children and the WHO reference children was on average 0.3 units at 48 months.

Figure 8. Relative growth of the study children in z-scores compared to the WHO standard, for boys and girls separately





5.6. Sensitivity analysis for assessing influence of incomplete follow-up

There were 459 boys and 424 girls who fulfilled the criteria for sensitivity analysis as having complete follow-up data between 0 and 12 months of age. Children who had complete follow-up data showed almost identical growth patterns as children in the whole data when 5th, 50th, and 95th centile curves and z-score curves were compared (data not shown).

5.7. Prevalence of growth faltering

The median (range) number of measurements included in the analysis at each age category and sex was 846 (256-9124) height measurements and 846 (256-9332) weight measurements. Most of the measurements were in the 0-6 month age group due to the many scheduled visits to the child health clinics at that age range.

5.7.1. Height growth faltering

Percentages of measurements that exceeded the height-for-age screening limits of the Finnish reference are presented in Table 2.a and the WHO standard in Table 2.b. Null z-score presents the median value of the reference data. The Finnish reference identified less stunted children than the WHO standard. Total percentages of measurements that exceeded the Finnish reference screening limits for stunting were 0.8 and 0.9 (<-2.7 SD) and the WHO standard 1.8 and 1.2 (<-2 z-score) for boys and girls respectively. In addition, 0.4% of boys' and 0.3% of girls' measurements exceeded the WHO limit for severe stunting. Largest proportion of growth faltering was found in the age groups of 0-6 months. The Finnish reference identified also less tall children than the WHO standard. Measurements that exceeded the screening limits for tallness were distributed

more evenly along the age groups, total percentages being 0.7 for boys and 0.5 for girls (>+2.7SD) compared to the Finnish reference and 6.6 for boys and 4.9 for girls (>+2 z-score) compared to the WHO standard. According to the WHO standard, total proportions of measurements of very tall (>+3 z-score) children were 0.7 in boys and 0.5 in girls.

Table 2.a. Proportions of measurements that exceed the Finnish reference screening limits for stunting or tallness

Age	Boys Height-for-age (HAZ)				Girls Height-for-age (HAZ)			
	Measurements	SD		Measurements	SD			
		<-2.7	>+2.7		<-2.7	>+2.7		
mo	n	%	%	n	%	%		
0-6	9124	1.2	0.7	8839	1.2	0.4		
7-12	3394	0.4	0.6	3293	0.6	0.2		
13-18	1889	0.1	0.9	1843	0.4	0.7		
19-24	1023	0.1	0.8	1024	0.0	0.6		
25-30	261	0.4	0.8	256	0.4	0.0		
31-36	669	0.0	0.8	640	0.3	1.6		
37-42	290	0.3	0.3	324	0.6	0.6		
43-48	509	0.0	1.4	488	0.2	1.3		
Total	17 159	0.8	0.7	16 707	0.9	0.5		

<-2.7 SD = stunted, >+2.7 SD = tall

Table 2 b. Proportions of measurements that exceed the WHO standard screening limits for stunting or tallness

Age	Boys Height-for-age (HAZ)					Girls Height-for-age (HAZ)				
	Measurements	Z-score				Measurements	Z-score			
		< -2	<-3	>+2	>+3		< -2	<-3	>+2	>+3
mo	n	%	%	%	%	n	%	%	%	%
0-6	9124	2.7	0.8	5.7	0.5	8839	1.8	0.5	4.5	0.4
7-12	3394	0.6	0.0	9.3	1.5	3293	0.4	0.0	6.4	0.7
13-18	1889	1.0	0.0	8.5	1.0	1843	0.7	0.0	5.6	0.7
19-24	1023	0.8	0.0	5.9	0.4	1024	0.4	0.0	4.9	0.5
25-30	261	1.5	0.0	4.6	0.8	256	0.4	0.0	3.9	0.0
31-36	669	0.8	0.0	3.7	0.3	640	0.9	0.3	3.6	0.5
37-42	290	1.4	0.0	3.8	0.0	324	1.2	0.0	2.2	0.0
43-48	509	0.4	0.0	4.1	0.4	488	1.0	0.2	3.1	0.6
Total	17 159	1.8	0.4	6.6	0.7	16 707	1.2	0.3	4.9	0.5

< -2 z-score = stunted, < -3 z-score = severely stunted, >+2 z-score = tall, >+3 z-score = very tall
 -2 z-score is equivalent to 2.3rd percentile and +2 z-score is equivalent to 97.7 percentile
 -3 z-score is equivalent to 0.1th percentile and +3 z-score is equivalent to 99.9th percentile

5.7.2. Weight growth faltering

Percentages of measurements that exceeded the weight-for-height screening limits of the Finnish reference are presented in Table 3a and WHO standard in Table 3b. The highest proportion of measurements that exceeded the screening limits for wasting were found in the age group of 8-13 months but after that, wasting had slightly decreasing pattern in both boys and girls. Proportions of obese children varied from age group to another. The Finnish Standard identified more wasting than the WHO standard. When compared to the Finnish reference, there were slightly more measurements from wasted girls (total 2.8%) than from wasted boys (2.4%) but in comparison with the WHO standard, there were slightly more measurements for wasted boys (1.5%) than for wasted girls (1.1%) in the sample. The Finnish reference found less obese children (2.9% of boys and 2.5% of girls) than the WHO standard (4.4% of boys and 3.0% of girls). According to the WHO standard, 0.6% of boys' measurements and 0.4% of girls' measurements were classified as severely obese.

Table 3a. Proportions of measurements that exceed the Finnish reference screening limits for wasting or obesity

	Boys Weight-for-height				Girls Weight-for-height		
	Age	Measure- ments	%		Measure- ments	%	
			<-15	>+20		<-15	>+20
mo	n	%	%	n	%	%	
0-6	9066	2.0	3.7	8757	1.9	3.0	
7-12	3392	3.0	2.2	3290	3.8	1.5	
13-18	1886	4.0	1.1	1841	4.9	2.0	
19-24	1022	3.4	1.4	1023	4.8	2.1	
25-30	261	1.9	3.1	256	2.7	2.3	
31-36	669	1.5	2.2	638	2.2	2.7	
37-42	290	1.4	2.8	322	1.9	2.2	
43-48	509	0.6	3.5	488	1.6	3.3	
Total	17 159	2.4	2.9	16 618	2.8	2.5	

<-15% = wasted, >+20% = obese

Table 3b. Proportions of measurements that exceed the WHO standard screening limits for wasting or obesity

Age	Boys Weight-for-height (WHZ)					Girls Weight-for-height (WHZ)				
	Measure- ments	Z-score				Measure- ments	Z-score			
		< -2	< -3	>+2	>+3		< -2	< -3	>+2	>+3
mo	n	%	%	%	%	n	%	%	%	%
0-6	9103	2.3	0.2	3.2	0.3	8815	1.5	0.1	1.7	0.1
7-12	3392	0.9	0.0	6.1	1.4	3290	0.8	0.2	4.2	0.6
13-18	1886	0.3	0.0	6.3	0.6	1841	0.4	0.0	5.1	0.7
19-24	1022	0.8	0.0	5.4	0.7	1023	0.6	0.0	4.8	0.6
25-30	261	0.4	0.0	6.9	1.9	256	0.4	0.0	4.7	1.2
31-36	669	0.6	0.0	4.3	0.8	638	0.5	0.0	4.1	0.9
37-42	290	0.3	0.0	4.8	1.4	324	0.0	0.0	4.9	0.0
43-48	509	0.2	0.0	5.1	1.2	488	0.4	0.0	3.9	0.6
Total	17 132	1.5	0.1	4.4	0.6	16 675	1.1	0.1	3.0	0.4

< -2 Z-score = wasted, < -3 z-score = severely wasted, >+2 z-score = obese, >+3 z-score = severely obese

Percentages of children who exceeded the weight-for-age screening limits of the WHO standard are presented in Table 3c. Finnish reference does not have screening limits for weight-for-age. Total percentages of measurements that exceed the screening limit for underweight and severely underweight were 1.6 and 0.3 in boys and 1.2 and 0.2 in girls respectively. All of the severely underweight boys and most of the girls were in the youngest age category. Total percentage of children classified as overweight were 5.1 in boys and 3.8 in girls and the measurements were distributed quite evenly along the age categories. There were some more severely overweight boys than girls with total percentages of 0.9 and 0.3 respectively.

Table 3c. Proportions of measurements that exceed the WHO standard screening limits for underweight or overweight

Age	Measure- ments	Boys Weight-for-age (WAZ)				Girls Weight-for-age (WAZ)				
		Z-score		Z-score		Z-score		Z-score		
		< -2	< -3	> +2	> +3	< -2	< -3	> +2	> +3	
(mo)	n	%	%	%	%	n	%	%	%	
0-6	9332	2.5	0.6	3.5	0.7	9055	1.8	0.4	2.5	0.1
7-12	3394	0.6	0.0	8.2	1.6	3291	0.6	0.0	5.2	0.6
13-18	1887	0.4	0.0	7.4	1.1	1844	0.4	0.1	6.1	0.4
19-24	1022	0.5	0.0	5.3	0.7	1025	0.6	0.0	6.0	0.5
25-30	261	0.4	0.0	7.7	1.2	256	0.0	0.0	5.5	0.8
31-36	669	0.8	0.0	3.4	0.5	639	0.3	0.2	4.9	0.8
37-42	290	0.7	0.0	5.2	1.4	324	0.9	0.0	3.7	0.0
43-48	510	0.6	0.0	4.5	0.8	488	0.4	0.2	3.9	0.4
Total	17 365	1.6	0.3	5.1	0.9	16922	1.2	0.2	3.8	0.3

< -2 Z-score = underweight, < -3 z-score = severely underweight, >+2 z-score = overweight, >+3 z-score = severely overweight

6. DISCUSSION

The aim of this study was to describe the current growth patterns of Finnish infants and young children by comparing the patterns with the Finnish national growth reference and the WHO growth standard which was published in 2006. Another aim was to assess the prevalence of growth faltering identified by the Finnish reference or the WHO standard by comparing the percentages of children who exceed the screening limits of the references.

In the study population, height was found to be following the Finnish reference pattern quite closely up to 12 to 14 months but then their height increased faster so that study boys were 1.4 cm taller and girls 1.0 cm taller at 48 months. Weight-for-age followed the Finnish reference patterns well up to 3 years but showed then slight increase but relative weight-for-height remained constantly lower than the reference values due to increased heights.

When compared to the WHO standard, study children were taller and heavier at each assessed age. The difference in heights was relatively constant over the age range being 1 cm at birth in both sexes and 1.4 cm in boys and 0.8 cm in girls at 48 months. Difference in weights increased so that at birth study children were on average 0.3 kg heavier but at 48 months boys were 0.9 kg heavier and girls 0.6 kg heavier than the WHO standard children. Relative weight-for-height was + 0.3 z-score above the standard values at 48 months in both sexes.

Relative growth curves showed remarkable fluctuation in growth patterns during the first year compared to the Finnish reference or the WHO standard.

When prevalence of growth faltering was compared, the WHO standard identified less wasted, slightly more obese or stunted and considerably more very tall children than the Finnish reference.

6.1. Strengths and limitations of the study

Sample size in growth studies has to be sufficient to provide reliable information on the mean, standard deviation and the distribution of the data and to fit the curves properly

with LMS method (Cole, 2006). The sample size of this study was relatively large and fulfilled all the criteria for adequate sample size for this kind of growth studies. Since the sample included children born during one year, the seasonality of growth did not distort the results either. In addition, data cleaning was done so that only one measurement for each measurement point was included from each child. By doing that, over presentation of extra measurements taken due to growth problems was avoided.

Finnish health care system has a long tradition of measuring almost every pre-school aged child regularly in the child health clinics. Because of that, the sample represents almost all 0 to 4 years old children and also the whole social class structure of children who lived in Tampere area during the period of which the data was collected. Tampere area has fairly mixed population originated from different parts of Finland. Sorva et al. (1985, 1989) compared growth of Finnish people living in Helsinki, which could at least to some extent be compared to Tampere regarding the population mixture, and growth of children from eastern Finland, whose growth was considered most likely to differ from the mixed city population. They found no significant difference between those two populations. Although in a study by Vuorela et al. (2008) rural areas had slightly higher obesity levels than urban areas and although this study was conducted in an urban area, the difference is small in children under 5 years of age and does not have a meaningful effect on the results. There is also a theoretical possibility that children born during the inclusion period grow somewhat differently than children born during other times but the probability for this is very small. Taking all this into consideration, the study sample represents well the entire Finnish population.

However, register studies like this have unavoidably some limitations. Anthropometric data that are collected retrospectively from registers include always some errors due to the way it is originally gathered and recorded and not all of them can be detected afterwards. Measuring a child, especially an infant, is not an unambiguous task if the child is not co-operating and that may have lead to measurement errors particularly in length measurements. In addition, the anthropometric measurements extracted for this study were originally taken by more than 230 different measurers who may have used slightly different measurement techniques resulting in systematic differences between the results. Since the data of this study was collected from several child health clinics, also several measuring equipment was used for taking the measurements. If the equipment had not been properly calibrated, it may have lead to some systematic errors

in the measurements. Another limitation is that some key in errors always occur when the data is entered into a register. However, a large sample size is likely to diminish the effect of all the errors since they are prone to cause both too high and too low measurements and thus likely to nullify each others effects and do not significantly distort the validity of the results. In a study conducted by Howe et al (2009), height/length and weight data that were collected during regular child health clinic visits, were assessed as having good accuracy for clinical and research use. In Finland, public health nurses are specially trained to take the measurements accurately using similar methods and same kind of good quality measurement equipment is used in each clinic. In conclusion, the data used for this study can be considered as the best possible in the absence of longitudinal measurements taken by anthropometrists.

The different inclusion and exclusion criteria of the reference populations and the sample population set some limits for this study. When the references were made children with disorders or illnesses affecting growth were excluded although excluding criteria based on health status are always somewhat subjective. When the study data were analyzed, children were not excluded due to their poor health status, firstly because following the same exclusion criteria as was used in the references would have been impossible, secondly because data that is detailed enough was not available or would have been very difficult to obtain and thirdly because proportion of children who would have been excluded on health grounds would have been very small and would have had very little effect on the fitted centiles. At the end, the study aimed to describe how Finnish children are growing, not only how healthy children are growing and that also is an argument for including all children disregarding their health status. However, if those children who had illnesses or disorders restricting growth were excluded also from the study population, it might have slightly increased the differences in growth between the study and the reference populations.

In addition, the exclusion limit for very low birth weight infants was set to 1.5 kg in this study although the exclusion limit in the construction of the Finnish reference and the WHO standard was 2.5 kg. The limit was set lower in order to avoid excluding term low birth weight infants since the length of gestation was not known. Setting limit into 1.5 kg is likely to include some preterm children who are known to have different growth patterns. Also those very low birth weight infants whose birth measurements were not recorded but some later measurements were, were not found by this method and thus

included in the study. That may have slightly affected the mean anthropometric values and may even have caused some very slight curve depression.

The LMS method and the LMS program used for growth curve smoothing have some advantages and disadvantages. An advantage is that the method uses continuous age range thus measurements do not need to be grouped by ages but all the measurements are included and affect the median values. A disadvantage is that choosing the optimal edf values that determine the smoothed median values for the anthropometric measurements is essentially a subjective process i.e. there are no unambiguously right edf values. Still, when edf values are changed, also the median values gradually change affecting the differences that are found between the reference values and the study population values. However, differences in results obtained from the feasible edf value combinations are not large and would not have affected considerably the magnitude of the differences. In addition, due to the nature of the LMS method, the LMS programme does not give confidence intervals for the obtained mean values. Obtaining confidence intervals for the LMS values would be a demanding statistical task which is out of the scope of this master's theses study.

In order to assess that there are no major errors in the data or in the smoothing process that would twist the curves, analysis of growth velocity was done. Growth velocity of the study children seemed to be following the normal growth velocity patterns reassuring that there were no major peculiarities in the data and the smoothing was done properly.

Lastly, a fact that affected the comparison of the study data and the Finnish weight-for-age standard is that weight-for-age median values for Finnish reference data are estimated from weight-for-height data and are relatively reliable only for those children who are close to the median but not at the extremes (Ignatius, personal communication). For this reason, in comparison with the Finnish reference, only 50th centiles were compared. For the same reason, comparison between proportions of growth faltering identified by the Finnish reference or the WHO standard could not be done concerning weight-for-age.

6.2. Scientific conclusions

6.2.1 Comparison with the Finnish reference

As it was discussed in earlier chapters, many maternal factors affect birth size and the factors may influence over several generations. Disregarding that, positive secular trend has never been detected in birth sizes (Cole, 2000b). The findings of this study support that earlier finding: birth length and weight of these sample children were found to be almost the same as the reference measurements although distinctive differences were found in older age groups. The finding that birth sizes have not changed indicates also that neither the socio-economic conditions nor other environmental factors affecting birth size, nor the length of gestation have changed remarkably since the construction of the reference.

Concerning the relative growth curves at early ages, a steep peak that can not be explained completely on biological grounds was seen at around two months of age. Some assumptions on the origins of the peak can still be made. Firstly, the distinctive variability in the relative growth curves during first months could result from different feeding practices affecting growth. It is known that predominantly breast fed infants grow faster than the formula fed infants during the first two months and then slower up to 24 months. This is seen especially in weight growth (Salmenperä et al, 1985; Dewey et al, 1995; Dewey, 2001). When the Finnish reference children were born, breast feeding levels in Finland were lower than at any other time in the recorded feeding history in Finland since 1920 and remarkably lower than when the study population was born (Verkasalo, 1980; Verronen, 1988; Hänninen-Nousiainen et al., 2004). It may show in this comparison as a peak at 2 months indicating faster growth for the study children than for the Finnish reference children and then as rapidly decreasing pattern when the growth rates of breast fed children decelerate compared to formula fed children. Somewhat similar peak was seen also in a comparison of breast fed infants with the CDC reference used in the United States (de Onis et al., 2007a). The decelerating pattern of the study children's relative height and weight after two month's peak might also result from different complementary feeding practises. At the time when the reference was made, complementary feeding was started earlier than today and with different food items (Siimes et al., 1985; Hasunen and Ryyänen, 2006).

The high peak in the relative growth curves at two months might also reflect peculiarities in the birth registry data used in the Finnish reference or in the birth data of the study children. If the reference birth lengths were 0.5 cm shorter or the study children's birth lengths 0.5cm longer, the relative growth curves would look more "normal". This may reflect the difficulties in measuring new born children. Length measurements are often difficult to obtain accurately (WHO, 1995b) and the measurement practises may have changed after the reference was made. However, none of these explanations fully explains such a steep peak in the curves but they may all contribute to it.

The finding that the length gain of the study children exceeds the reference growth at 12 to 14 months leading to 1.4 cm difference in boys heights and 1 cm difference in girls heights at 48 months, most probably indicates positive secular changes in growth. As it was explained earlier, first year's growth is mostly continuity of intrauterine growth and is nutrition dependent (Karlberg, 1989). The increased breast feeding levels, changed complementary feeding practises and the fact that breast fed children grow slower after two months of age and catch up the formula fed children sometimes around two years, might explain why the positive secular change in height is seen only after infancy. Findings of this study might also indicate that child growth environments have been improved in Finland since the construction of the reference leading to accelerated growth after infancy.

In generally, secular changes can be seen in both accelerated growth velocity in early life and in increase in final height. It has been suggested that secular changes in height are present already at two years of age (Cole, 2000a; Larnkjaer et al., 2006). In this view, the 1 cm acceleration in boys' height and 0.7 cm acceleration in girls' height, that was present at 24 months in these study children, would be seen also in their final heights and the rest of the height increase would result from secular changes in the timing of growth velocity.

When weights of the study children were compared with the Finnish reference, their weight-for-age patterns were found to be following the reference centiles quite closely. However, since the average heights have increased, the sample children were actually slightly lighter than the reference children up to four years. This can also be seen in the relative weight-for-height values which are lower than the reference values in most of

the age groups. Similarly as the length/height growth patterns, the weight growth patterns of the sample children can also be explained by changed feeding practises. Since remarkably more infants are now breast fed, their slower weight growth may have diminished the otherwise positive secular trend at early ages. After three years of age, the prevalence of obesity started to increase and was slightly higher in the sample population than in the reference population. Earlier studies conducted in Finland have shown that obesity levels have increased remarkably in older children and adolescents and that the excess weight gain starts around three to five years of age (Hakanen et al., 2006; Kautiainen et al., 2002; Vuorela et al., 2008).

6.2.2. Comparison with the WHO reference

It is well known that maternal stature and nutritional status is related to the birth size of their infants and that the impacts of these intrauterine conditions diminish by 12 months of age (Herngreen et al., 1994; Buuren and Wouwe, 2008). Explanation for the slightly higher birth lengths and weights of the study children compared to the WHO standard might be that the study children's mothers were taller and heavier than the mothers of the standard children. Although the mothers of the standard children lived in affluent environments, they might not have reached their full genetic growth potential due to epigenetic constrains and that might have affected also the size of their infants. It has been suggested that secular changes are close to plateau in Northern European countries (Larnkjaer et al., 2006) but the trend may still be strong in some of the countries where the WHO data was extracted from. In fact, the birth measurements of the Norwegian cohort included in the WHO standard (Baerung et al., 2004; WHO, 2006b) were closer to the birth measurements of this study population than the standard measurements indicating intrauterine growth constrain in some other WHO cohort children.

Concerning the relative growth curves of the study children, similar bend that was seen in comparison with the Finnish reference at two months was also seen in comparison with the WHO standard but to opposite direction. Some assumptions of its origins can be made also in this comparison. If prenatal growth is restricted due to the maternal size, faster catch up growth usually occurs soon after birth as was explained in earlier chapters. Catch up growth of small born WHO children, which is not seen in the study children, might explain the deep dip in the relative growth curves of the study children at two months. Same kind of drop soon after birth was found also in Britain when the use of WHO standard was assessed (Wright et al., 2008).

The dip in the first months and faster growth of the Finnish children thereafter might also be explained again by the different feeding patterns. Although breast feeding levels have increased remarkably in Finland, only about 55% of Finnish infants were exclusively breast fed at 2 months at the time when the study children were born (Hasunen and Ryynänen, 2006) compared to 100% of the WHO standard children. This may explain why the standard children grew faster than the sample children during the first months and slower thereafter. In addition, the finding that differences between the growths of the study population and the standard population increase noticeably at six months might be related to different timing of introduction of complementary feeding, different complementary feeding frequencies or varying diets. However, only feeding practises could probably not explain these relatively large differences in growths of Finnish children and the standard population at that age.

Another possible explanation for the fluctuation in the relative growth curves during the first months might be some technical peculiarities in the WHO data analysis concerning birth measurements of the standard children. The standard's birth measurements seem to be quite low compared to the later measurements and this may show as "too fast" growth in the first months, causing also a deep dip in the relative growth curves of this study population. If the WHO standard's birth measurements were more consistent with the later measurements, the dip in the curves would diminish. It would also diminish if the birth measurements of the study children were slightly lower as was mentioned in the previous chapter.

Lastly, although it is estimated that most of the genetic variability of humans resides within populations and only 10 -15% between populations (Jorde, 2000; Jorde and Wooding, 2004), the genetic variability might also explain some differences between the sizes of the Finnish children and the standard children.

6.2.3 Growth faltering identified by the references

When cut-off points for growth faltering were assessed, the Finnish reference identified slightly more children as stunted or tall than it should have identified if the sample population was representative of the reference population. Most of the stunted children were seen in the youngest age category. This is most probably due to the different exclusion criteria when the Finnish reference excluded all premature children but there were some of them in the study data. Over presentation of tall children is explained by positive secular trend in height growth. Because Finnish weight-for-height screening

rules don't tell anything about the distribution of the reference data, the numbers of children exceeding the screening limits can not be compared to the numbers in the reference population as such.

In similar assessment of the WHO standard, the standard classified slightly more children as severely stunted and clearly less children as stunted as it should have classified if the sample population was representative of the standard population. All the severely stunted boys and most of the girls were in the youngest age group reflecting again the different inclusion criteria of the standard population and the sample and especially the inclusion of some premature children in the sample data. The WHO standard classified also fewer children as wasted, more as obese, severely obese or very tall and much more children as tall indicating different distribution of the sample data and the standard.

When The Finnish reference and the WHO standard were compared, the WHO standard identified fewer children as wasted, slightly more as obese or stunted and considerably more as very tall than the Finnish reference. This is mostly due to different cut-off points for growth faltering but also due to different reference populations.

6.3. Relation to previous studies

6.3.1. Previous studies compared to the Finnish reference assessment

As to my knowledge studies concerning the linear growth of Finnish children have not been published since the construction of the Finnish national growth reference thus the results of this study can not be compared with other recent studies on linear growth of Finnish children per se.

Some studies on secular trend in growth of Finnish children have however conducted in 70's and 80's. A study by Dahlström et al. (1984) suggested that in 70's, increase of average adult height had already stopped in Finland but the positive secular trend was still seen in the timing of high height and weight growth velocity in childhood and adolescence indicating earlier growth spurts. The earlier timing of high growth velocity was also seen in a longitudinal study by Sorva et al. (1985), but they reported also 0.8 cm average increase in girls' final heights and 1.1cm increase in boy's final heights

compared to the old Finnish reference published in 1964 by Backström-Järvinen. Consistent with these earlier studies, my study indicated that there has been a positive secular trend in the timing of high height growth velocity and in heights of 48 months old children since 60's and early 70's. However, it was not possible to conclude if the trend has now ceased and if it is has ceased, when this has happened.

Some studies on obesity levels of Finnish children and adolescents have also been published recently. Although prevalence of obesity has increased remarkably between 1977 and 1999 among Finnish 12-18 years old adolescents (Kautiainen et al., 2002; Vuorela et al., 2008), findings of this study suggest that the obesity levels have not increased among 0-4 years old children although a slowly increasing trend in obesity levels was seen at four years. That finding is consistent with the STRIPP study conducted in Turku, in which the obesity levels of Finnish children started to increase slowly at 3 to 4 years and at 5 years steeply (Hakanen et al., 2006). The findings are also somewhat consistent with a study by Vuorela et al. (2008) who reported that obesity prevalence was increased only slightly amongst 5 years old girls and not at all amongst 5 years old boys between 1986 and 2006. They concluded that younger children are more resistant to the obesogenic environment and another explanation might also be the spontaneous activity of younger children. Results similar to the Finnish studies were also found in a study by Wang et al. (2007) conducted in the USA in which obesity levels increased slower in 2 to 5 years old children compared to older ones.

Vuorela et al. (2008) found also some differences between the obesity levels of urban and rural children in 2006 but not in 1986 when Tampere area and surrounding rural areas (Vilppula, Virrat and Ruovesi) were compared, rural areas having higher levels of obesity. Same kinds of results have also been reported from Sweden (Neovius et al. 2006). This study included only children from an urban area and the results might slightly differ if also rural areas were included although the differences would not be large in young children.

Since Norway and Finland resemble each others closely in many ways, including population characters and social conditions, it is reasonable to compare this study also to the recently published study on current growth of Norwegian children conducted by Juliusson et al. (2009). Constant with the findings of my study on Finnish children, their

study showed only marginal secular changes in lengths of infants and weights of 0-4 years old Norwegian children compared to the currently used Norwegian reference constructed according to the growth of children in the 1970's and 1980's. However height and especially weight-for-height of older Norwegian children has altered remarkably compared to the reference.

6.3.2. Previous studies compared to the WHO standard assessment

Findings of this study are in accordance with studies carried out in several other developed countries comparing the national references and the WHO standard: Children in many developed countries grow faster than the WHO standard population, particularly after 6 months of age. Especially weight percentiles in many European national growth charts are higher than in the WHO growth charts (Ziegler and Nelson, 2007). In the recent study by Juliusson et al. (2009) conducted in Norway, the growth patterns of Norwegian children resembled closely the patterns of this Finnish study population when compared to the WHO standard. In the study population, all percentile lines were generally positioned above the WHO standard percentile lines at births and in the age groups of 6 months to 5 years.

Contrary to the other studies and also to this study, length and height growth of children in United Kingdom were found to be following the WHO growth curves at all ages after birth but like in other studies in developed countries, their weight gain deviated considerably from the WHO standard data. UK infants were also larger at birth than the standard children (Wright et al., 2008).

When levels of growth faltering were studied in other developed countries, findings were also similar with this study. For example in United Kingdom, considerably less infants were classified as underweight or wasted and higher proportion of children as obese when using WHO reference than when the national reference was used (Wright et al., 2008). When growth of South-African and Canadian children were assessed, WHO standard identified also more stunted and overweight children than the National Centre for Health Statistics (NCHS) and the Centre for Disease Control (CDC) references (de Onis et al., 2006b; Norris et al., 2009). In addition, in a comparative study carried out in Peru, Vietnam and India, the nutritional status of children was different when WHO standard was used than when NCHS reference was used but the direction and magnitude of the differences were not consistent (Fenn and Penny, 2008).

6.4. Public health implications and further research proposals

As was earlier discussed, prerequisite for successful growth assessment is a reliable growth reference or standard against which to compare the growth of children. Currently the Finnish national reference does not accurately reflect the contemporary height growth of Finish children. This may leave some pathologically growing children unidentified and also lead to some unnecessary referrals, especially in tall children who are close to the cut-off points. However, most of the truly pathological cases are found at the extremes of the distribution and not close to the cut-off points thus it is unlikely that many pathological cases are now left out. It is also known that more important that the child's position on the growth chart is that the child follows his or her own "growth channel". Updating the reference would enable more accurate height growth assessment especially close to the cut-off points, but it would also mean that large amounts of children that are currently visiting the clinics would cross their own "growth channels" disrupting the detection of truly pathological growth. The weight reference reflects current growth patterns of 0 to 4 years old children quite well but if obesity levels have increased in older ages, like some previous studies indicate, updating the reference would "normalize" higher weights in those ages which would not be beneficial. In addition, updating the reference would also require costly updates of the software used in child health clinics. Before any decisions can be made, advantages and disadvantages of updating the growth reference should be carefully considered. In addition, growth patterns of older children and adolescents should also be studied.

The Finnish national growth reference and the WHO growth standard have different reference populations and also different cut off points for growth faltering. The selection of a growth reference is important for interpretation of growth patterns, detection of growth faltering and identification of the onset of excess weight gain. There is more and more evidence that very fast growth in infancy is associated with increased risk of obesity in later childhood and in adulthood (Baird et al., 2005; Ong and Loos, 2006). Prevalence of obesity, cardiovascular diseases, diabetes and other chronic diseases, that are reported to be associated with high weight gain, have increased also in Finland. That is an argument for a growth reference that allows earlier identification of excess weight gain than the Finnish reference. Adoption of the WHO standard in Finland would have significant impacts on the interpretation of young children growth, especially the weight gain. If the WHO standard was adopted, more children would be classified as obese and fewer as wasted. This would probably make

the parents more aware of their children's risk of becoming overweight already when the excess weight gain starts since more children would be growing above the median (50th centile) than now when the national reference is utilized. That might promote healthier diets and allow earlier interventions against obesity. It is known that children who are in risk of being obese in adulthood should be identified in early childhood to allow effective prevention (Katiola et al., 2003; Cheung et al, 2004).

Many previous studies have confirmed that the WHO standard is better than the national references in assessment of growth of predominantly breast fed children (de Onis et al., 2006b; de Onis et al., 2007a; van Dijk and Innis, 2009). If infants that are fed according to the recommendations seem to be having growth faltering although the growth is normal, it may lead to adverse consequences: anxiety in parents, unnecessary investigations, changing breast feeding to formula feeding, overfeeding with formula or too early introduction of complementary feeding. Adoption of the WHO standard in Finland would allow slower and more optimal weight gain in infancy and it might lead to longer exclusive or predominant breast feeding, which is currently considered as the best way of nourishment for infants.

However, there will always be some children who are for various reasons exclusively formula fed. The WHO standard would classify most of them as overfed which might also have adverse consequences in forms of anxiety among parents and possible underfeeding. That would need to be taken into account in child health clinics.

Adoption of WHO standards would probably decrease the number of children who are referred to paediatricians due to growth retardation. However, an important question that should be further studied is that are those children that are identified as having growth faltering by one reference but not by the other one really healthy or adequately nourished or are they truly pathological. It has been proved that slight growth faltering is very rarely associated with major social or medical disorders (Wright and Parkinson, 2004) and over diagnosing growth faltering may lead to unnecessary anxiety among parents (Spencer, 2007). At the end, a reference that identifies as many truly pathological children as possible and as few false pathological cases as possible would be the ideal one.

Also the increasing ethnic diversity of the Finnish population speaks for adoption of the WHO standard. International standard would serve better in assessment of growth of children who are not of Finnish origin.

A disadvantage in the adoption of the WHO standard in Finland would be that the current reference and the data collected since the publication of the reference would not be comparable with the new ones unless the old data were re-analyzed using the new standards. That would cause difficulties in the continuity of the follow up of children's growth. It would also require considerable amount of money and effort to replace the old software used in child health clinics and to re-train the public health nurses and paediatricians in the use and interpretation of the new charts. Misinterpretations could also occur at the beginning.

One more issue to consider is that the WHO standards are constructed only for children up to 5 years of age consisting of two charts, one from birth to 2 years and another for age 2 to 5 years. In 2007 WHO launched also a reference for children over 5 years of age and adolescents constructed from the old WHO reference to allow its usage until adulthood. However, that is a reference, not a standard since it would be impossible to control environmental effects that affect older children and adolescents (de Onis, 2007b). Adoption of the WHO standard in Finland would require usage of several different growth charts which would be somewhat confusing. In Britain, a working group that has been assembled to investigate if Britain should switch to WHO standards instead of the national reference is likely to recommend that the WHO standard should be used during the first 2 years of life and the national reference thereafter. That would optimise slower weight gain in infancy and early childhood but would be more representative in later childhood (Cole, 2007; Wright et al., 2008). That kind of a solution might be feasible also in Finland.

Lastly, different growth charts and cut-off points used in different countries makes the comparison of growth of different populations difficult. Adoption of the WHO standard in Finland would remarkably improve the comparison making the growth of Finnish children more comparable globally. In conclusion, advantages and disadvantages of the adoption of the WHO standard in Finland should be thoroughly evaluated and the adoption considered.

7. CONCLUSIONS AND RECOMMENDATIONS

Average height of Finnish children has increased but relative weight has decreased or remained constant in most ages between 0 to 48 months since construction of the Finnish national growth reference. Discussion is needed whether 1.5 cm increase in boys' height and 1cm increase in girls' height at 48 months justifies the updating of the reference. In addition, further study is needed to evaluate if the same growth pattern as was seen in 0-4 years old children in this study applies also to older children and adolescents.

Compared to the WHO standard, Finnish children are slightly taller and heavier at each assessed age between 0 to 4 years. The WHO standard identifies fewer wasted and more obese children than the Finnish reference and its standard values for heights and weights are lower than the Finnish reference values. Since the WHO standard values for weights are lower and it shows higher levels of obesity, its adoption in Finland should be considered and the public health implications of the adoption evaluated. Utilization of the WHO standard would also make the growth of Finnish children more comparable internationally.

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REFERENCES

- Aber J, Bennerr N, Conley D, Li J. The effect of poverty on child health and development. *Ann Rev Public Health* 1997;18:463-483
- Asworth A, Shrimpton R, Kazi J. Growth monitoring and promotion: review of evidence of impact. *Maternal and Child Nutrition* 2008;4:86-117
- Baerung A, Bjoerneboe G-E, Tufte E, Norum K. Implementation of the WHO Multicentre Growth Reference Study in Norway. *The United Nations University, Food and Nutrition Bulletin* 2004;25(1) Suppl 1
- Baird J, Fisher D, Lucas P, Klejnen J, Roberts H, Law C. Being big or growing fast: systematic review of size of and growth in infancy and later obesity. *BMJ* 2005;331:929
- Barker D, Osmond C, Forsten T, Kajantie E, Eriksson J. Trajectories of growth among Children who have coronary events as adults. *N Engl J Med* 2005;353:1802-9
- Berenson G, Srinivasan S, Bao W, Newman W, Tracy R, Wattigney W. Association between multiple cardiovascular risk factors and atherosclerosis in children and young adults. The Bogalusa heart study. *New Engl J Med* 1998;338:1650-6.
- Bogin B. The Evolution of Human Growth. In: Cameron N, editor. *Human Growth and Development*. Academic Press, London, 2006.
- Borghi E, De Onis M, Garza C, Van den Broeck J, Frongillo A, Grummer-Strawn L, et al. Construction of the World Health Organization child growth standards: selection of methods for attained growth curves. *Statist Med* 2006;25:247-265
- Bramswig J. Short and tall stature. *An Nestle* 2007;65:117-127
- Bray G. Overweight is risking fate. Definition, classification, prevalence, and risks. *Ann NY Acad Sci* 1987;499:14-28
- Bruining G. Association between infant growth before onset of juvenile tye-1 diabetes and autoantibodies to 1A-2. *Lancet* 2000;356:655-6
- van Buuren S, van Dommelen P, Zandwijken G, Grote F, Wit J, Verkerk P. Towards evidence based referral criteria for growth monitoring. *Arch Dis Child* 2004;89:336-41
- van Buuren S, Fredriks M. Worm plot: a simple diagnostic device for modelling growth reference curves. *Statistics in Medicine* 2001; 20:1259-1277
- van Buuren S, van Wouwe J. WHO Child Growth Standards in action. *Arch Dis Child* 2008;93:549-551
- Cameron N. Human growth curve, canalization and catch-up growth. In: Cameron N, editor. *Human growth and development*. Academic Press, London, 2006

- Cheung YB, Machin D, Karlberg J, Khoo KS. A longitudinal study of pediatric body mass index values predicted health in middle age. *Journal of Clinical Epidemiology* 1994; 57:1316-1322
- Cole T. Babies, bottles, breasts: Is the WHO growth standard relevant? *Significance* 2007;March:6-10
- Cole T. Galton's midparent height revisited. *Ann Hum Biol* 2000a;27:401-5
- Cole T. Growth References and Standards. In: Cameron, editor. *Human growth and development*. Academic Press, London. 2006.
- Cole T. Secular trends in growth. *Proceedings of the Nutrition Society* 2000b;59:317-324
- Cole T. The LMS method for constructing normalized growth standards. *Eur J Clin Nutr* 1990; 44: 45-60
- Cole T. The secular trend in human physical growth: a biological view. *Econ Hum Biol* 2003;1:161-8
- Cole T, Freeman J, Preece M. British 1990 growth reference centiles for weight, height, body mass index and head circumference fitted by maximum penalized likelihood. *Stat Med* 1998;17:407-29
- Cooper R, Kaufman J, Ward R. Race and genomics. *N Engl J Med* 2003;348:1166-70
- Dahlström S, Viikari J, Åkerblom H, Uhari M, Dahl M, Lähde P-L, et al. Suomalaisten lasten pituus, paino ja menarke vuonna 1980. *Duodecim* 1984;100:838-848
- Dewey K. Nutrition, growth and complementary feeding of the breastfed infant. *Pediatr Clin North Am* 2001;48:87-104
- Dewey K, Pearson J, Brown K, Krebs N, Michaelsen K, Persson L, Salmenperä L, Whitehead R, Yeung D and WHO Working Group on Infant Growth. Growth of Breast-Fed Infants deviates from current reference data: A Pooled Analysis of US, Canadian and European Data Sets. *Pediatrics* 1995;96:497-503
- Dietitians of Canada, Canadian Paediatric Society, The College of Family Physicians of Canada, and Community Health Nurses Association of Canada. The use of growth charts for assessing and monitoring growth in Canadian infants and children. Position statement. *Paediatr Child Health* 2004;9(3):171-80
- van Dijk C, Innis S. Growth curve standards and the assessment of early excess weight gain in infancy. *Pediatrics* 2009;123(1):102-108
- Ekblom O, Oddsson K, Ekblom B. Prevalence and regional differences in overweight in 2001 and trends in BMI distribution in Swedish children from 1987 to 2001. *Scand J Public Health* 2004;32:257-63.

- Erkkola M, Pigg H-M, Virta-Autio P, Hekkala A, Hyppönen E, Knip M, Virtanen SM. Infant feeding patterns in the Finnish type 1 diabetes prediction and prevention nutrition study cohort. *European Journal of Clinical Nutrition* 2005;59:107-113
- Fayter D, Nixon J, Hartley S, Rithalia A, Butler G, Rudolf M, et al. Effectiveness and cost-effectiveness of height screening programmes during the primary school years; a systematic review. *Arch Dis Child* 2008;93:278-84
- Fenn B, Penny M. Using the World Health Organization Growth Standards: Differences From 3 Countries. *J Pediatr Gastroenterol Nutr* 2008;46(3):316-321
- Fenton T, Sauve R. Using the LMS method to calculate z-scores for the Fenton preterm infant growth chart. *Eur J Clin Nutr* 2007 Feb:1-6
- Flegal K. Curve smoothing and transformations in the development of growth curves. *Am J Clin Nutr* 1999;70(suppl):163S-5S
- Garner P, Panpanich R, Logan S. Is routine growth monitoring effective? A systematic review of trials. *Arch Dis Child* 2000;82:197-21
- Garza C. New Growth Standards for the 21st Century: A Prescriptive Approach. *Nutrition Reviews* 2006;64(5):S55-S59
- Garza C, De Onis M. A new international growth reference for young children. *Am J Clin Nutr* 1999;70(Suppl):169S-72S
- Garza C, De Onis M. WHO Multicentre Growth Reference study Group. Rationale for developing a new international growth reference. *Food Nutr Bull* 2004;25(Suppl 1):S5-14
- Grantham-Mc Gregor S, Cheung YB, Cueto S, Glewwe P, Richter L, Strupp B, and the International Child Development Steering Group. Developmental potential in the first 5 years for children in developing countries. *Lancet* 2007;369:60-70
- Grote F, van Dommelen P, Oostdijk W, de Muinck Keizer-Shrama S, Verkerk P, Wit J, van Buuren J. Developing evidence-based guidelines for referral for short stature. *Arch Dis Child* 2008;93:212-217
- Hakanen M, Lagström H, Kaitosaari T, Niinikoski H, Nanto-Salonen K, Jokinen E, et al. Development of overweight in an atherosclerosis prevention trial starting in early childhood. The STRIPP study. *Int J Obes (Lond)* 2006;30:618-26
- Hasunen K, Rynänen S. Imeväisikäisten ruokinta Suomessa vuonna 2005. Sosiaali- ja terveystieteiden tutkimuskeskuksen selvityksiä 2005:19. Helsinki 2006.
- Herngreen W, van Buuren S, van Wieringen J, Reerink J, Verloove-Vanhorick S, Ruys J. Growth in length and weight from birth to 2 years of a representative sample of Netherlands children (born in 1988-89) related to socio-economic status and other background characteristics. *Ann Hum Biol* 1994;21:449-63
- Hindmarsh P. Endocrinology of growth. In: Cameron, editor. *Human growth and development*. Academic Press, London, 2006.

Hindmarsh P, Geary M, Rodeck C, Kingdom J, Cole T. Factors predicting ante- and postnatal growth. *Pediatr Res* 2007;63:99-102

Hochberg Z, Albertsson-Wikland K. Evo-devo of infantile and childhood growth. *Pediatric Research* 2008;64(1):2-7

Howe L, Tilling K, Lawlor D. Accuracy of height and weight data from child health records. *Arch Dis Child*, published online 17 Aug 2009

Hui L, Schooling C, Cowling B, Leung S, Lam T, Leung G. Are universal standard for optimal growth appropriate? Evidence from a Hong Kong Chinese birth cohort. *Arch Dis Child* 2008;93:561-565

Hänninen-Nousiainen P, Pietilä A-M, Koponen P, Vehviläinen-Julkunen K. Rintaruokinnan trendit väestön terveysseurannassa - tuloksia Terveys 2000-tutkimuksesta. *Kätilölehti* 2004;7:258-259

Isanaka S, Villamor E, Shepherd S, Grais R. Assessing the Impact of the Introduction of the World Health Organization Growth Standards and Weight-for-Height z-score Criterion on the Response to Treatment of Severe Acute Malnutrition in Children: Secondary Data Analysis. *Pediatrics* 2009;123:e54-e59

Jorde L, Watkins W, Bamshad M, Dixon M, Ricker C, Seielstad M, Bazer M. The Distribution of Human Genetic Diversity: A Comparison of Mitochondrial, Autosomal, and Y-Chromosome Data. *Am J Hum Genet* 2000;66:979-988

Jorde L, Wooding S. Genetic variation, classification and 'race'. *Nat Genet* 2004;36 Suppl 11:S28-33.

Juliussen PB, Roelants M, Eide GE, Moster D, Juul A, Hauspie R, et al. Growth references for Norwegian children [Norwegian]. *Tidsskrift for den Norske Laegeforening* 2009;129(4):281-286

Kaitosaari T, Rönnemaa T, Raitakari O, Talvio S, Kallio K, Volanen V, et al. Effect of 7-year infancy-onset dietary intervention on serum lipoproteins and lipoprotein subclasses in healthy children in the prospective, randomized special Turku coronary risk factor intervention project for children (STRIP) study. *Circulation* 2003;108:672-7

Kajantie E, Barker D, Osmond C, Forsten T, Eriksson J. Growth before 2 years of age and serum lipids 60 years later: The Helsinki Birth Cohort Study. *Int J Epidemiol* 2008;37:280-289

Karlberg J. A biologically-oriented mathematical model (ICP) for human growth. *Acta Paed Scand* 1989;350(Suppl):70-94

Karlberg J, Jalil F, Lam B, Low L, Yeung CY. Linear growth retardation in relation to the three phases of growth. *Eur J Clin Nutr* 1994;48(Suppl 1):S25-S44

Kautiainen S, Rimpelä A, Vikat A, Virtanen S. Secular trend in overweight and obesity among Finnish adolescents in 1977-1999. *Int J Obes Relat Metab Disord* 2002;26:544-552

Knip M, Reunanen A, Virtanen SM, Nuutinen M, Viikari J, Åkerblom HK. Does the secular increase in body mass in children contribute to the increasing incidence of type 1 diabetes? *Pediatric Diabetes* 2008;9(Part II):46-49

Kramer M. Intrauterine growth and gestational duration determinants. *Pediatrics* 1987;80(4):502-511

von Kries R, Kolezko B, Sauerwald T, von Mutius E, Barnert D, Grunert V, von Voss H. Breast feeding and obesity: cross sectional study. *BMJ* 1999;319:147-50

Laitinen J, Power C, Jarvelin MR. Family social class, maternal body mass index, childhood body mass index, and age at menarche as predictors of adult obesity. *Am J Clin Nutr* 2001;74:287-94.

Larnkjaer A, Schroder S, Schmidt I, Jorgensen M, Michaelsen K. Secular change in adult stature has come to a halt in northern Europe and Italy. *Acta Paediatrica* 2006;95:754-755

Lejarraga H. Growth in Infancy and Childhood: A Pediatric Approach. In: Cameron N, editor. *Human Growth and Development*. Academic Press, London 2006.

Lobstein T, Baur L, Uauy R, IASO international Obesity Task Force. Obesity in children and young people: a crisis in public health. *Obes Rev* 2004;5(Suppl 1):4-104

Mahoney LT, Burns TL, Stanford W. Coronary risk factors measured in childhood and young adult life are associated with coronary artery calcification in young adults: the Muscatine study. *J Am Coll Cardiol* 1996;27:277-84.

Markkula H. *Pediatrator software, version 7.2.0.2, 2005*

Mc Cormic M. The contribution of low birth weight to infant mortality and childhood morbidity. *N Engl J Med* 1985;312:82-90

Mei Z, Ogden C, Flegal K, Grummer-Strawn L. Comparison of the prevalence of Shortness, Underweight, and Overweight among US Children Aged 0 to 59 Months by Using the CDC 2000 and the WHO 2006 Growth Charts. *J Pediatr* 2008;153:622-8

Must A, Strauss RS. Risks and consequences of childhood and adolescent obesity. *Int J Obes Relat Metab Disord* 1999;23(Suppl 2):S2-11

Neovius M, Janson A, Rossner S. Prevalence of obesity in Sweden. *Obes Rev* 2006;7:1-3

Norgan N. Nutrition and growth. In: Cameron N, editor. *Human Growth and Development*. Academic Press, London 2006

Norris S, Griffiths P, Pettifor J, Dunger D, Cameron N. Implications of adopting the WHO 2006 Child Growth Standards: case study from urban South-Africa, the Birth to Twenty cohort. *Ann Hum Biol* 2009;36(1):21-27

Nuutinen O, Nuutinen M. Lapsuusiän lihavuus lisää sepelvaltimotaudin vaaraa. *Duodecim* 2001;117:1356-62

Ong K, Loos R. Rapid infancy weight gain and subsequent obesity: systematic review and hopeful suggestions. *Acta Paediatr* 2006;95:904-8

de Onis M, Garza C, Onyango A, Borghi E. Comparison of the WHO Child Growth Standards and the CDC 2000 Growth Charts. *J. Nutr.* 2007a;137:144-148

de Onis M, Garza C, Onyango A, Martorell R, editors. WHO Child Growth Standards. *Acta Paediatrica*,2006a;96(Suppl 450)

de Onis M, Garza C, Victora C, Onyango A, Frongillo E, Martines J. The WHO Multicentre Growth Reference Study: Planning, study design, and methodology. *Food Nutr Bull*, 2004a;25(Suppl 1):S15-26

de Onis M, Onyango A, Borghi E, Siyam A, Nishida C, Siekmann J. Development of the WHO growth reference for school-aged children and adolescents. *Bulletin of the World Health Organization* 2007b;85:660-7

de Onis M, Onyango A, Borghi E, Gartz C, Yang H, for the Multicentre Growth Reference Study Group. Comparison of the World Health Organization (WHO) Growth Standards and the National Centre for Health Statistics/WHO international growth reference: implications for child health programmes. *Public Health Nutrition* 2006b;9(7):942-947

de Onis M, Onyango A, van den Broek J, Chumlea W, Martorell R, WHO Multicentre Growth Reference Study Group. Measurement and standardization protocols for anthropometry used in the construction of a new international growth reference. *Food Nutr Bull* 2004a;25(Suppl 1):S27-36

de Onis M., Wijnhoven T., Onyango A. Worldwide practices in child growth monitoring. *Journal of Pediatrics* 2004c;144:461-465

Onyango A, de Onis M, Caroli M, Shah U, Sguassero Y, Redondo N, Caroli B. Field-testing the WHO Child Growth Standards in four countries. *J Nutr* 2007;137:149-152

Onyango A, Pinol A, De Onis M, WHO Multicentre Growth Reference Study Group. Managing data for a multicountry longitudinal study: experience from the WHO Multicentre Growth Reference Study. *Food Nutr Bull*. 2004;25:Suppl 1:S46-52

Pan H, Cole T. User's guide to LMS Chart Maker. Medical Research Council, UK 1997-2005

Pere A. Comparison of two methods for transforming height and weight to normality. *Ann Hum Biol* 2000;27(1):35-45

Pere A. Discussion: Conditional Growth Charts. *The Annals of Statistics* 2006; 34(5):2105-2112

Perheentupa J, Pere A. Pituuden ja painon seuranta neuvolassa. In: Simell O, editor. *Neuvolakirja*. Orion Yhtymä OY, 1997.

Pringle P, Geary M, Rodec C, Kingdom J, Kayamba-Kay's S, Hindmarsh P. The influence of cigarette smoking on antenatal growth, birth size, and the insulin –like growth factor axis. *J Clin Endocrinol Metab* 2005;90:2556-2562

Roosenbloom A. Physiology of growth. *Ann Nestlé* 2007;65:97-108

Salmenperä L, Perheentupa J, Siimes M. Exclusively breastfed infants grow slower than reference infants. *Pediatric Research* 1985;19(3):307-312

Schell L, Knutson K. Environmental effects on growth. In: Cameron N, editor. *Human growth and development*. Academic Press, London, 2006.

Schmidt I, Jorgensen M and Michaelsen K. Height of conscripts in Europe: is postneonatal mortality a predictor? *Annals of Human Biology* 1995;22(1):57-67

Seal A, Kerac M. Operational implications of using 2006 World Health Organization growth standards in nutrition programmes: secondary data analysis. *BMJ* 2007;334(7596):733

Shrimpton R, Victora C, de Onis M, Lima R, Blössner M, Clugston G. Worldwide timing of growth faltering: Implications for nutritional interventions. *Pediatrics* 2001;107(5)

Siimes M, Salmenperä L, Perheentupa J. Pitkääkestoinen, yksinomainen rintaruokinta. *Duodecim* 1985;101:458-464

Singhal A, Lucas A. Early origins of cardiovascular disease: is there a unifying hypothesis? *Lancet* 2004;363:1642-5

Sorva, R., Lankinen, S., Tolppanen, E-M, and Perheentupa, J. Variation of growth in height and weight of children. II. After Infancy. *Acta Paediatrica Scandinavica* 1990;79:498-506

Sorva R, Tolppanen E-M, Lankinen S, Perheentupa J. Growth evaluation: parent and child specific height standards. *Archives of Disease in Childhood* 1989;64:1483-87

Sorva R, Tolppanen E-M, Lankinen S, Perheentupa J. Lasten kasvu ja sen arviointi. *Duodecim* 1985;101:465-476

Sosiaali ja Terveysministeriö. Imeväisikäisen lapsen ruoka. Sosiaali ja terveysministeriön oppaita 2004:17

Spencer N. Failure to think about failure to thrive. *Arch Dis Child* 2007;92:95-6

Tanner J. *A history of the study of human growth*. Cambridge 1981, Cambridge University Press

Tanner J. *Fetus into Man. Physical Growth from Conception to Maturity*. Cambridge, Massachusetts: Harvard University Press 1990. Revised edition.

Towne B, Demerath E, Czerwinski S. The Genetic epidemiology of growth and development. In: Cameron N, editor. *Human Growth and Development*. Academic Press, London, 2006.

Ulijaszek S. Between-population differences in human growth. In: Ulijaszek S, Preece M, editors. *The Cambridge Encyclopedia of Human Growth and Development*. Cambridge, UK: Cambridge University Press, 1998:361-379

Verkasalo M. Rintaruokinta yleistynyt. *Suomen Lääkärilehti* 1980;24:1981-83

Verronen P. Rintaruokinnan edistäminen synnytyssairaalassa ja lastenneuvoloissa. Tampereen Yliopisto, Tampere 1988

Vuorela N, Saha M-T, Salo M. Prevalence of overweight and obesity in 5- and 12-year-old Finnish children in 1986 and 2006. *Acta Paediatrica* 2008;98(3):507-512

Walker S, Wachs T, Gardner J, Lozoff B, Wasserman G, Pollit E, Carter J, and the international child development steering group. Child development: risk factors for adverse outcomes in developing countries. *Lancet* 2007;369:145-57

Wang X, Zuckerman B, Coffman G, Corwin M. Familial aggregation of low birth weight among whites and blacks in the United States. *N Engl J Med* 1995; 333:1744-49

Wang Y, Beydoun M. The obesity epidemic in the United States – gender, age, socioeconomic, racial/ethnic, and geographic characteristics: a systematic review and meta-regression analysis. *Epidemiol Rev* 2007;29:6-28

Waterland R, Jirtle R. Early nutrition, epigenetic changes at transposons and imprinted genes, and enhanced susceptibility to adult chronic diseases. *Nutrition* 2004;20:63-68

Waterlow J, Buzina R, Keller W, Lane J, Nichaman M, Tanner J. The presentation and use of weight and height data for comparing nutritional status of groups of children under the age of 10 years. *Bulletin of the World Health Organization*, 1977;55:489-498

WHO and UNICEF. WHO child growth standards and the identification of severe acute malnutrition in infants and children. WHO and UNICEF, 2009.

WHO. Obesity: preventing and managing the global epidemic. Report on a WHO consultation. Technical Report Series, No 894. WHO, 2000.

WHO Multicentre Growth Reference Study Group. Enrollment and baseline characteristic in the WHO Multicentre Growth Reference Study. *Acta Paediatr Suppl*. 2006a;450:7-15

WHO Multicentre Growth Reference Study Group. WHO Child Growth Standards. Length/height-for-age, weight-for-age, weight-for-length, weight-for-height and body mass index-for-age. Methods and development. 2006b. Geneva: World Health Organization, 2006.

WHO Multicentre Growth Reference Study Group. Reliability of anthropometric measurements in the WHO Multicentre Growth Reference Study. *Acta Paediatr Suppl* 2006c;450:56-65

WHO. Physical status: the use and interpretation of anthropometry. Report of a WHO Expert Committee. Technical Report Series No. 854. Geneva, WHO, 1995a.

WHO, UNICEF. Global Strategy for Infant and Young Child Feeding. WHO 2003

WHO Working Group for Infant Growth. An evaluation of infant growth: the use and interpretation of anthropometry in infants. *Bulletin of the WHO* 1995b;73(2):165-174

WHO working group on the Growth Reference Protocol and the WHO Task Force on Methods for the Natural Regulation of Fertility. Growth of healthy infants and the timing, type and frequency of complementary foods. *Am J Clin Nutr* 2002;76:620-7

van Wieringen J. Secular Growth Changes. In: Falkner F, Tanner JM, editors. *Human Growth, 2 Postnatal Growth*. London, Baillière Tindall, 1978

Wright C, Callum J, Birks E, Jarvis S. Effects of community based management in failure to thrive: randomised controlled trial. *BMJ* 1998;317:571-4

Wright C, Lakshman R, Emmet P, Ong K. Implications of adopting the WHO 2006 Child Growth Standard in the UK: two prospective cohort studies. *Arch Dis Child* 2008;93:566-569

Wright C, Parkinson K. Postnatal weight loss in term infants: what is normal and do growth charts allow for it? *Arch Dis Child Fetal Neonatal Ed* 2004;89:F254-7

Ziegler E, Nelson S. The new WHO growth standards. Comparison with other growth charts. *Ann Nestlé* 2007;65(3):109-115

APPENDICES

Appendix 1.

Data that was collected from the Tampere municipality child welfare clinic register (Pegasos patient register)

Baseline characteristics of children
Social security number
Identification code
Birthday
Sex
Place of residence (health centre code)
Amount of siblings
Amount of fetuses (singleton, multiple)
Gestational age at birth
Anthropometric measurements of children
Height
Weight
Head circumference
Date of measurement
Parental characteristics
Age of the mother
Parity
Maternal smoking during pregnancy
Parental smoking after pregnancy
Single parenthood

Appendix 2.

Appendix 2.1. Height-for-age, 5th, 50th and 95th centile values for boys 0-48 months of age, sample population compared to the WHO standard and the Finnish reference.

AGE (mo)	SAMPLE adj			WHO			SAMPLE			FIN		
	5	50	95	5	50	95	5	50	95	5	50	95
0	46.9	50.9	53.8	46.8	49.9	53.0	46.9	50.9	53.8	47.6	50.7	53.8
3	58.1	62.2	65.4	58.1	61.4	64.8	58.1	62.2	65.4	58.2	61.7	65.2
6	65.1	69.0	72.6	64.1	67.6	71.1	65.1	69.1	72.6	65.5	69.1	72.8
10	70.8	74.8	78.7	69.5	73.3	77.0	70.8	74.8	78.7	70.7	74.7	78.7
12	73.1	77.1	81.2	71.8	75.7	79.7	73.1	77.2	81.3	72.9	77.0	81.1
15	76.2	80.5	84.8	75.0	79.1	83.3	76.2	80.5	84.9	75.5	79.9	84.2
18	79.2	83.7	88.3	77.8	82.3	86.7	79.2	83.7	88.2	78.0	82.7	87.4
21	82.0	86.7	91.5	80.4	85.1	89.9	81.7	86.4	91.2	80.9	85.7	90.6
24	84.5	89.5	94.5	82.8	87.8	92.8						
24	83.8	88.8	93.8	82.1	87.1	92.1	83.9	88.9	93.8	83.0	88.0	93.1
27	85.9	91.1	96.3	84.3	89.6	94.9	85.9	91.0	96.2	84.9	90.2	95.6
30	87.8	93.2	98.6	86.3	91.9	97.5	87.8	93.1	98.5	86.6	92.1	97.7
33	89.6	95.2	100.8	88.2	94.1	99.9	89.6	95.2	100.7	88.3	94.0	99.8
36	91.4	97.2	102.9	90.0	96.1	102.2	91.4	97.2	102.9	90.0	95.9	101.8
39	93.1	99.1	105.0	91.7	98.0	104.3	93.1	99.1	105.0	91.7	97.8	103.9
42	94.8	101.0	107.1	93.3	99.9	106.4	94.8	101.1	107.2	93.3	99.6	106.0
45	96.4	102.9	109.2	94.9	101.6	108.3	96.5	102.9	109.2	94.9	101.5	108.0
48	98.0	104.7	111.2	96.4	103.3	110.2	98.0	104.7	111.2	96.5	103.2	110.0

SAMPLE adj = Sample population data, adjusted height measurements to follow WHO standard methods, see chapter 4. Methods

Sample population centiles obtained using LMS method and LMS Pro software

Finnish reference data obtained from PEDIATOR database [mean and SD from the database, centiles calculated from mean and SD values with a formula: 5th centile= M-(SD*1.645); 95th centile= M+(SD*1.645)]

WHO reference data obtained from World Health Organization (WHO, 2006b)

Appendix 2.2. Height-for-age, 5th, 50th and 95th centile values for girls 0-48 months of age, sample population compared to the WHO standard and the Finnish reference.

AGE (mo)	SAMPLE adj			WHO			SAMPLE			FIN		
	5	50	95	5	50	95	5	50	95	5	50	95
0	46.4	50.1	52.9	46.1	49.1	52.2	46.4	50.1	52.9	47.3	50.2	53.1
3	56.8	60.6	63.7	56.3	59.8	63.3	56.8	60.5	63.7	57.3	60.5	63.8
6	63.5	67.2	70.7	62.0	65.7	69.5	63.5	67.2	70.7	64.2	67.7	71.2
10	69.0	73.0	76.8	67.4	71.5	75.5	69.0	73.0	76.8	69.4	73.3	77.2
12	71.3	75.4	79.4	69.8	74.0	78.3	71.3	75.4	79.4	71.5	75.6	79.8
15	74.5	78.8	83.1	73.0	77.5	82.0	74.5	78.8	83.1	74.4	78.8	83.2
18	77.5	82.1	86.6	75.9	80.7	85.5	77.5	82.1	86.6	77.1	81.8	86.5
21	80.4	85.3	90.0	78.6	83.7	88.7	80.1	85.0	89.7	79.3	84.2	89.1
24	83.0	88.1	93.1	81.1	86.4	91.7						
24	82.3	87.4	92.4	80.4	85.7	91.0	82.4	87.5	92.5	81.6	86.8	92.0
27	84.5	89.9	95.1	82.7	88.3	93.8	84.4	89.7	94.9	83.7	89.0	94.4
30	86.5	92.0	97.5	84.9	90.7	96.5	86.3	91.9	97.3	85.6	91.2	96.7
33	88.3	94.1	99.7	86.9	92.9	99.0	88.2	94.0	99.6	87.5	93.2	98.9
36	90.0	96.0	101.9	88.8	95.1	101.3	90.0	96.0	101.8	89.3	95.2	101.0
39	91.7	97.9	104.0	90.6	97.1	103.6	91.7	97.9	104.0	91.0	97.1	103.1
42	93.4	99.8	106.1	92.4	99.0	105.7	93.4	99.8	106.1	92.6	98.9	105.2
45	95.0	101.7	108.2	94.0	100.9	107.8	95.0	101.7	108.2	94.2	100.7	107.3
48	96.6	103.5	110.2	95.6	102.7	109.8	96.6	103.5	110.2	95.8	102.5	109.3

SAMPLE adj = Sample population data, adjusted height measurements to follow WHO standard methods, see chapter 4. Methods

Sample population centiles obtained using LMS method and LMS Pro software

Finnish reference data obtained from Peditator database [mean and SD from the database, centiles calculated from mean and SD values with a formula: 5th centile= M-(SD*1.645); 95th centile= M+(SD*1.645)]

WHO reference data obtained from World Health Organization (WHO, 2006b)

Appendix 2.3. Weight-for-age, 5th, 50th and 95th centile values for boys 0-48 months of age, sample population compared to the WHO standard and the Finnish reference (50th centile only).

AGE (mo)	SAMPLE			WHO			FIN
	5	50	95	5	50	95	50
0	2.7	3.6	4.3	2.6	3.3	4.2	3.6
3	5.3	6.6	7.9	5.2	6.4	7.7	6.2
6	6.9	8.4	10.1	6.6	7.9	9.5	8.4
10	8.2	9.7	11.8	7.7	9.2	10.9	10.0
12	8.6	10.2	12.4	8.1	9.6	11.5	10.5
15	9.2	11.0	13.2	8.6	10.3	12.3	11.2
18	9.8	11.7	14.1	9.1	10.9	13.1	11.8
21	10.4	12.3	14.8	9.6	11.5	13.9	12.5
24	10.8	12.9	15.5	10.1	12.2	14.7	13.0
27	11.3	13.5	16.2	10.5	12.7	15.4	13.6
30	11.8	14.0	16.9	11.0	13.3	16.2	14.1
33	12.2	14.5	17.6	11.4	13.8	16.9	14.6
36	12.6	15.1	18.3	11.8	14.3	17.5	15.1
39	13.1	15.7	19.0	12.2	14.8	18.2	15.5
42	13.5	16.2	19.8	12.5	15.3	18.9	15.9
45	13.9	16.7	20.4	12.9	15.8	19.5	16.4
48	14.3	17.2	21.1	13.3	16.3	20.2	16.8

Sample population centiles obtained using LMS method and LMS Pro software

Finnish reference data obtained from PEDIATOR database (mean only)

WHO reference data obtained from World Health Organization (WHO, 2006b)

Appendix 2.4. Weight-for-age, 5th, 50th and 95th centile values for girls 0-48 months of age, sample population compared to the WHO standard and the Finnish reference (50th centile only).

AGE (mo)	SAMPLE			WHO			FIN
	5	50	95	5	50	95	50
0	2.6	3.5	4.2	2.5	3.2	4.0	3.5
3	4.9	6.0	7.1	4.7	5.8	7.2	5.8
6	6.4	7.7	9.3	6.0	7.3	8.9	7.9
10	7.5	9.0	11.0	7.0	8.5	10.4	9.1
12	8.0	9.5	11.6	7.3	8.9	11.0	10.0
15	8.6	10.2	12.4	7.9	9.6	11.8	10.7
18	9.2	11.0	13.3	8.4	10.2	12.6	11.4
21	9.7	11.6	14.1	8.9	10.9	13.4	12.0
24	10.2	12.2	15.0	9.4	11.5	14.2	12.6
27	10.7	12.9	15.8	9.9	12.1	15.0	13.1
30	11.2	13.5	16.6	10.4	12.7	15.7	13.6
33	11.7	14.0	17.3	10.8	13.3	16.5	14.1
36	12.1	14.5	18.0	11.3	13.9	17.3	14.6
39	12.5	15.1	18.7	11.7	14.4	18.0	15.1
42	12.9	15.6	19.4	12.1	15.0	18.8	15.6
45	13.3	16.2	20.2	12.5	15.5	19.6	16.0
48	13.7	16.7	20.9	12.9	16.1	20.4	16.5

Sample population centiles obtained using LMS method and LMS Pro software
 Finnish reference data obtained from PEDIATOR database (mean only)
 WHO reference data obtained from World Health Organization (WHO, 2006b)