Energy intake, macronutrient composition and nutritional status among children (4-17 years) with Cystic Fibrosis in Scandinavia

A cross-sectional study

Master thesis by

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Kristine Wingård Johansen

Summary

Introduction and aim of the thesis

Cystic fibrosis (CF) is the most common recessively inherited genetic disorder among Caucasians. Genetic mutations in CF patients cause dysfunction in exocrine glands and disturbances in cell membranes. This causes frequent lung infection, shortness of breath and poor weight gain and growth. Pancreas insufficiency (PI) is seen among 90 % of the patients and malabsorption is the greatest negative outcome of this. It is estimated that CF patients have increased energy requirements compared to healthy peers and 120-150 % EAR have been used as a guideline for patients. To increase the energy intake in total, the range of 35-45 % from fat has been used as recommendation. CF patients are recommended to supplement their diet with fat-soluble vitamins to avoid deficiencies. The aim of this thesis was to increase the knowledge about the energy and macronutrient intake of CF patients in Scandinavia. This is important to determine whether the nutritional treatment of the patients is optimal to support normal growth.

Method

"The Scandinavian nutritional multicentre study in patients with CF" was a cross-sectional study and totally 442 children with CF recruited from Denmark, Norway and Sweden when in clinically stable condition. Data were gathered at yearly hospital check-ins. A 7 day diet record using pre-coded national food diaries, and these were analyzed for energy and nutrients at the national institutions. Anthropometrical and clinical measurements were performed and questionnaires detecting nutritional supplements of energy and vitamins were collected. A draw-out of 212 children (4-17 years) with CF and PI and food record was studied in this master thesis.

Results

CF participants seemed to have on average a general satisfying energy and nutrient intake compared to the recommendations. There were no differences in energy intake or macronutrient composition among the genders. Interestingly, participants from

Sweden had a higher energy intake than Norwegian participants. The intake of fat in E % was generally within the lower range of the recommendations. CF participants had a higher energy and fat E % intake compared to healthy peers. The serum values of fat-soluble were on average within the laboratory reference, except for vitamin D. CF participants had on average a satisfying dietary intake of selected micronutrients.

Conclusion

Even though the dietary intake of CF patients seems to have improved over time, there is still a potential for improvement, especially at the individual level. Increased energy requirements and serum values of fat-soluble vitamins below reference values pose a risk to malnutrition and poor clinical outcome. Certain individuals with CF have serum values below the reference point and should be routinely monitored.

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Abbreviations and explanation of words

BMI	Body Mass Index
CF	Cystic Fibrosis
CHO	Carbohydrates
EAR	Estimated Average Requirement
EFA	Essential fatty acids
FEV_1	Forced Expiratory Volume in 1 second
IBW	Ideal Body Weight
NBS	Newborn screening
NNR	Nordic Nutrition Recommendations
PERT	Pancreatic Enzyme Replacement Therapy
PI	Pancreas insufficiency
PS	Pancreas sufficiency
PUFA	Poly unsaturated fatty acids
RDA	Recommended Daily Allowance
REE	Resting energy expenditure
WHO	World Health Organization

1 Background

1.1 Cystic fibrosis

Cystic fibrosis (CF) is the most common recessively inherited genetic disorder in Caucasians. The disease includes a variety of symptoms including persistent coughing, frequent lung infection, shortness of breath, poor growth/weight gain and greasy bulky stools or difficulties with bowel movement and salty tasting skin. Cystic fibrosis is a multi-organ disease, clinical most important are the affection of the lungs and digestive system due to viscous mucous (1).

The mean prevalence of CF in EU is calculated to 0.737/10 000 which means that it still is a rare disease defined as lower than 5 per 10 000 (2). The incidence is highest in Ireland, 1:1353 live births, and lowest in Finland, 1:25 000 (2). The incidence in Denmark is 1:4700 and in Sweden 1:5600 (2). The incidence in Norway is not known, but probably near the incidence in Denmark or Sweden. There are 283 known cases of CF in Norway in 2011 (3). In Scandinavia there are ca. 1300 patients diagnosed with CF (3-5).

The incidence among non-Caucasians is lower than among Caucasians (6).

The gene responsible for CF was localized in 1989 (6). CF is recognized by mutations in the CF trans-membrane conductance regulator (CFTR) gene. This gene is positioned on chromosome 7q31.2 and the different mutations make up five categories of which CF is classified depending on the phenotype (2). More than 1,600 mutations have been found, and the most common mutation is named ΔF508 (2).

The CF-mutations causes widespread dysfunction in exocrine glands with disturbances in sodium, chloride and water transport through cell membranes in epithelial-cells (6). The result is abnormally dehydrated viscous secretions and multi-organ disease such as chronic lung disease with inflammation, airway obstruction and recurrent or chronic infections, exocrine pancreas insufficiency with steatorrhea, intestinal obstruction in

neonates and older participants, abnormally high sodium chloride levels in sweat and other complications such as liver CF liver disease, CF related diabetes and osteoporosis (6;7) .

Cystic fibrosis (CF) is a life-shortening disease and lung failure is the main cause of death. Previously CF was considered lethal in childhood, but survival has improved over time (6). This is probably mostly due to better, more aggressive and preventive treatment (6). In Norway about 60 % of the CF-population are ≥ 18 yrs old in 2011 (3). The life expectancy of CF participants is improved and many live through their thirties, however about 15-20 % of children in US and Canada die before they turn 10 years old. Studies from the US and Canada support the need for close follow-up of the CF participants for better survival rate (8). A United Kingdom model predicts an estimated median survival of 50 years for a child born with CF in 2000 or later (9).

1.1.1 Diagnosis

A consensus from 1998 states that diagnosis of CF should be determined by one or more of the following criteria: history of CF with a sibling, positive sweat test, positive newborn screening test and laboratory result of CFTR genetic mutation either shown as elevated chloride levels in sweat or identification of mutations known to cause CF (10).

The Cystic Fibrosis Foundation classifies the sweat test as the gold standard for diagnosing CF. Amount of chloride in the sweat is measured by applying a chemical to the arm or the leg. An electrode is placed over the spot and a weak electrical current is applied to produce sweat. The sweat is collected and analyzed for content of chloride. More chloride than normal is seen among patients with CF. A chloride level of ≥ 60 mmol/L diagnoses CF (11). The diagnostic working group on CF present two algorithms that have come out of discussions between experts (12). The first algorithm is diagnosis based on the sweat test, and the second is based on the genetic mutations. They highlight that both algorithms are important to manifest the disease, especially in patients with mild CF.

Newborn screening

Newborn screening (NBS) have been used for years in Australia. From 2011 neonatal screening for CF will be implemented in Norway (13). This is a method that determines immunoreactive trypsinogen (IRT) levels in newborn babies. In babies with CF IRT is elevated. The sweat test is a follow up test if IRT levels are elevated (14). Mckay et al. (14) emphasize the importance of NBS and early diagnosis of CF. These two parameters linked with the suitable treatment suggests a reduction in morbidity, supports growth in the first years of life and prevent malnutrition and vitamin deficiency.

Failure to grow is a general symptom among CF patients. A randomized control trial in Wisconsin, USA states that there was an odds ratio of 3.5 for children diagnosed with NBS, compared to those diagnosed conventionally with an odds ratio of 3.1 (14).

Cystic fibrosis is a complex disease requiring a holistic approach to treatment. A multidisciplinary team is recommended for the best outcome. The medical, nutritional and physiotherapy treatments are the cornerstones in CF-care (15).

1.1.2 Affected organs in CF

Chronic lung disease

As a result of the secretion of at thicker mucus than normal, there is a drastic decrease in the clearance of the lungs (1;7) This is one important reason for the chronic bacterial colonization/infection. Inflammation represents a basal status already at birth. Inflammation and bacterial infection are the origin of a vicious circle in CF patients causing damage in the lung and in end lung failure (7). Lung transplant is then the option.

The most common bacteria infections among participants with CF are *Staphylococcus aureus, Haemophilus influenza* and *Pseudomonas aeruginosa* (16). *Haemophilus influenza* and *Staphylococcus aureus* are most frequent in childhood. *Pseudomonas aeruginosa* is most frequent among adults. More than 50 % of adults in Scandinavia are chronic carriers of *Pseudomonas aeruginosa* (17) . When the bacterium is present,

a drop in the lung function is often seen. Early treatment is important for easier handling of the microbe. Parents are advised to ensure that children with CF are tested for colonization every 6th week (16).

Treatment and prevention of lung infections

The treatment involves a combination of lung physiotherapy, the use of bronchodilators and antibiotic treatment of the microbes (16).

The microbes are often difficult to eradicate with antibiotics. Early treatment and high doses of antibiotics are important for easier handling of the microbe (16).

Daily lung physiotherapy is highly important contributing to reduction of chronic infections. Inhalation and mucous mobilization techniques are used to preserve the lung function and clean the airways for viscous mucous. Coughing techniques, physical activity and the use of inhalation of medication are parts of the lung therapy (18).

Pancreas insufficiency (PI)

The most common gastrointestinal problem among CF participants is exocrine pancreas insufficiency (PI). Pancreas is classified as insufficient when > 90 % of acinar function is lost. The damage is first seen in the fetus, and the result is replacement of acinar cells with fibrous tissue and fat (19). Meconium ileus is seen among 15 % (20) of CF patients in the US with PI and is manifested 48 hours after birth as intestinal obstruction. Meconium is normally present at birth and enzymes from the pancreas help pass the substance with feces (20).

An estimation around 90 % of CF patients have pancreas insufficiency (PI) (6;19). In the study material for this thesis, 89 % of the children had PI. The pancreas secretes digestion enzymes that aids in digestion and ultimately the absorption of protein, fat and fat-soluble vitamins. PI is characterized by viscous secretions from pancreas, that after prolonged time will cause autodigestion of pancreas. The digestion enzymes of the pancreas build up within the pancreas and eventually destroy its own tissue. PI is diagnosed by a fecal test. Fecal pancreatic elastase 1 (EL 1) is normally synthesized in

the acinar cells. Reduction in the levels of EL1 suggest pancreatic lesion. A fecal test is delivered, and very low values are shown in patients with PI (19).

Malabsorption with steatorrhea is the greatest negative outcome of pancreas insufficiency (21). Especially fat, protein, nitrogen, bile, fat-soluble vitamins and vitamin B_{12} are affected (6). Malabsorption increases the risk of poor growth, impaired muscle function and poor respiratory function (6). Energy loss may also come from vomiting, and undiagnosed glycosuria. Hyperglycemia due to destruction of the cells of Langerhans can develop and some CF participants experience diabetes mellitus as a result of the disease (6). Patients with PI have the lowest prognosis (9).

Other gastrointestinal problems

Celiac disease, rectal prolapsed, acute pancreatitis, gastro-esophageal reflux, ulcer and Crohn's disease have been reported among CF patients (6).

1.1.3 Pancreatic enzyme replacement therapy

Pancreatic replacement therapy is used to treat participants with PI, highly common among CF participants. Participants with PI must take an oral supplement of pancreatic enzymes to avoid steatorrhea. A normal functioning pancreas secretes digestive enzymes such as lipase, protease and amylase into duodenum. The breakdown of fat, protein and carbohydrate (CHO) is then facilitated. When the pancreas is malfunctioning the patient suffer from weight loss, cramps, flatulence, bloating and greasy stools, and inappropriate digestion of CHO and protein contributes to malnutrition as well as the fat maldigestion (22).

Enteric-coated microspheres are mostly used (22). Enteric-coated enzymes are protected from stomach acid, and are activated when pH climb above 5.5 in duodenum (6). Fat absorption between 85-95 % of intake should be possible to achieve with enzyme preparations. Timing in relation to meal and adjusting the enzyme dosage to fat intake is important. It is necessary to review the pancreatic enzyme replacement therapy regularly to optimize uptake of fat (19).

1.2 Deficiencies and nutritional recommendations

Resting energy expenditure

Energy expenditure determines the energy requirement of the body and can either be measured or calculated (23). Resting energy expenditure is defined as an estimate of the basal metabolic rate (6). Many studies report that CF patients have increased REE compared to healthy individuals. Some researches believe that increased REE is one of the main reasons for malnutrition among the CF participants. Infection of the lungs and chronic inflammation is associated with increased workload for the respiratory system causing and increase in REE (23). Noteworthy, antibiotic treatment of infections have been associated in a decline in REE (6). Total energy expenditure is composed of REE, dietary thermo-genesis and the cost of physical activity. An increase in REE does not always mean an increase in total energy expenditure (TEE) according to McCloskey et al. (24).

Interestingly, the discussion around genotype and REE conflicting. Some studies found participants with the ΔF508 to have a higher REE than participants with other genotypes. On the other hand other studies have found that REE is not dependent on genotype (6).

Low energy intake

Growth failure among CF participants have been linked to poor dietary intake (6). Appetite is often reduced during illness, and especially around infections. Some other factors that may be of importance are poor use of pancreatic enzymes, behavioral feeding problems, media pressure to healthy, depression, eating disorders (6).

1.2.1 Malnutrition among CF patients

Malnutrition is characterized by divergence between energy and nutrient requirement and a person's food intake affected by malabsorption in the body (25) This complicated condition can affect growth when lasting for more than 4 months (26). Malabsorption and malnutrition is seen early among CF participants and growth retardation is often a consequence (27). Symptoms of malabsorption include pale,

loose and foul smelling stools. Patients with good appetite who experience poor growth and weight gain are likely to have malabsorption. If not identified early, severe consequences can be malnutrition and growth failure (23).

Among CF participants, wasting is highly correlated to poor prognosis and impaired survival (28). Sharma et al. reported in 2001 that survival is highly dependent on percentage ideal weight after correction for age, gender, % predicted FEV_1 (Forced Expiratory Volume in one second), PaO_2 (partial pressure of oxygen in arterial blood) and $PaCO_2$ (partial pressure of carbon dioxide in arterial blood). Patients managing to obtain >85 % ideal body weight had an 84 % survival rate after five years. Comparably participants with ≤ 85 % ideal body weight had 53 % survival rate (29).

According to the Cystic Fibrosis Foundation optimal nutrition and growth is important for treatment of malnutrition and to improve quality of life for participants living with CF. Normalization and maintenance of weight for adults, and optimization of growth for children is achieved through management of gastrointestinal and pulmonary symptoms, energy intakes, psychosocial and financial issues (1). There has been improvement in the nutritional intake of CF participants during the past twenty years by increasing total energy intake, and energy percentage from fat. The improvement in pancreatic enzyme supplements have also contributed to this (28). In children, the importance of improving nutritional status contributes to optimized essential fatty acids, vitamin and mineral status and minimizes the risk of pubertal delay (30).

1.2.2 Energy and macronutrients

The symptoms of CF, such as chronic lung infection and malabsorption symptoms may contribute to decreased appetite. Decreased fat absorption from the food means loss of energy, and lung infections and decreased lung function may contribute to increased energy expenditure. This heightens the risk of not meeting energy requirements. The recommendations discussed below take into account the increased energy needs of infection, cost of breathing and loss due to malabsorption.

Energy

Dietary Reference Intakes is a collective term of reference values. The Estimated Average Requirement (EAR) is the intake level for a nutrient at which meets the needs of 50 % of the population (31). Recommended Dietary Allowance (RDA) is the daily intake of a nutrient considered sufficient by the Food and Nutrition Board to meet the requirements of nearly all healthy individuals in each life stage and gender group. It is set to approximately 20 % higher than EAR (31). Estimates suggest that CF patients may need up to 120 – 150 % EAR for age and gender (6). Ramsey et al 1992 emphasize the need for a diet > 120 % RDA as well as 40 % from fat and 15 % from protein (32).

The Cystic Fibrosis Foundation in the US strongly emphasizes the importance of nutritional guidance from health personnel to children who struggle with growth. In the United States, the CF Foundation states that less than 50 % of the CF children have a BMI percentile ≥ 50. Stark et al. (33) compared children receiving behavioral intervention with dietary counseling compared to children receiving only dietary counseling. The results after nine weeks led to improved energy intake among the first group. The children showed improved nutritional status with an energy intake of 120 % of recommendations and increased BMI z-score, emphasizing the importance of nutritional guidance (33). It is important to note that pulmonary infections may require a higher energy intake in periods. Some children grow normally by consuming the EAR for energy for normal population (6). American guidelines have been developed to establish good routines around dietary and vitamin supplements along with enzymatic treatment. The American Cystic Fibrosis Foundation reported in 2005 through the CF Patient Registry Report that 23% of children in the US are below the 10^{th} percentile weight for age and sex. The same report states that 22% of adults (aged 18-30) are underweight with a body mass index < 18.5 (25). The current guidelines for children with CF are based on consensus. The clinical American guidelines are from 2002 and identify children at risk for as well as children with nutritional failure and their anthropometric measurements in relation to reference standards. Clinicians have

found the standards difficult to work with, and the guidelines have sometimes resulted in incoherent risk classifications of participants (25).

Fat

Fat is the most concentrated energy source as well as the only source of essential fatty acids (EFA). CF patients are recommended to keep their fat intake around 35-45 % of total intake to get enough energy (6). Many studies use a limit set at fat intake to 40 E% when investigating the dietary intake of CF patients (30;34).

EFA deficiency is frequently reported in CF and symptoms include impaired wound healing, increased susceptibility to infection and reduced platelet aggregation (6). The precursor EFA, linolenic acid, α-linolenic acid and omega 3 long chain polyunsaturated fatty acids (such as EPA, DHA) are found to be low in plasma and tissue of these patients. Essential fatty acid deficiency is associated with changes in membrane and cellular functions, changes in immune function as well as renal, hepatic and pulmonary functions (23).

The effects of low weight and negative energy balance associated with CF influence beta-oxidation of PUFA. Thus low concentrations of PUFA are caused by increased destruction of the fatty acids in the participants who also might have infections, low antioxidant status and increased oxidative stress (23).

Protein

It is still unclear around protein requirements for CF patients and the European consensus does not give any recommendation on protein (23). The British Dietetic Association, pediatric group recommend that protein should provide 15 % of the total energy intake (6). Patients with increased loss of nitrogen in the feces, and those that have increased protein turnover should keep their protein intake around 15 % of total intake (6).

Fiber

Normally children with CF may have a diet low in fiber as they are recommended to keep a high fat and sugar intake. Fiber is known to increase stool frequency, and many

CF children suffer from more abdominal pain, especially when diet is low in fiber (6). Nordic Nutrition Recommendations (NNR) 2004 recommends an intake of 10 g/day of fiber for children from the age of 4. The intake should gradually increase to recommended level for adults 25-35 g/day or 3 g/MJ (35).

1.2.3 Fat soluble vitamins

Routine supplementation with fat soluble vitamins A, D and E are especially important for patients with CF and PI due to the increased risk of malabsorption. The dose recommended is based on the levels that will normalize serum values through monitoring levels in most participants with CF without causing hypervitaminosis (23). Routine supplementation of vitamin K is still controversial (23).

Vitamin A plays a large role in eye function, immune system, reproduction, growth and development. People failing to meet the required needs of vitamin A, deficiency symptoms such as impaired vision and decreased resistance to infections develop (35). Poor clinical status and impaired lung function in patients with CF are associated with low serum levels of vitamin A (23).

Ultraviolet light from sunlight is the major source of vitamin D for humans, depending on seasons and geographical position. Supplementation of vitamin D is not necessary when sun exposure is adequate. Low serum levels of vitamin D binding protein have been found among CF patients and may cause the low serum levels of vitamin D (23).

Vitamin E, known to protect the lipoproteins and cell membranes is highly important for neurological activity and is considered one of the body's antioxidants. As CF patients are prone to chronic inflammation their oxidative stress is increased. The antioxidant activity is recognized by vitamin E's role in defending against free radicals such as peroxidation of fatty acids. Symptoms of deficiency such as hemolytic anemia, trombocytosis and edema have been described among premature low birth weight infants (35). Whether vitamin E supplementation protects against oxidative lung damage in patients with CF is still not determined (23).

1.3 Improvement of nutritional status in CF

1.3.1 The importance of good nutritional status on lung function

The Cystic Fibrosis Foundation made evidence-based recommendations for nutritional management of children and adults with CF and PI based on results of a systematic review, and found that normal weight and growth associated with better lung function (FEV_1) (25). Steinkamp et al investigated the effect of malnutrition and colonization of *P.aeruginosa* on FEV_1, and found that lung function was related to both parameters independent of gender. Patients with malnutrition were found to have decreased lung function , independent of bacterial colonization. Patients with both colonization of bacteria and malnutrition had the worst lung function (36).

Another classical experiment that involved nutritional intervention among CF patients in Boston, USA and Toronto, Canada (8). This study began the investigation of the effect of nutritional intervention on weight gain and clinical improvement of the disease. When studying participants at clinics in Boston and Toronto, the researches found large differences when looking into the diet and pancreatic enzyme supplementation regimes. While Toronto emphasized a high fat, high calorie diet with 20 – 30 enzyme capsules per day, Boston maintained a low fat, high calorie diet with less enzymes per meal. When looking at survival rate of CF patients, researchers found significantly higher survival rate among Toronto patients. Toronto patients had a median survival age of 30, while it was 21 years in Boston. (8).

1.3.2 Strategies to improve nutritional status among CF patients

Current American recommendations have come out of an evidence based review from 2005, where 1,008 articles from 1998-2005 were examined. Articles evaluated energy intake and pancreatic enzyme replacement therapy (PERT), and were used to develop recommendations for patients with CF. The articles based on clinical trials showed that a higher energy intake was related to improved weight gain. The recommendations based on reviews for children over 2 years of age and adults is an energy intake greater

than the general population ranging from 110-200% (25). It is important to note that energy requirement is highly dependent of presence and level of malabsorption. Dietary habits using a 24 hour recall sheet and food recording for 3-5 consecutive days are useful tools in assessing energy intake. Physical activity, lung status and malabsorption should be added to basal metabolic rate (BMR) to estimate energy requirement (32). To achieve an energy intake of 110-200% of the healthy population nutritional supplements, both oral and enteral along with the food intake is required. The dietary recommendations are set high to balance out the energy losses from infections, increased breathing and malabsorption (25).

The European Consensus from 2002 (23) advises patients with CF to hold their food intake above 120 % EAR, however many of the participants do not manage to keep their intake this high. Different strategies have been tested to increase the appetite of patients suffering from low intake. Anabolic medicines and muscle stimulation are shown to increase appetite, and body weight. Side effects such as diabetes and adrenal suppression is further yet to be studied (23).

White et al. emphasizes a fat intake of 40 % of total energy intake (30;34). Oral nutrition support is a concept for improving nutrition intake. Nutritional booster is the technique of adding calories to a meal without increasing the amount of food noteworthy. This method considers the patients' food likings and adds energy to the patients usual diet. Examples are to add butter or margarine to potatoes, rice or pasta and to make soup with milk or cream instead of water. Adding snacks in between meals such as nuts, cheese, peanut butter, whole milk and pizza is often a better way to increase fat intake more so than to eat snacks such as pop or fruit juice. Home made supplements such as smoothies or milkshake may be a good supplement. Even though commercial supplemental drinks can be more convenient, the recipes offered for home made supplemental drinks often taste better and can be easier to modify, according to Patchell (6).

1.3.3 Nutritional supplements

Nutritional drinks

For those patients that struggle to get their daily intake of food above 120 % of the recommended intake, nutrient dense supplements have been used for a long time to increase energy intake. There are different supplements, depending on country, hospital and what the patient prefer.

A study by Kalnins et al in Toronto, Canada investigated the effect of oral supplements on energy intake and nutritional status over a 3 month period. The oral supplement was intended to increase the energy intake with 20 % over this time period. The study group looked at the effects of oral supplements on malnourishment among CF participants. Findings of the study included no significant differences in body weight or energy intake after three months. Interestingly, they found no differences in FEV_1 as well. Explanations to why this was the case is based on the theory that the nutritional supplements substitute normal food, and thus do not lead to additional energy (37). The use of dietary advice and monitoring alone is an appropriate approach in children with CF who are moderately malnourished. Nutritional supplements may be used but should not be regarded as an essential part of care (38).

Enteral tubefeeding

When weight for height drops less than 85 %, a weight loss for more than 2 months or no weight gain for 3-6 months enteral tube feeding may be used among CF patients. Around 5 % of CF patients need tube feeding to support nutritional intake in the UK. Most of these are adolescents (6). This method for improving nutritional status is well documented, and includes supplements introduced to the body via the nose or stomach. Nasogastric or gastronomic tubes are usually activated during continuous feeding over night. Improvements in body fat, height and muscle mass is linked to tube feeding (6).

Supplementation of fat soluble vitamins in CF

Supplements intended for CF patients have been used in both Europe and the US. Fat soluble vitamin supplements should be taken with a fat containing meal in the

morning, with the addition of enzymes for best absorption (32). Daily doses of fat soluble supplementation of vitamin A is recommended, with a current daily intake between 1100 and 3400 µg (23).

The European Census Report on Cystic Fibrosis also states that dosage should never be above 6,000 µg if RBP is low. Water soluble supplementation of vitamin A is thought to be more toxic than viscous supplements such as fish oil. Serum levels of vitamins should be routinely measured and monitored in CF to ensure optimal supplementation (23).

CF patients are recommended to take 10-20 µg of daily of a vitamin D supplement. Doses up to 50 µg have been given to patients with severe deficiencies (23). The Nordic countries, having seasonal changes and low sun exposure during the winter have seen positive outcomes after introducing 25-OH vitamin D_3 supplementation to infants during the past 30 to 40 years. (35). A report from the UK (2008) recently stated that serum values in CF should be within the range of 75-150 nmol/L is desirable (39).

According to the NNR 2004 supplementation of vitamin E might amplify the risk of hemorrhagic stroke and lower the risk of ischemic stroke among people with hypertension (35). Supplementation between 70-250 mg is recommended (23).

Vitamin K, being one of the fat soluble vitamins are usually not taken in consideration, however new methods for determining vitamin K deficiency are studied (40). Vitamin K is also regulated by the gut flora, however how this affect vitamin K status is still discussed. On the other hand is antibiotic therapy of infections may affect the gut flora and synthesis of vitamin K in the intestines (41).

Table 1.1 *Recommended supplement intake of fat soluble vitamins A, D and E for CF participants*

Vitamin	CF patients needing supplements	Starting dose
Vitamin A	PI	4000- 10 000 IU (1,100- 3,000 µg)
Vitamin D	PI, northern countries	400-800 IU (10-20 µg)
Vitamin E	PI	100-400 IU (70-250 mg RRR tocopherol)

Requirements for CF participants from the European consensus report (23).

Special considerations in children with CF

In pre-school age, children have developed their own taste for certain foods. Children aged 6-12 years can have difficulties managing the disease and compliance of treatment such as enzyme therapy, and some children may feel that they are differentiated from the other children in their class. This age range is also well known for peer pressure, also around food choices. Children and youth aged 13-18 years have a higher energy need to support the development of the body that takes place during puberty. On the other side, lung infections are more frequent in this age range, adding to the energy need. Peer pressure is even more common among children in this age range, and especially girls may increase their risk of not maintaining their energy need. (32).

1.4 Monitoring growth

1.4.1 Assessment of growth

Numerous guidelines have been published to optimize the care for CF patients to evaluate, monitor and detect complications and prevent a negative outcome. A dietetic interview along with a diet record make up a dietary assessment, which is recommended practice at CF centers at least once a year (15). It should be taken into consideration that CF children often have delayed puberty, and assessment of pubertal stage is useful to determine the risk of malnutrition. BMI, percentage weight for age, height for age and weight for height is routinely used in the United States. These measurements can be useful to assess growth, however should be used carefully with children (6), as BMI must be interpreted on the basis of comparison with age and gender specific references (23).

Routine measurement of weight and height should be recorded at every visit with their physician. BMI should be calculated, and growth should be plotted on growth charts for most accurate monitoring (19). To determine nutritional status, standard deviation scores or z-score should be used. Z-scores of height, weight and BMI can be used to track changes over time (19).

BMI

Body mass index (BMI) is calculated by weight/height^2 and is used among children and adults to evaluate over- and underweight in research and at clinics (42). As child growth is an important indicator on nutritional status the World Health Organization (WHO) have determined a set of standards to monitor populations. Wasting is defined as low weight for height and stunting as low height for age. Stunting is a result of long term nutritional deprivation, and poor diets and chronic infections is often the main reason (42).

As BMI vary among the genders and age, age specific reference values are used for comparison and these are expressed as z-scores. The values are best evaluated through

comparison with national reference values. Nysom et al. (43) investigated the national reference values for healthy Danish people between the age of 0 and 45. These values have been compared to other public European reference values. Danish girls aged 6-18 had a significantly higher BMI than female German, French and older Danish reference populations. To diagnose and treat CF appropriate standards and methods are needed at clinics (43).

1.5 Studies on nutritional intake and nutritional status and on CF

Studies on CF children present findings of participants consuming more energy than controls, however guidelines are often not reached (30).

Stark et al. compared the growth outcomes of 67 CF children receiving nutritional intervention to CF children receiving standard care. Improvement in BMI z-score was investigated from baseline and after 2 years. The children in the intervention group received nutrition education over the course of 9 weeks. The results of the study showed that children in the intervention group had a significantly less decline in BMI z-score over time than those children receiving standard care (33).

White et al (30) highlight that adolescents and young adults have an energy need that is 25-80 % higher than healthy peers. In their retrospective case-control they examined 94 dietary and pulmonary assessments and recorded height and weight. The mean intake of the participants was 114 % of EAR None of the participants had a fat intake within the recommendation of 40 % of total intake (30).

A study on energy intake and nutritional status of preadolescent and adolescent children with CF in Toronto found dietary intake of the children to be 116 % for girls and 112 % of EAR for boys (44). The children (n=56) were 10-15 years of age an completed a 3 day food diary and completed anthropometric and pulmonary assessment. The children had a mean intake of 35 E% from fat, in both genders. Nutritional status was normal in both genders, as determined by weight as percentage

of ideal weight for height, mean triceps skin fold thickness and mid-arm muscle circumference (44).

Kawchak et al completed a 3-year longitudinal prospective study of 25 children with CF and PI at the mean age of 7.8 (±1.3) at the start of year 1. Energy intake, nutritional status and pulmonary function were analyzed. Results were compared to a healthy control group of 26 children within the same age. They report that energy intake was close to or exceeding 100 % RDA. A high fat, high energy diet was prescribed for the CF participants before and during the food record assessment. Findings from the study state that CF participants had a higher energy and fat intake than the controls. However CF participants had a mean fat intake of 33 E%, an intake which does not fall within the recommended intake of 35-40 % of total intake. No significant difference was found in the energy intake between the genders within the CF participants (45).

1.5.1 Scandinavian dietary population studies in healthy children

We wanted to compare the distribution of macronutrients and investigate the participants with CF in this study with children without CF at the same age. For this purpose we used national surveys from each country.

The objectives of three Scandinavian studies (46-48) conducted around the same time line, approximately 2000-2003 include children and their food intake as a mean to promote and proactively support healthy living. The studies were performed among children in primary school. Ungkost 2000, Riksmaten 2003 and Dietary Habits in Denmark 2000-2002 investigate children and teenager's food choices, intake, food routine and composition of the meal. The subjects registered their food intake and physical activity for 7 consecutive days. All three studies show that the Scandinavian children's food intake is much close to the Nordic Nutrition recommendations, however there are some weak attributes. The children have a higher intake of saturated fat and added sugar than recommended. The intake of foods rich in dietary fiber such as bread and potatoes are lower than recommended.

For example did the children's protein intake range between 14-16 E%, fat intake from 31-32 E% and CHO from 53-54 E%. The intake of fat and sugar was mainly added sucrose and saturated fats. Only 3.6-3.7 % of the fat intake included unsaturated fatty acids.

1.5.2 The Scandinavian nutritional multicentre CF study

The thesis is a part of "The Scandinavian nutritional multicentre study in patients with CF". This is a cross-sectional study initiated and designed by the Scandinavian Cystic Fibrosis Study Consortium (SCFSC) where the main objective was to determine the nutritional status of CF patients in Scandinavia. The study was performed at CF centers in Denmark, Norway and Sweden. Data were collected from September 2003-May 2006. Other objectives are to find out whether there are any differences between the countries and to find possible relations contributing to the findings on nutritional status. The study is ethically approved by Regional Ethics Committees in all three countries, and informed consent signed by all participants. The team leader of this study is Lena Hjelte MD, PhD, Associate Professor and the leader of Stockholm CF centre, Karolinska University Hospital Huddinge.

2 Aim of the thesis

This master thesis aims to investigate

- The energy and nutrient intake and the nutritional status among children (4-17.9 years old) with cystic fibrosis (CF) and pancreas insufficiency (PI) in Scandinavia (Denmark, Norway and Sweden).

- Factors that can influence the energy and nutrient intake and nutritional status.

Objectives

- To investigate the clinical (FEV_1) and nutritional status (BMI, height and weight) among children with CF and PI

- To investigate the dietary intake of energy and nutrients among the children with CF and PI and determine whether there are any differences in the dietary intake among participants from Denmark, Norway and Sweden, younger and older children and between the genders.

- To compare the macronutrient composition in the diet of children with CF and PI to that of healthy children in Scandinavia.

- To determine to what degree there is a correlation between fat intake in E % and energy intake in % of EAR and the distribution of macronutrients in the diet of children with CF and PI.

- To identify the proportion of children with CF and PI that use nutritional drinks, how much they use and how much energy this adds to their total intake. In addition to investigate the correlation between intake of nutritional drinks and BMI

- To compare the daily supplementation of fat soluble vitamins (A, D and E) from supplements with the recommendations for CF and PI, and to investigate if there are any associations between use of supplements and serum values for these vitamins.

3 Material and methods

3.1 Study design and inclusion criteria

The participants were recruited from two Norwegian, two Swedish and one Danish hospital from 2003-2006. They were consecutively included when in clinically stable condition. Participants using pancreatic enzymes were defined as pancreatic insufficient. Patients with CF diagnosed by repeated positive sweat test (Chloride :Cl > 60mmol/L) and pulmonary or gastrointestinal symptoms or positive mutational analysis compatible with the diagnosis of CF. Patients using pancreatic enzymes were defined as pancreatic insufficient. The following inclusion and exclusion criteria were used:

Table 3.1 *Inclusion criteria for participants in the study*

Inclusion criteria
Confirmed CF diagnosis based on clinical features
≥ two positive sweat tests (Cl > 60mmol/l) and/or presence of known disease-causing mutation on each CFTR gene

A total of 898 participants were included in the study, and 442 of these were under 18 years of age. The patients were invited to the study through their CF centre, and an information letter was sent to each patient and their parents (Appendix 1). Informed consent was gathered from all patients participating in the study (Appendix 2,3).

This master thesis includes data on 212 children (4-17.9 years of age) with PI who have recorded their dietary intake from "The Scandinavian nutritional multicentre study in patients with CF". The dietary record forms were not valid for children younger than 4 years of age, thus children < 4 years have been excluded from the thesis.

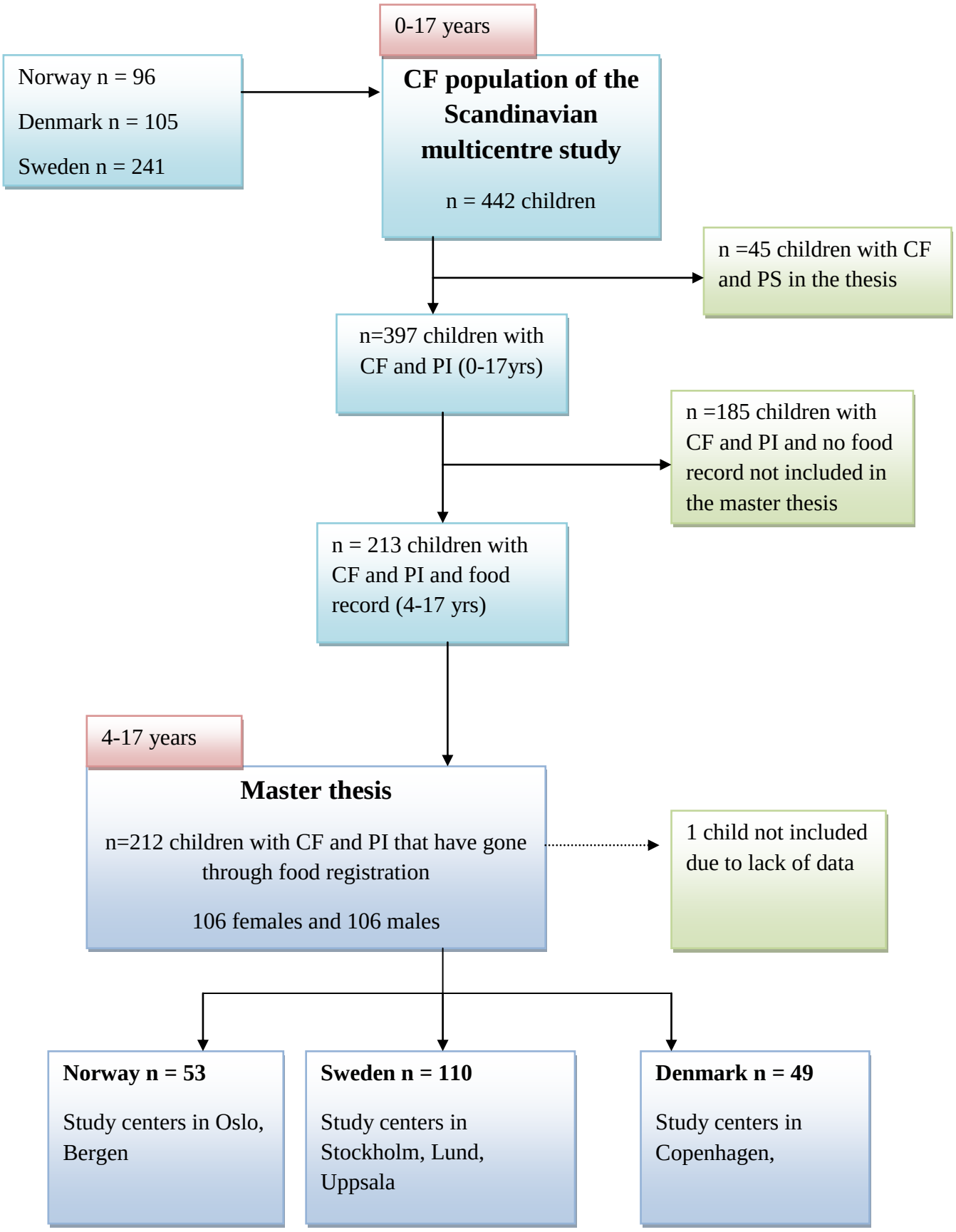

Figure 3.1 *Flow chart depicting the participants included in the Scandinavian CF study and in this thesis:*

3.2 Methods

The data were gathered at yearly hospital check-ins and included blood samples , anthropometrical measurements, tests and examinations as well as a 7-day diet record. A doctor interviewed the participants about their disease, complications, symptoms and treatment .

3.2.1 Nutritional intake

Diet record

A dietitian at each centre was instructed on how to inform the participants on the food registration (Appendix 4). The dietitian instructed the participants and the parents on how to register their intake of food, and oral or enteral energy supplements. Day care providers and kinder garden assistants were provided a written instruction on how to register food intake (Appendix 5).

The participants completed a 7 day diet record by using pre-coded national food diaries. The dietary intake was recorded on 7 executive days in a food diary corresponding to each country. The food diary in Norway included lists of typical foods and food groups within each country. Every food group had an open box, where the participants could register their individual intake. Foods not included in the diary could be written down at the end of each page. Quantity was given in defined household measurements such as cups, tablespoon or portions illustrated by pictures.

A written instruction (Appendix 6) and a picture booklet on portion sizes were also distributed to the participants and parents. The picture booklet is somewhat different in each country. The Norwegian pre-coded food diaries (Appendix 7) have been validated (49), and included 277 foods including drinks and meals. The food diary had foods and meals listed on the left side and time slots at the top. Quantity was given in defined household measurements such as glasses, table spoons or portions estimated with the help of the picture booklet. The picture booklet (Appendix 8) included 13 colored photo series, with 4 different portion sizes ranging from small to large. Every

participant described their eating pattern by filling out how many units he/she had of each food at what time.

The Swedish (50) and Danish (51) pre-coded forms are also validated. Examples of the Swedish picture booklet (Appendix 9) and the Danish pre-coded food diary (Appendix 10) are depicted in appendices.

Table 3.2: *The national institutions and programs used to analyze food records*

Country	Coding and analyzing of food records	Software
Denmark	Danish National Food Institute	GIES
Norway	Department of Nutrition, University of Oslo	KBS
Sweden	National Food Administration	MATs and the database PC-kost

The calculation of energy intake has been standardized so that all three countries have used the same values to calculate energy content of the food.

Table 3.3: *Factors used for calculation of energy intake (35)*

Macronutrient (g)	Energy (kJ)	(kcal)
Protein	17	4
Fat	37	9
Alcohol	29	7
Carbohydrate (dietary fiber not included)	17	4

Relative values (i.e. percentage of energy from the various macronutrients and the total energy intake have been used when presenting the results across the wide age range of the participants.

The reported energy and nutrient intake is the sum of food intake and oral- and enteral energy supplements. Vitamin supplements are recorded on a separate international sheet (Appendix 11).

The energy intake as a percentage of EAR was calculated for each person using reference values for energy intakes and physical activity level in groups of children. (***Table 1.5 NNR***). Percentage energy contribution from macronutrients was calculated for each assessment (35).

3.2.2 Questionnaires

Nutritional drinks and supplementation of vitamins

The usual intake of nutritional drinks, nutritional and vitamins have been recorded on separate forms distinguishing types, how often and quantity ingested (Appendix 3, 4, 5, 6) .

Participants were systematically interviewed by a dietitian about their usual supplementation of vitamins, minerals, trace elements, omega-3-supplements and their intake of nutritional drinks and enteral nutrition. The questionnaires were filled out by the dietitian in conjunction with the patient interview.

Demographics and clinical data

Demographical data such as age, gender and country are used to investigate differences between countries and groups.

Anthropometrical data such as height, weight, BMI (z-score is calculated). For calculation of BMI z-score the reference values of Nysom were used (43). *The weight was taken in the morning fasting having emptied the urinary bladder and bowel. Weight of garments was deducted from the measured weight (jeans, 0.6 kg and t-shirt 0.1 kg).* (Appendix 12)

Pulmonary function was performed at inclusion by dynamic spirometry at each centre. From measured forced vital capacity and expiratory volume in one second (FEV_1) in liters, percentage of predicted values were calculated using Solymar reference

equations for participants < 19. FEV_1 > 80 % predicted was defined as normal or mildly lung dysfunction

The biochemical analysis of serum vitamins (vitamin A, D and E) was done at the Research Laboratory Department of Pediatrics, Haukeland University Hospital, Bergen, Norway. Iron status was clinically evaluated at the CF centers.

3.2.3 Statistical preparation and analysis of data

The data on the 212 children were drawn out of the total of 442 children. SPSS PASW Statistics version 18 for Windows was used to analyze the data (SPSS, Inc., Chicago, Illinois, USA). Microsoft Excel and Word have been used to present results.

$P<0.05$ was considered statistically significant.

Histograms, Normal Q-Q plots and the Kolmogorov Smirnov test were used to evaluate whether each of the analyzed variables were normally distributed. An $n < 30$ in study groups usually indicates that one should consider using non-parametric tests (52).

Dietary intake, percentage of fat, protein and CHO of total intake are presented as mean, min, max and standard deviation.

When comparing only two groups, for example males and females or older and younger children Independent-samples *t*-test was used to verify statistical difference.

ANOVA One Way analysis was used for comparison between more than two groups, to determine differences in energy intake in percentage of EAR, macronutrient intake in percentage of total intake and other continuous variables between the independent groups. Post hoc tests were used to determine which groups that are significantly different from another. A Tukey HSD test for multiple comparisons was conducted. In order to adjust for type I errors when testing for multiple comparisons, the Bonferroni correction was applied to the P-value of 0.05 (52). With three comparisons, such as comparisons between the countries the adjusted P-value was considered significant at

P<0.017. With four comparisons, such as those between age-groups the adjusted P-value was considered significant at P<0.013.

Correlation analysis using Pearson Product-Moment coefficient was used to investigate the correlation between supplemental intake of fat soluble vitamins and serum values of fat soluble vitamins (A, D, E) and the correlation between total energy intake and fat intake in E % of total intake.

3.2.4 Comparison of macronutrient intake in E% of CF participants and healthy Scandinavian children

The dietary habits of the Nordic CF participants have been compared to the dietary habits of healthy children in Scandinavia. The Norwegian CF children have been compared to healthy children from Ungkost, the Swedish CF children have been compared to healthy children from Riksmaten and the Danish CF participants have been compared to the healthy children from the Dietary habits in Denmark study. The children compared within each country are within the same age range. The master student was not able to perform statistical analysis on this, but have made comparisons based on the numbers from the population studies.

4 Results

4.1 The subjects

A total of 212 children with PI and completed diet record (106 females and 106 males) from Denmark, Norway and Sweden completed the study. Forty-nine children were from Denmark (25 females, 24 males), 53 from Norway (25 females, 28 males) and 110 participated from Sweden (56 females, 54 males).

Table 4.1 *Distribution of participants within age-groups*

Age years (NNR age-groups)	Denmark n	Norway n	Sweden n	Total n
2-5	6	8	19	33
6-9	16	24	32	72
10-13	12	11	39	62
14-17	15	10	20	45
Total	49	53	110	212

4.1.1 Demographics

Table 4.1 depicts the children categorized into the age groups by the Nordic Nutrition Recommendations 2004. Thirty-three percent of the children are between 6 and 9 years old, and 29 % are between 10 and 13 years. Since the youngest children included this thesis are 4 years, the group labeled 2-5 years have the lowest number of children. The mean age of all participants is 10.4 years (4-17.9 years).

Table 4.2 *Overview of anthropometrical and clinical values for all participants*

Variable	n	Mean	St.Dev	Min	Max	Reference values
Age, years	212	10.4	3.8	4	17.9	
Height, z-score	212	-0.2	1.0	-3.1	2.0	
Weight, z-score	212	-0.2	1.0	-1.9	5.2	
BMI, z-score	212	0.2	0.92	-2.2	3.1	
		Mean	**St.dev**	**Min**	**Max**	
FEV_1, % predicted	199	89	17	37	131	
S-retinol, µmol/l	200	1.4	0.5	0.2	2.8	>0.7
S-vitamin D, nmol/l	200	57.3	24.4	6	180.9	75-150*
S-tocopherol, µmol/l	200	22.7	9.2	6.9	83.2	14-50
		Median	**Interq range**	**P25**	**P75**	
S-ferritin	194	25	20	16.5	38	7-142

*Haukeland University Hospital (vitamin A and E), Report from Leeds (vitamin D) (39).

Table 4.2 presents anthropometrical data, measurement of lung function and serum values for all participants. The reference values for serum concentrations of fat soluble vitamins are also included.

4.1.2 Anthropometrical measurements

Due to the wide age span, the weight of the children varied from 14.7 to 96.4 kg with a median (mean) weight of 32 (35.6) kg. Mean z-score for weight and mean z-score for height are both slightly negative. This results in a slightly positive mean BMI z-score (0.2). This is significantly different from the healthy Danish reference population (P=0.02).

Only 2 participants have a BMI z-score at -2 SD from the mean, and 2 participants have a BMI z-score + 2SD from the mean. The distribution of BMI z-scores for the age-groups are depicted on the following pages.

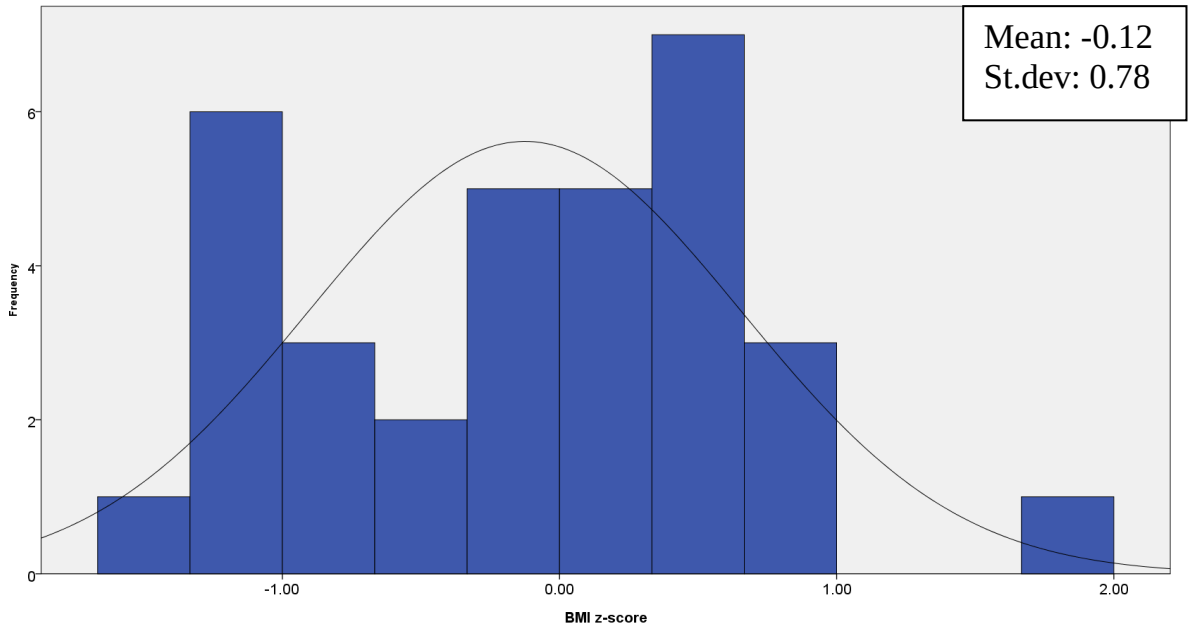

Figure 4.2 *Distribution of 4-5 year olds (N=33) on their BMI z-score*

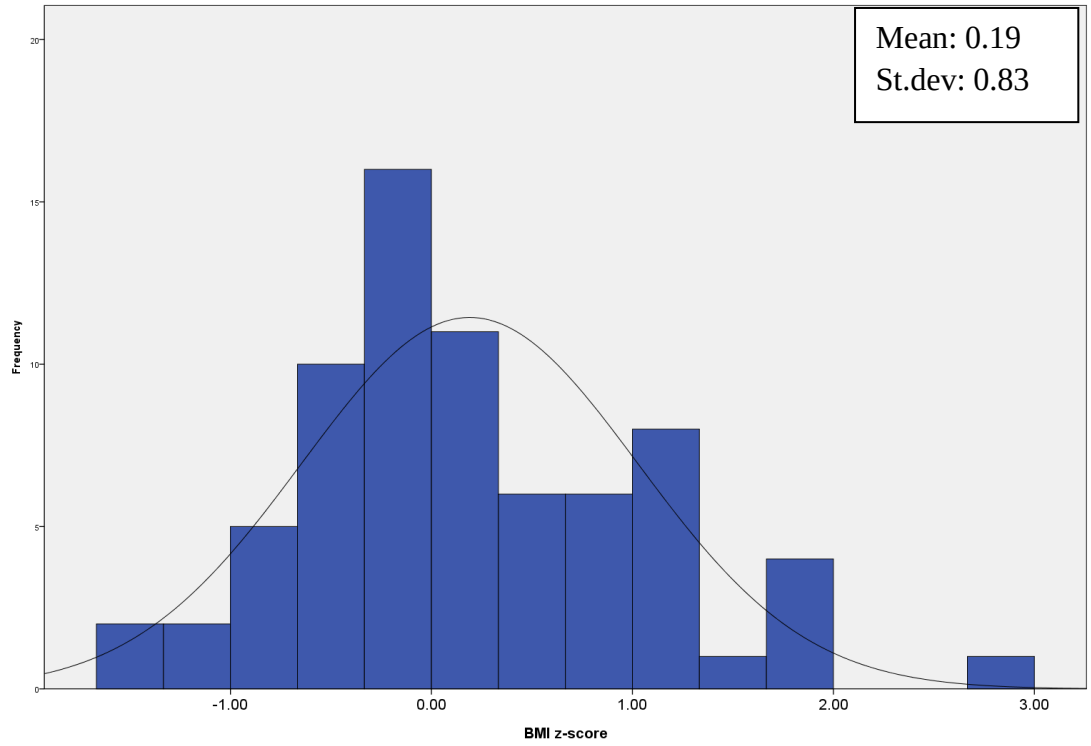

Figure 4.3 *Distribution of 6-9 year olds (N=72) on their BMI z-score*

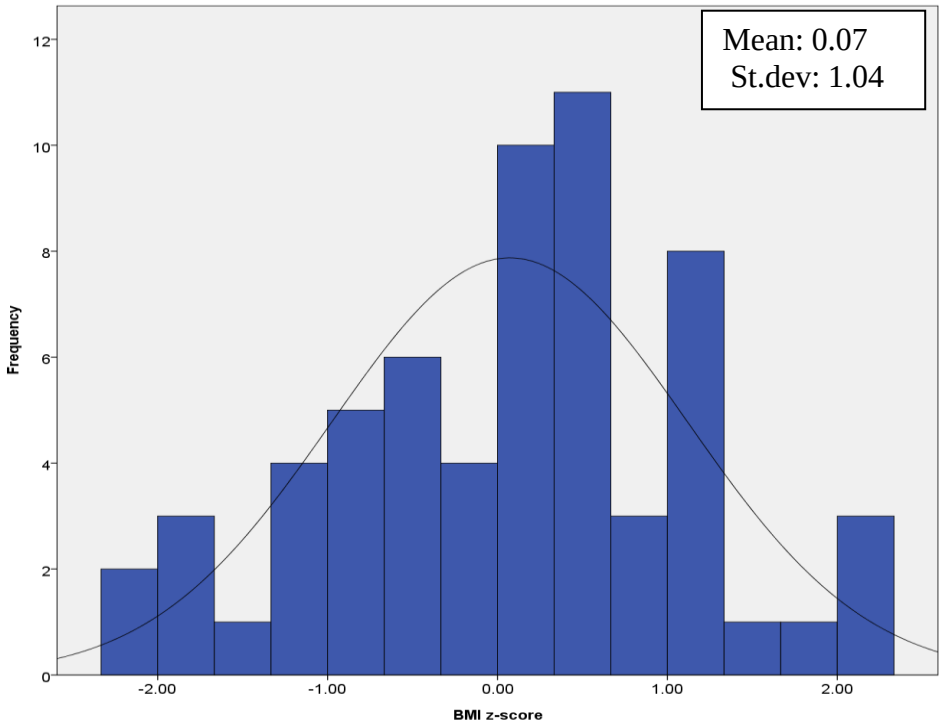

Figure 4.4 *Distribution of 10-13 year olds (N=62) on their BMI z-score*

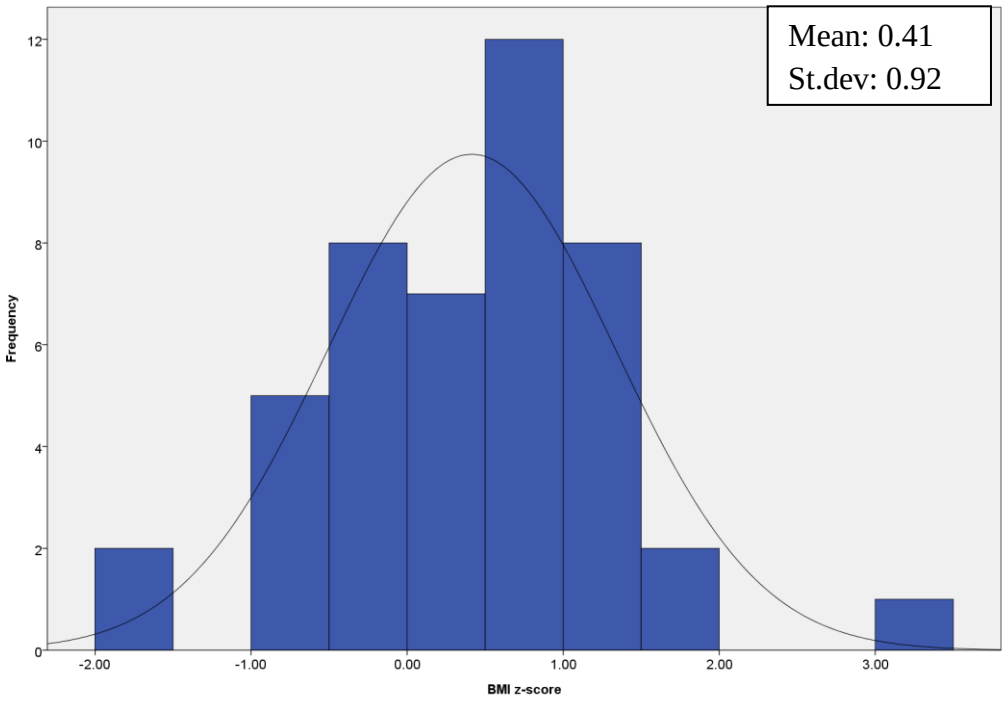

Figure 4.5 *Distribution of 14-17 year olds (N=45) on their BMI z-score*

4.1.3 Clinical values

FEV_1

The participants in this study had a mean expected value of 89 %. Forty-six of the children had an FEV_1 % predicted value < 80 %. The following table gives an overview of the mean FEV_1 % predicted values of the children within the age-groups. Significant differences between groups are highlighted with an asterix:

Table 4.3 *The FEV_1 % predicted values of the children within the age-groups*

Age	n	Mean FEV_1 % predicted value
4-5	22	98.6*
6-9	70	91.4
10-13	62	84.1*
14-17	45	88.2

*p-value= 0.003

Children aged 4-5 years old have a significantly higher FEV_1 % predicted value than participants aged 10-13 years.

Serum values of fat soluble vitamins

The mean serum value of vitamin D among the CF population in this study was 57 nmol/l. Among the participants, 167 (79 %) had serum levels of vitamin D lower than 75 nmol/l, and (69) 32 % were below 50 nmol/l. A mean value of 1.37 µmol/l on serum retinol (ref: > 0.7 µmol/l), however 6 of the children were below the reference value for vitamin A.

The average CF participant has a mean (22.7 µmol/l), which are within the laboratory reference range. Of the participants, 30 are below the reference range.

4.2 Energy and Macronutrient intake

4.2.1 Energy intake compared to recommendations

Table 4.4 *Energy intake in % of EAR of selected groups*

Group	n	Mean	St.dev	Min	Max	P-value
All	212	132.6	40.1	21	342	
Boys	106	135.0	39.4	21	295	0.262
Girls	106	129.0	40.6	58	342	0.262
≤ 10 years	105	144.0	43.0	21	342	<0.01
> 10 years	107	120.5	32.9	58	295	<0.01
Denmark	49	128.3	36.7	21	200	0.05
Norway	53	118.6	35.4	61	230	0.002
Sweden	110	141.1	41.7	61	342	0.002

As shown in ***Table 4.4***, no statistically significant difference was found between boys and girls with respect to energy intake as % EAR. Children older than 10 years had a significantly lower energy intake expressed as % EAR than the younger children, and the Swedish CF children had higher values than their Norwegian counterparts. Children from Denmark did not differ significantly in their total energy intake in % of EAR compared to Swedish or Norwegian CF children. When studying the energy intake % compared to recommendations, the values were highly spread out. Energy intake > 120 % EAR was found for 128 (60.4 %) whereas the minimum intake was 21 %.

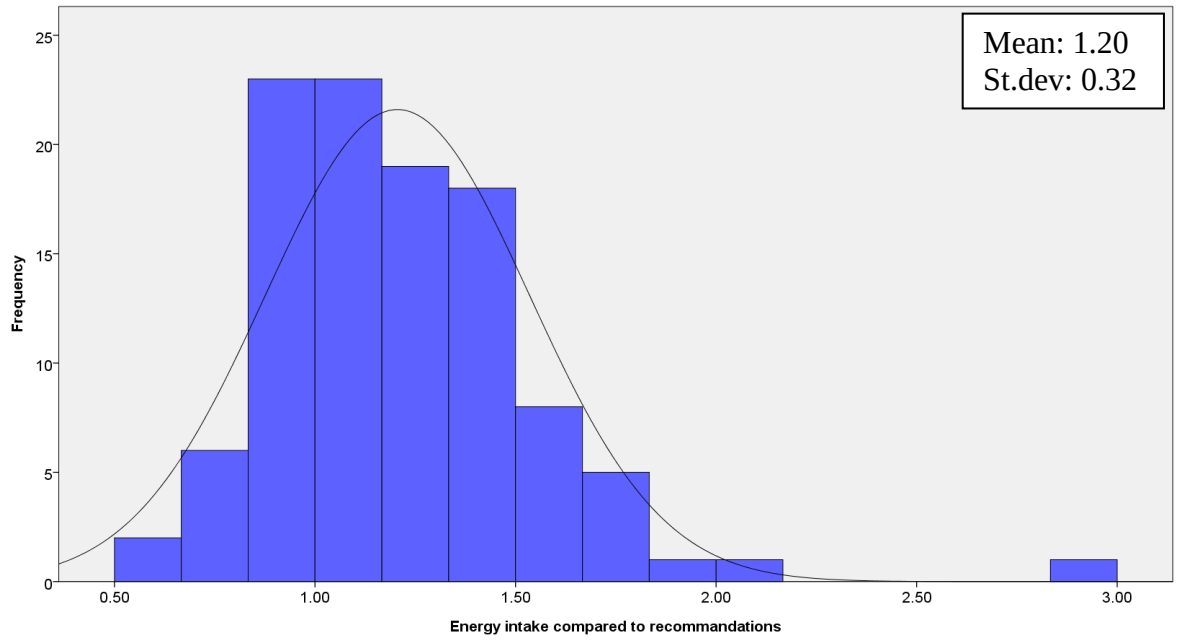

Figure 4.6 *The energy intake of participants > 10 years of age*

Children over the age of 10 have a mean energy intake of 120.5 % EAR. The distribution among the children is shown above.

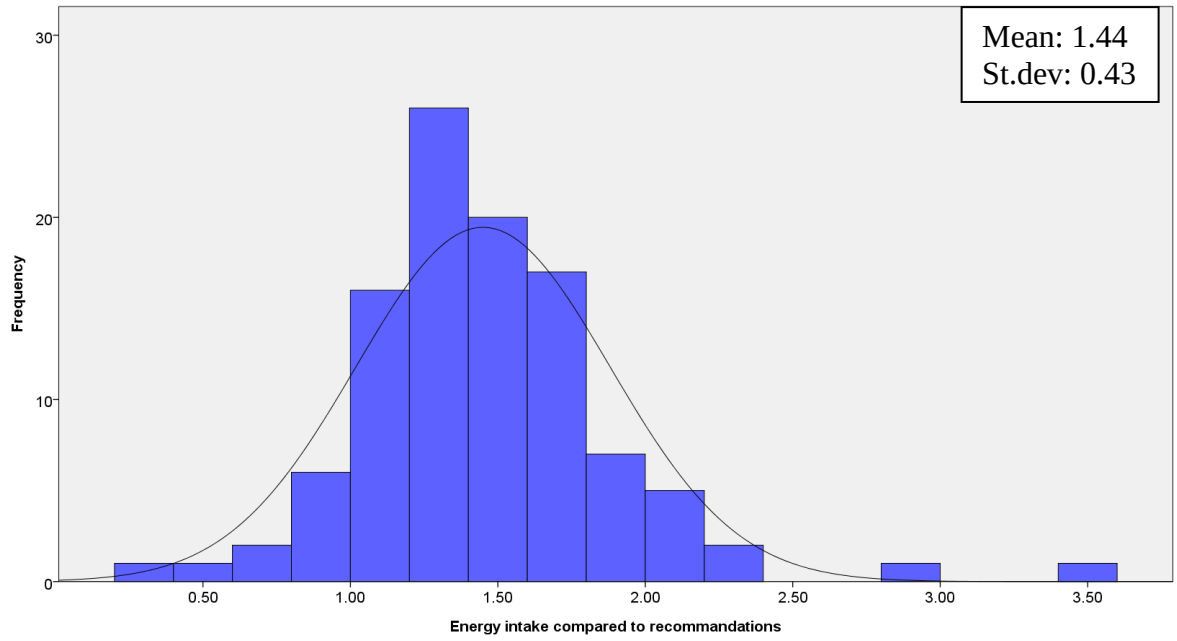

Figure 4.7 *The energy intake of participants ≤10 years of age*

Children under the age of 10 have a mean energy intake of 144 % EAR.

4.2.2 Macronutrients in E % of total energy intake

Table 4.5 *Distribution of macronutrients in E %*

	n	Protein, E %	CHO, E %	Fat, E %	PUFA, E %
All participants	212				
Mean		13.8	49.3	36.6	5.9
St.dev		2.4	6.9	6.1	2.4
Min-max		1.8-20.5	34.0-96.4	1.7-51.0	0.3-6.0
Females	106	13.9	49.5	36.1	5.7
Males	106	13.6	48.9	37.1	6.0
≤10 years	105	13.3	49.7	37.6	6.4
>10 years	107	14.2	48.8	35.6	5.4
Denmark	49	13.1	48.9	36.8	4.4
Norway	53	13.4	52.0	34.6	6.5
Sweden	110	14.3	48.1	36.6	6.2

Table 4.5 shows the distribution of energy-yielding nutrients among selected groups and comparisons between them. The significant differences between the groups remains when performing the Bonferroni correction on P-values. There were no significant difference found between boys and girls in any of the macronutrients in % of total energy intake. Children over the age of 10 had a significantly higher E% from protein (P= 0.006). The children under the age of 10 had a significantly higher intake of fat and PUFA in % of EAR compared to those children over the age of 10 (P= 0.002, 0.003). Participants from Sweden were found to have a significantly higher protein intake in E% than participants from Denmark and Norway (P=0.001). The Danish participants had a significantly lower intake of PUFA in E% compared to Swedish and Norwegian participants (P< 0.001). The CHO intake in E% is higher among Norwegian participants compared to the two other Nordic countries (P =0.002).

The relationship between energy intake and E % from fat

Correlation analysis was performed to investigate the relationship between total energy intake and distribution of fat E%. There was a slightly positive correlation (r =0.286, P <0.001) between the two variables.

4.2.3 Supplementation of nutritional drinks

Among 204 of the children (data missing on 8), 145 did not use nutritional drinks to supplement their diet. Fifty-nine of the children supplemented their diet with nutritional drinks. Twenty-nine of these obtained less than 400 kcal per day from nutritional drinks and 30 participants received over 400 kcal per day. Of the children with the highest intake (> 800 kcal/day), 11 of the children were over 10 years of age. The highest intake was 1525 kcal/d.

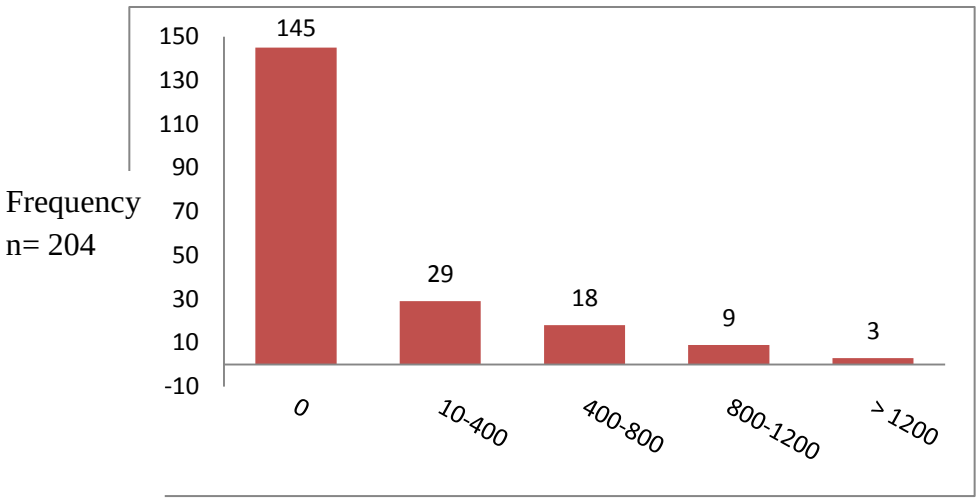

Figure 4.9 *Energy intake from nutritional drinks*

Figure 4.9 gives an overview of the participants and their energy intake from nutritional drinks. Amount of kcal have been categorized into appropriate groups Of the 59 participants who supplemented their diet with nutritional drinks, about half (28 participants) had between 101 and 300 ml daily.

Table 4.6 *Supplementation of nutritional drinks within each country*

Country	n	Energy (kcal/d) Mean	St.dev
Denmark	6	534.7	505.0
Norway	8	277.2	185.6
Sweden	45	514.5	359.2

As ***Table 4.6*** depicts, there were no significant difference between the countries in the intake of nutritional drinks when comparing the 59 participants that registered their use of nutritional drinks (P= D-S: 0.43, D-N:0.92, N-S:0.25).

4.2.4 The association between nutritional drinks and energy intake

Table 4.7 *The energy intake in % of EAR of participants consuming nutritional drinks compared to those who do not consume these*

Nutridrinks	n	Mean	St.dev	Min	Max
Yes	59	137	41.9	21	342
No	144	130	39.4	60	295

P-value = 0.068

Comparing the energy intake in percentage of EAR did not give a significant difference between participants consuming nutritional drinks and those who did not. The P-value were however just above 0.05 and we can expect tendency for higher energy intake among participants consuming nutritional drinks

When investigating the use of nutritional drinks and the effect on fat E%, there was no significant difference found between participants who used nutritional drinks and those who did not (P=0.06).

4.2.5 Nutritional drinks and BMI z-score

The addition of nutritional drinks establishes an interesting question around variations in BMI z-score among the participants.

Table 4.8 *The relationship between BMI z-score and supplementation of nutritional drinks*

Nutridrinks	n	Mean	St.Dev	Min	Max
Yes	59	0.20	0.96	-2.04	3.07
No	144	0.024	0.80	-2.17	1.88

P-value: 0.167

Interestingly, there were no significant difference on BMI z-score between participants supplementing their diet with nutritional drinks compared to participants who do not use nutritional drinks (P-value 0.167)

4.3 Supplementation of fat soluble vitamins and serum values

Table 4.9 *Supplemental intake of fat-soluble vitamins*

Vitamin Supplement n=205	Median	Min	Max	Interquartile range	25/75 Percentile	P-value	Recommended supplement intake[1]
Vitamin A Re µg	1,350	0	14,400	1,000	860/1860	0.00	1,100-3,000
Vitamin D µg	15.3	0	343	19	10/29.1	0.00	10-20
Vitamin E α-TE mg	161.6	0	2,436	105	115/220	0.00	100-200

[1] European Consensus on Cystic Fibrosis (23).

Of the 212 children in this study, 200 reported taking a supplement of fat soluble vitamins. The median intake of vitamin A did not fall within the recommendations for

CF. For vitamin A, the maximum value was extreme, 14,400 µg. The median intake of vitamin D was 15.3 µg, and falls within the recommendations for CF. The maximum intake of vitamin D was also high, being 343 µg. The child having the highest supplemental intake of vitamin D also had the highest intake of vitamin E (2,436 mg α-TE). The median intake of supplemental vitamin E was 161.6 mg α-TE. The data on supplemental intake of fat soluble vitamins were not normally distributed.

Table 4.10 *Serum values of fat-soluble vitamins*

Serum values	n	Mean	Min	Max	St.Dev	Recommendations[1]
S-retinol µmol/l	200	1.4	0.2	2.8	0.5	>0.7 µmol/L
S--25-hydroxy vit D nmol/l	200	57.3	6.0	180.9	24.4	75-150 ng/L
S-vit E tocopherol µmol/l	200	22.7	6.9	83.2	9.2	>11.6 µmol/L

[1]**Haukeland University Hospital (vitamin A and E), Report from Leeds (vitamin D) (39).**

The serum values of fat soluble vitamins varied between the participants and were presented in table 4.12. The serum values for retinol were above lower reference value of serum vitamin A. Six participants did not meet the reference serum value > 0.7 µmol/l. The mean value for serum vitamin D (57.3 nmol/l) was lower than the laboratory reference of 75-150 ng/l, newly recommended in CF. Thirty-three of the participants (16.5 %) were within the reference for serum vitamin D. The mean serum value for serum tocopherol was 22.7 µmol/l, and this is within the reference (>11.6 µmol/l). Twenty-nine of the children (14.5 %) had serum values below the laboratory reference.

The relationship between supplement intake and serum values of fat soluble vitamins

Correlation analysis using Pearson Product-Moment coefficient was used to investigate the correlation between supplemental intake of fat soluble vitamins and serum values of fat soluble vitamins (A, D, E). A negative correlation was found between supplemental intake of vitamin A and serum values of retinol (r= -0.3,

n =195, p =0,05). No correlations was found between supplemental intake of vitamin D and E and serum values of these.

4.3.1 Other micronutrients

The dietary intake of thiamine, vitamin C, calcium, and iron have been investigated to understand the participants nutritional intake of certain micronutrients from their diet. The data that were not normally distributed are presented as median and interquartile range and highlighted with an asterix.

Table 4.11 *The intake of selected micronutrients of CF participants by age-groups*

Micronutrient	Age group	Mean/Median*	St.dev/ Interquartile range*	Recommendations NNR (M/F)
Thiamine, mg/d	4-5 (n=33)	1.2	0.38	0.6
	6-9 (n=72)	1.4*	0.67*	0.9
	10-13 (n=62)	1.7	0.9	1.0/1.2
	14-17 (n=45)	1.7	0.7	1.1/1.4
Vitamin C, mg/d	4-5 (n=33)	72.7*	67*	30
	6-9 (n=72)	85.4*	57*	40
	10-13 (n=62)	82.5*	69*	50
	14-17 (n=45	102*	72*	50/60
Calcium, mg/d	4-5 (n=33)	1168	353	600
	6-9 (n=72)	1228	549	700
	10-13 (n=62)	1614	564	900
	14-17 (n=45	1328	605	800
Iron, mg /d	4-5 (n=33)	9.0*	3.5*	8
	6-9 (n=72)	9.1*	4.4*	9
	10-13 (n=62)	11.7*	5.0*	11
	14-17 (n=45	11.2*	3.8*	15/9

*Median and interquartile range are presented with an asterix

As ***Table 4.11*** illustrates children within all age groups had on average a higher intake of thiamine than the recommendations. The average intake of vitamin C was above the recommendations for dietary intake among all age groups. The calcium intake among the participants was on average higher than recommended as well. The average intake of iron was just within the recommended intake, except for girls within the 14-17 age group. The median intake of iron for participants between 14-17 years was 11.2 mg/d, and the recommended intake from food is 15 mg/d for girls and 9 mg/d for boys.

4.4 Macronutrient intake in E % of CF children compared to healthy Scandinavian children

From the studies on the healthy children, a weighted average have been used to represent the mean. Suitable age groups corresponding to the age of the children within the studies were used to get a reasonable number of participants to compare with.

4.4.1 Compared with Ungkost 2000

For this comparison CF children between 8-14 years were selected as the healthy children were 4th and 8th graders. Comparing the intake of macronutrients of CF children and healthy children from Norway (Ungkost 2000) gives the following results:

Table 4.12 *Macronutrient intake in E% of Norwegian CF participants compared to healthy children of Ungkost*

Macronutrient	CF n =30	Ungkost n =1824
Protein, E%	12.6	14.3
Fat, E%	34.6	31.1
CHO, E%	52.8	54.4
Added sugar, E %	18.5	17.5
PUFA, E%	6.8	5.6

All values are expressed as mean values

From ***Table 4.12*** it seems that CF children had a slightly higher energy percentage from fat and PUFA than Ungkost children. It seems that the energy percentage from protein and CHO intake was a little lower in CF participants.

Added sugar

For the Norwegian children we were also able to compare the intake of added sugar. The intake of added sugar is 1% higher among CF children compared to healthy children.

4.4.2 Compared with Riksmaten 2003

The Swedish participants aged 6-11 years were compared to the participants of the study on healthy children from Sweden.

Table 4.13 *The macronutrient intake in E% of Swedish CF children compared to healthy children of Riksmaten aged 4, 7 and 10 years*

Macronutrient	CF n = 59	Riksmaten n = 2495
Protein, E%	14.3	15.2
Fat, E%	38.6	31.7
CHO, E%	47.3	53.2
PUFA, E%	6.5	3.7

All values are expressed as mean values

From the numbers it seems that the Swedish CF children had a higher fat intake compared to healthy 4 year olds, 2nd and 5th graders in Riksmaten. The CF children had a higher PUFA intake in % of total intake, compared to children from Riksmaten. Healthy second graders and 5th graders had a slightly higher protein intake in E% compared to CF children. It is expected that the healthy children in the Riksmaten study had a higher mean CHO intake (above 50 % of total intake) compared to CF children (47.3 % of total intake).

4.4.3 Compared with Dietary habits in Denmark 2000-2002

The healthy Danish participants in the dietary study have been arranged into two groups, 4-9 and 10-17 years. All Danish CF participants (4-17.9 years) have been included to compare with the Danish dietary study.

Table 4.14 *The macronutrient intake in E% of Danish CF children compared to healthy children of Dietary habits in Denmark*

Macronutrient	CF n =49	Dietary Habits in Denmark n = 1379
Protein, E%	13.3	14.0
Fat, E%	36.8	33.0
CHO, E%	48.9	51
PUFA, E%	4.4	4.5

All values are given as mean for both gender unless specified

The Danish CF children had the lowest intake of protein in E% of total intake. However when looking at the healthy Danish children, their protein intake seemed to not be as high as the other healthy children in Scandinavia. As for the other countries, the Danish CF children seemed to have a higher fat intake compared to the healthy children in Denmark. It seems that the Danish children in general had a lower PUFA intake in E% of total fat intake when compared to the other two countries. Both the CF children and the healthy children had an equal intake of PUFA (E%).

Comparing the Scandinavian CF children with children in the Nordic dietary surveys, we can assume a higher average fat intake among the CF participants. CF children of Norway and Sweden have a higher PUFA intake than healthy children, but this is not seen among CF children in Denmark. Healthy children have a higher mean CHO intake compared to CF children. The protein intake is on average higher among healthy children.

When investigating the energy intake in kcal, the following was seen:

Table 4.15 *The energy intake (kcal) of CF participants compared to healthy children in Scandinavia*

Group	Age	n	Mean kcal intake
Dietary habits of Denmark	4-17	1379	2067
Danish CF children	4-17	49	2589
Ungkost	9 and 13	1824	2019
Norwegian CF children	8-14	30	2290
Riksmaten	4,7,10	2495	1792
Swedish CF children	6-11	59	2720

CF children seem to have a higher mean energy intake (kcal) than healthy peers within Denmark, Norway and Sweden, as shown in ***Table 4.15.***

5 Discussion

This thesis is part of a cross-sectional study, and advantages as well as limitations to the study are discussed below.

Other studies have also investigated the energy intake of CF patients, and the results of this thesis will be discussed and put in context of findings in other studies.

5.1 The study group and method

5.1.1 The study group

The participants were children with cystic fibrosis and pancreas insufficiency in Scandinavia. Other studies have investigated groups of CF patients and their energy intake, however no one, as far as we know have studied and compared the energy and macronutrient intake of CF children in Denmark, Norway and Sweden. There was no significant differences in energy intake and macronutrient intake in percentage of total intake between the genders among the participants in this study. Results were thus not expressed within the genders. A study conducted in Australia on 29 CF children correlates to this. The researchers emphasize that the differences are seen among the older children over 15 years of age (53). The results in this thesis emphasize that there were significant differences among children over and under the age of 10, and will be discussed further.

The results from this thesis is based on analyses of 212 children who originally were drawn out of a data set of 422 children. Two centers in Scandinavia did not have the opportunity to partake in the study, one center in Gothenburg, Sweden and one in Århus, Denmark. Results may have been different if these were included in the study. Of the 442 children, 45 were pancreatic sufficient and 184 PI patients did not register their food intake. I wanted to present some of the clinical and anthropometrical values for the children with PI who did not register their food intake. This to establish whether the draw-out of participants correlate clinically and anthropometrically to that

of those who were not included. The mean age of the children with PI who were not included was slightly higher (12.3) than the average CF child in the study group (10.4 years). Overall the clinical and anthropometrical values were comparable. The lung function, height z-score and weight z-score were quite similar, so were the mean values for serum retinol, tocopherol and vitamin D. The mean BMI z-score was a little closer to the healthy population within the group of children who were not included in the thesis (0.01) compared to the study group of this thesis (0.16). The results can be generalized to Scandinavian children with CF and PI within the age groups discussed. The children who were not included in the study seems to have the same anthropometrical and clinical values as the participants.

Table 5.1 *Clinical and anthropometrical values of children who were not included in the thesis*

Variable	n	Mean	St.Dev	Min	Max	Reference values
Age, years	101	12.3	3.7	4	17.9	
Height, z-score	101	-0.4	1.1	-3.2	2.2	
Weight, z-score	101	-0.2	0.9	-2.9	3.9	
BMI, z-score	101	0.01	0.9	-2.1	3.6	
FEV_1, % predicted	101	87.8	17.8	47	132	
S-retinol, µmol/l	101	1.3	0.5	0.3	3.0	>0.7
S-vitamin D, nmol/l	101	54.1	24.9	4.1	150.9	75-150*
S-tocopherol, µmol/l	101	24.0	10.6	5.5	57.1	>11.6
		Median	**Interq range**	**P25**	**P75**	
S-ferritin	101	32	24	15.5	36	7-142

*recommendations specific for CF (39)

5.1.2 Method

Standardized methods were used to collect the data material. High accuracy can be expected from the measurements of serum values for vitamins and minerals and lung function. Data based on self reporting (for instance food intake, nutritional

supplements and vitamin supplements) are potentially biased. To decrease the bias as much as possible, standard instructions and questions were used in all three countries.

Advantages of the method

Several comparisons can be studied at once within cross-sectional studies, as variables are collected at one point in time. The advantage of cross-sectional studies compared to studies such as case-control studies and cohort studies, is that you avoid recall bias and loss to follow up. This study design is also relatively inexpensive compared to other types of research (52).

The study that this thesis could correlate mostly to is the research by White et al., 2007. They performed a case-control study on 58 CF children at regional CF centers in England. Their data were gathered from 2000-2001, approximately the same time period as in this study (2003-06). They divided their participants into appropriate age groups (5-8, 9-12 and 13-16 years), that can be compared to the age groups in this thesis.

The same method for gathering data material on CF participants as other studies was used. Kawchak et al (45) used the same method as we when investigating the dietary intake of children with CF. Food records and measurement of height and weight as well as evaluation of lung function were analyzed. This eases the comparisons and support of other studies. White et al. (30) used a 4-day food record, an in this study there was used a 7-day record. The reason for using 7 day food recording was to eliminate biases related differences in food intake and meal composition on weekdays and weekends within the countries. Measurements of height, weight, lung function (FEV_1), energy intake in % EAR, macronutrient intake in E% and the intake of some micronutrients could be directly compared to results by White et al. (30).

Food record as used in this thesis is valuable when investigating dietary behavior and quality (54). Olveira et al. suggest that under reporting among CF patients is low, and they suggest that some of the participants may have over reported their energy intake (54). This might have been the situation in our study as well.

The food records were analyzed in national food composition tables, that corresponded to each country's food choices, meal composition and foods. The estimation of energy intake in EAR % and macronutrient E% was standardized according to NNR (2004) and valid for all three countries (35). The Nordic countries have quite the same food preferences, however there are some differences in meal types among them.

The doctors, nurses and dietitians involved in the collection of the data were instructed through the same guidelines on how to perform the measurements and tests. The tests have been standardized as best way possible for an international study. On the other hand, weights were not calibrated and this might propose a bias in results including weight.

Limitations

Cross-sectional studies examines one point in time events. As many cross-sectional studies may be started through inviting the participants, non response may cause a problem. Volunteer bias may be a problem as those who are particularly interested respond to the questionnaires. One of the largest limitations of cross-sectional studies is that one cannot determine clear inference of causality (52).

The drawback of receiving a database with data gathered by someone other than yourself automatically provides less control. Not being able to have seen the tests, blood work and the examinations on the participants disables the researcher got get the full picture of the study. It was not possible to attend the data gathering as this was done from 2003-2006. Since this is an international study, it was not possible for one researcher to attend all CF centers.

5.1.3 Statistics

Parametric test such as Independent samples *t*-test and One Way Anova analysis of variance were used to compare the different groups. Parametric tests are more powerful than non-parametric tests, as they are used on larger study samples (55).

BMI z-score was used to evaluate the participants' growth. Other studies emphasize the importance of using BMI percentiles when studying children, as BMI is not constant across childhood. Ideal body weight percentage (IBW %) is another measurement reported in many studies on children, when reporting on patients at risk for nutritional failure (56). Results on BMI z-scores from this study cannot be compared directly when investigating results from studies with other ways of presenting growth.

5.2 Discussion of results

5.2.1 Anthropometrical and clinical measurements

Height and BMI

White et al (30) state that cross-sectional studies of children with CF compared to healthy controls imply that CF children have more deficits than the healthy subjects, and the decline needs to be addressed.

Laing et al. (57) compared 42 CF children with 42 healthy controls and found that the average CF child were significantly shorter than controls. This study supports their findings, and as ***Table 4.2*** depicts, the average CF participant had a slightly negative height z-score compared to healthy Danish reference population.

The average BMI z-score of the CF participants was slightly more positive (0.2).). Z-scores for mean height and weight were both slightly negative, height more than weight This may indicate that CF children have a larger weight for height compared to healthy children. The difference was found to be significant when comparing the BMI z-score of CF participants to that of Danish reference population (P=0.02). The negative weight and height z-score may indicate that some of the children slightly shorter than healthy peers. Only 2 participants are more than 2 SD from the mean, which have been used as a critical point for growth (42). White et al. (30) investigated the differences between CF children grouped into age groups (5-8, 9-12 and 13-16 years). They found that CF children aged 5-8 years had a lower z-scores of weight,

height and BMI compared to controls. The older children had even lower z-scores compared to healthy controls. When investigating the differences in BMI z-score between the age groups of this thesis, no significant differences were found among the CF children.

Other studies have investigated the effect of nutritional intervention on BMI z-score over time. Hankard et al (26) have looked at studies on nutrition and growth in CF, and report that BMI z-score improved slightly when participants underwent intervention.

FEV_1

It is expected that the decline in lung function comes with age among CF patients. Forty-six children had a FEV_1 under 80 %, and of these 32 % (n=15) were under the age of 10. Thirteen (86 %) of these had the most severe mutation merely the ΔF508 genetic mutation, which affect lung function the most (58). When investigating the entire study group (n=212), it was found that the average CF child had normal lung function expressed as FEV_1 in percentage of predicted (89 %). Stark et al. (33) investigated the effect of nutritional intervention on growth and pulmonary function, compared to that of standard care. They found no significant difference in FEV_1 over 27 months between children in the intervention compared to those receiving standard care. They emphasize that reports from the Cystic Fibrosis Foundation show that persons with better nutritional status have better lung function.

When investigating lung function as presented by FEV_1, I found a significant difference between the children aged 4-5 and 10-13 years as presented in ***Table 4.3***. This may be due to the fact that there are nearly three times as many children in the 10-13 age group, which may affect the distribution. A study by Corey et al. investigated the FEV_1 of children in Toronto and Boston within the same age range as we. They had approximately the same number of children in each group and found no significant differences within the age groups when comparing lung function (8). Keller et al. (58) found that lung function declined significantly at 13-16 years compared to 5-8 and 9-12 year age groups. White et al. (30) reported mean values < 80 % within all

age groups, and decline in lung function with age was seen. From the ***Table 4.3*** it seems that lung function declined with age.

Steinkamp et al. (36) investigated the effect of malnutrition on lung function. They found that malnourished CF patients within all age groups had a significantly worse lung function than nourished patients. When performing a correlation analysis on energy intake in EAR % and FEV_1, there was no correlation found within the study group of this thesis. The relationship between nutritional status and lung function seems to be important to monitor (36).

5.2.2 Do CF participants reach their energy and fat recommendations?

Energy

The past two decades have been revolutionary in terms of nutrition improvements among patients with CF. High calorie and fat diets and the improvement in pancreatic enzyme replacement therapy have improved the nutritional support of this patient group (28). Interestingly, the findings from this study correlate to other studies when investigating the total energy intake of CF participants. Several other studies report that CF patients have a higher energy intake than controls, but that they fail to meet the recommendations. The children within this study had on average a higher energy intake than reported in other studies, and the intake was on average within the recommendations.

CF patients are recommended to have an energy intake between 120 and 150 % of EAR, (23) emphasized among clinicians in Europe . A wide degree of variation in energy intake was seen between the Scandinavian countries. Norwegian CF participants had a mean intake of 117.6 %, slightly below the recommended level. This was significantly different from the Swedish CF children, who had a mean energy intake of 141.1 % of EAR.

The Swedes have a different diet routine than both Denmark and Norway, as they often have two hot meals during the day (lunch and dinner). One cannot know whether

the method for food recording could be biased. It is known that the Swedish CF clinics are more centralized and staffed with multidisciplinary teams than in Norway, and as a consequence the Swedish patients may get more regular input from dietitians. The different routines within each country may affect the nutritional treatment of the CF children.

These results were based on 7 consecutive days of food registration. One Danish child has an energy intake of 21 % of EAR. This child has normal serum values, so the low intake might suggest that he has been sick for the seven days of food recording. This child also contributes to the minimum value on energy % for CHO, fat and proteins.

Studies by other investigators support the findings of this study on energy intake. Kawchak et al (45) found that participants had a mean energy intake of 100-107 % Recommended Dietary Allowance (RDA). In our study we compare our results to EAR, a value that represents the requirement for the average person and commonly used in Europe. Findings cannot be generalized when comparing with studies that report intake in % of RDA, because this value represents more than the average requirement but assumptions can be made. Recommendations may also vary between countries, even though they are surprisingly similar across the world (35). RDA is calculated based on EAR and is usually 20 % higher than EAR (59).

The trends of other studies can be compared. Kawchak et al. state that CF patients are recommended to keep their intake at 120 % of RDA, indicating that participants did not reach their recommendations. Other studies also report that CF participants do not reach the recommended values. The findings of this thesis was that 84 (39.6 %) of participants did not reach the recommended intake for CF children between 120 and 150 % of EAR. As illustrated in ***Table 4.4***, when dividing into groups, only the Norwegian participants did not have a mean energy intake > 120 % EAR.

The accuracy of food recording in this thesis can be discussed as there are so many people involved in registering the diet intake of the children. Parents, day care providers and the children have been involved in the food recording. This may affect the reporting of food intake. As CF children are recommended to have a higher energy

and fat intake than healthy children we can expect that some individuals over report. Olveira et al. (54) report that their study on 37 children with CF revealed a mean intake of 132 % of EAR. This is within the same range as found in this thesis when dividing study population of the thesis into reasonable groups, as ***Table 4.4*** illustrates. Findings from White et al., when studying 94 food diaries revealed a mean energy intake of 116 % EAR (30). The findings from this study compares to the findings of other studies on energy intake among participants with CF and it may suggest that dietary guidelines have an impact on the dietary intake of CF children. The results from this thesis was that many of the CF participants obtained an energy intake within the recommendations, suggesting that it is also highly achievable among the CF population.

Fat

Only 62 (29 %) of the participants had a fat intake > 40 % of total intake. Of these 39 (35%) participants are from Sweden, 17 (35%) from Denmark and 6 (11%) from Norway. Kawchak et al found that their participants had a mean intake of 34 E % from fat. This is below the recommended intake for CF patients. Our study support that average fat intake in E% is on the lower scale of recommendations of 35-45 % of total intake. A mean intake of 36.6 E % within the entire tudy population, and varying from 34-37 E % among the groups as depicted in ***Table 4.5***. Olveira et al. (54) found the mean intake of fat to be 39.2 E %, and Bentur et al found the fat intake among their participants to be 35 E% (44). White et al. emphasize that their study group had a mean fat intake of 38.7 E% among children on enteral nutrition, and 34.8 E % among children who did not supplement their diet (30). The findings in this thesis support results of other studies, that CF patients do not achieve the recommended intake of fat in percentage of total intake. I also found no significant difference in fat E % intake between the children supplementing their diet with nutritional drinks and those who did not (P =0.06).

Laing et al (57) investigated the food preferences of CF children compared to healthy children and found that CF children had a significantly higher liking for high-fat foods than controls. The foods liked more were typical high-fat foods such as biscuits, pizza,

hamburger, peanut butter and mayonnaise. The investigators found no significant difference in BMI between CF children and controls. In this thesis I was not able to study the food choices of the CF children.

There is assumed that as patients with CF are advised to keep a high fat intake from childhood on to increase their total energy intake, their liking for high fat foods may be increased. As several studies on CF and dietary intake report a fat intake close to 40 % of total intake.

Importantly, there were more children participating from Sweden in this study. Almost twice as many participants as the two other countries respectively. This may have caused the results of the Swedish children to be higher on energy intake in EAR % and fat E%.

The Danish participants had a significantly lower PUFA E % intake (P= <0.001), however I was not able to investigate the food choices among the countries. Controversy exists among PUFA supplementation. Strandvik (60) recently stated that supplementation of PUFA improved lung function by 8 months, but that another study reported negative effects among adult CF patients after 3 months of intravenous administration.

The relationship between energy intake and fat E %

I found a small positive correlation between total energy intake in EAR% and fat E % among the children (r =0.286, P <0.001). These results are lower than the findings of White et al. (30), who found that percentage of energy from fat also gave a positive correlation (r =0.52, P <0.001). Their participants received advise on how to maximize dietary energy and fat intake at the clinic before the study. The children in this study were recording their intake, based on national instructions on dietary intake and did not get any additional advise on how to maximize intake as the objective was to study the dietary intake at the point in time. This may be the reason of the lower correlation between total intake in EAR% and fat E% among the participants of this thesis.

Protein and CHO

Swedish children were found to have a significantly higher mean protein intake in E % compared to both Denmark and Norway (P=0.001). As mentioned, the Swedish meals are structured a little different than the other two countries respectively. The Swedish lunch is often a hot meal, and could possibly increase the protein E% among the Swedish participants. The Norwegian children had a significantly higher CHO intake (P=0002) than the other countries. As I was not able to look into food choices among the participants it is not possible to tell if the difference was due to sugar or complex CHO as illustrated in ***Table 4.12***. The intake of sugar in percentage of energy intake in Norwegian CF- children was not very different from healthy Norwegian children. The average protein and CHO intakes in E% among participants within this study are within the average range of the protein and CHO E% intake of participants from White et al (30).

5.2.3 Comparing younger and older children

Table 4.2 provides an overview of the energy and macronutrient intakes in % of total intake and compared to EAR. Children above 10 years had a significantly lower total energy intake in % of EAR compared to children under the age of 10. The children over 10 years of age had a lower fat and protein E % intake as well. White et al. (30) investigated the energy and macronutrient intake of CF children within age groups. They found that there was a trend for older CF children to have a higher fat intake (g) compared to healthy controls.

A lower energy intake in % of EAR in participants more than 10 years old may be due to the increased control teenagers have on food intake. These children spend more time in school and many have the option of bringing food or buying it at the school canteen. As mentioned in the introduction, there are special considerations around teenagers. The peer pressure, puberty and social settings may affect appetite and energy intake. Some teenagers may find it embarrassing to take enzymes before every meal and therefore do not eat at school, and may worry about looking different to people around them. They might also feel awkward about consuming a higher fat meal compared to

peers (6). Truby et al. emphasize that as CF children age they may become more aware that they are in a different position than other children (61).

5.2.4 Nutritional drinks

In this study 59 children (27.8 %) used nutritional drinks to supplement their diet. Olveira et al (54) report that 30 % of the children in their study used nutritional drinks to increase energy intake. There was no significant difference in the intake of nutritional drinks in kcal among Denmark, Norway and Sweden in this study. Kalnins et al. (37) studied the effect of nutritional supplements on energy intake and nutritional status in CF patients over a 3 month period. They state that neither dietary supplements or nutritional counseling improved nutritional status of the participants during the 3 month period. They highlight that supplements may replace food intake, indicating that total energy intake will not be increased. Our findings may support this as supplementation of nutritional drinks did not give a significant difference on total energy intake in percentage of EAR. However, there can not be drawn specific reasons on the effect of the nutritional drinks as one cannot know if the usage improved the total energy intake for the individual participant. As Kalnins et al. (37) found, we also found that nutritional drinks did not improve nutritional status as measured by BMI z-score at the selected point in time. Smyth et al. (38) investigated the use of oral supplements among CF participants over a 3 month period and found no significant difference in BMI centile.

5.2.5 Micronutrient intake

Supplementation of fat-soluble vitamins and serum values

Aird et al. (62) emphasize that vitamin A levels in serum vary widely among CF patients and is significantly correlated to FEV_1. They found no correlation between serum vitamin E and pulmonary function.

It was found in this thesis that almost all children had serum concentrations of vitamin A within the reference value. Only six participants had serum values lower than recommended. Patients with CF and decreased retinol concentrations have been found to have disturbed night vision, which was reversed by supplementation of vitamin A (23). Supplementation within Scandinavia seems to be generally good but monitoring of each patient could improve clinical outcome at the individual level.

The average serum values for vitamin D (57.3 nmol/l) were not within the reference values (75-150 nmol/l). Robberect et al. (63) report that low serum concentrations of 25-OH vitamin D increases the risk of bone disease and fractures among CF patients over time. They emphasize that holding supplementation solely responsible for the average low serum values may be underestimating the first source of 25-OH vitamin D, merely sunlight. Robberect et al. (63) state that many studies report low serum 25-OH vitamin D values among CF patients, but that the results may vary depending on the severity of the disease. They emphasize that serum concentrations of 25-OH vitamin D are expected to be low among CF patients as 22-97 % of healthy controls are below the laboratory reference. When in sunlight, up to 85 % of the 25- OH vitamin D comes from the sun. In the Nordic countries the dermal vitamin D uptake is high in the summer, and lower in the winter (63).

The CF children in this study had a mean serum vitamin E concentration (22.7 µmol/l) within the reference range (14-50 µmol/l), and 30 (14 %) were below the reference. Clinical deficiency of vitamin E is rare among CF patients, even though low serum levels are often found among them (23). Studies have shown that long term deficiency will eventually cause irreversible neurological damage. One cannot know whether vitamin E supplementation protect against oxidative lung damage among CF patients, however supplementation is recommended to decrease the risk of long-term deficiency (23).

Dietary intake of other vitamins and minerals

The European consensus report on CF states that iron deficiency may be a concern among children with CF, as serum ferritin might be false elevated when the child have

an infection (56). CF participants of this study had a normal to high dietary intake of iron, and their serum ferritin values were within the normal range. White et al. (30) investigated the intake of some vitamins and minerals within age groups of CF participants. They found that CF participants had a higher intake of almost all vitamins and minerals compared to healthy controls. Their average values for iron, calcium and vitamin C are comparable to my findings of dietary intake.

5.2.6 Investigating the macronutrient intake of CF children compared to healthy peers

Scandinavian population studies on healthy children within the same age as the CF participants were compared to the results of CF participants to estimate whether the macronutrient intake in E% was different among CF children. It seemed that within all countries, that CF participants had a higher E% from than their healthy peers. Both in Sweden and Norway the E% from PUFA seemed also higher.

Some assumptions could be made of the dietary intake (kcal) of the participants compared to their peers. The CF children seemed to have a higher energy intake (kcal) compared to healthy peers as shown in ***Table 4.15***. As for the analyses of energy intake in % EAR, the same trend is seen when comparing kcal intake. It seems that the smallest difference in energy intake in kcal is seen among the Norwegian CF patients and their healthy peers. As differences cannot be statistically determined only assumptions can be made. Biases cannot be excluded, concerning the gathering of dietary data among the countries. The organization of CF care may be of relevance. CF care in Sweden and Denmark is more centralized they may have better access to therapy and health personnel involved with nutrition. The Danish CF centers are also more centralized than in Norway, however there were no significant differences in average energy intake in EAR % between Norway and Demark (P=0.05) as seen in ***Table 4.4***. One can discuss the tendency for significance among the countries, and assume that the difference would have been significant if the sample size was larger.

6 Future implications

The findings in this thesis have generated new knowledge, but also created questions and hypotheses in the field of CF and the patients' energy, macro- and micronutrient intake.

It is known that CF patients have increased energy requirements compared to the healthy population, and many of the participants in this thesis had a general satisfying dietary intake. In the future it would be interesting to investigate the participants as part of an intervention study. This could reveal interesting findings about the CF patients nutritional status over a time period. A longitudinal study could help in the questions asked around the negative impact of malnutrition in CF patients.

Other interesting questions to be studied are concerning CF patients and the optimal treatment and therapy. For this thesis I was not able to study the individual food preferences of the children. To establish what types of food are chosen among CF patients, future studies could possibly investigate food choices and meal composition.

The importance of vitamin D supplementation to decrease the risk of poor bone health could be investigated further, to establish guidelines for the Nordic CF patients who do not get adequate sunlight exposure throughout the year.

Under- or over-reporting among CF participants could be interesting to detect. I was not able to look into this within the thesis, but it is an interesting aspect of future research.

7 Conclusion

CF children had a general satisfying energy intake compared to recommendations, with about 60 % of participants receiving more than 120 % of EAR. No differences were seen among the genders. The results from this thesis may suggest that the dietary intake of CF patients, compared to older studies have improved. Furthermore it may be thought to be improvement in information and guidance to patients with CF as the importance of optimal nutrition have been revealed. It is important to highlight that the CF participants in this thesis are slightly shorter than healthy peers. According to the recommendations they have a satisfying energy intake, but improvements may be significant to support normal growth. Nutrition therapy is an important parameter for patients with CF, as some groups may not reach the recommended values.

The children did not reach the target for fat of 40 % of total intake. Many of the children (67 %) were within the lower end of the range, above 35 % of total intake. Swedish participants had a significantly higher protein intake in E % compared to the other Nordic countries. Danish participants had a significantly lower PUFA intake in E % compared to Norway and Sweden.

The participants using nutritional drinks did not have a significantly higher average BMI z-score than those who did not use nutritional drinks. Furthermore these children did not have a higher mean energy intake compared to those who did not use nutritional drinks. Other studies suggest that nutritional drinks may replace the intake of regular food.

In general CF children had a satisfying intake of supplemental fat-soluble vitamins. Vitamin D is of special concern for CF patients in the Nordic countries as seasonal changes may affect the serum values of 25-OH vitamin D, and this might affect the bone health long-term. The average vitamin D status for the participants was below the laboratory reference.

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Appendix 1

Oslo, januar 2004

Kjære CF-pasienter og foreldre til barn med CF.

Vi er snart i havn med pseudomonasstudien som de fleste av dere har deltatt i. Bakteriestammer og oppsamlede blodprøver vil nå bli sendt til Sverige og Danmark for analyser. Når resultatene av disse analysene foreligger, vil vi kunne trekke konklusjoner fra studien.

Det skandinaviske forskningssamarbeidet har så langt vært svært vellykket og gruppen har nå utarbeidet en protokoll for en grundig undersøkelse av ernæringssituasjonen hos personer med CF. Vi mener dette er viktig fordi ernæringen har stor betydning for sykdomsforløpet. Ved en nøyaktig gjennomgang av både næringsinntaket og blodprøveanalyser, samt et røntgenbilde av hånden (under 18 års alder) for å se på utviklingen av skjelettet, kan vi danne oss vi et godt bilde av status, og komme med konkrete råd til den enkelte person med CF. Vi vil også se på om det er forskjeller mellom Norge, Sverige og Danmark når det gjelder ernæringssituasjonen og høste erfaringer av det. Hos enkelte pasienter ønsker vi også å undersøke en avføringsprøve mht elastase-aktivitet (bukspyttkjertelfunksjon).

Undersøkelsene til studien tenker vi utført i forbindelse med en ordinær årskontroll eller en storkontroll. Da skal det likevel tas blodprøver, og studien innebærer at det kun tas et par ml ekstra blod i tillegg til de ordinære prøvene som uansett inngår i en årskontroll. For å få pålitelige data mht næringsinntak, er det nødvendig å registrere inntaket i løpet av 7 dager. Dette er 3 dager lenger enn en ordinær kostregistrering som gjøres ved vanlig årskontroll/storkontroll. Dette er nødvendig for å kunne sammenligne data mellom de forskjellige landene. Ernæringsfysiologene Inger Elisabeth Moen og Torild Grønnerud vil gå gjennom opplegget med hver enkelt.

Vedlagt følger mer utfyllende informasjon om prosjektet som er godkjent av etisk komité og av Datatilsynet.

Vi håper at dere etter å ha lest informasjonen, kan tenke dere å delta. I løpet av 2004 og første del av 2005 håper vi at flest mulig er inkludert i studien. Tidspunktet for når den enkelte vil få tilbud om å være med, avhenger bl.a. av når årskontroll ble gjennomført forrige gang. Dere vil da få nærmere informasjon.

Med vennlig hilsen
På vegne av CF-teamet ved Ullevål Universitetssykehus

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HELSE ØST

Appendix 2

Samtykkeerklæring
(barn 14 år og yngre)

Jeg vil gjerne delta i prosjektet "Ernæringsstatus hos skandinaviske pasienter med cystisk fibrose". Jeg gir samtykke til å bruke opplysninger fra min pasientjournal. Jeg er innforstått med at data fra studien om forekomst av pseudomonas (såfremt jeg er deltaker i det prosjektet) vil bli benyttet som basisdata for det aktuelle prosjektet. Det gis tillatelse til at data kan lagres i prosjektets database i inntil 15 år fra innrulleringsdato og kan benyttes som basisdata for fremtidig forskning om cystisk fibrose. Blodprøven tillates lagret. Det tillates også at blodprøven avidentifiseres og sendes til Sverige for analyse. Det tillates at avidentifiserte data sendes Sverige og Danmark for felles skandinavisk bruk.
(Data til felles skandinavisk bruk forutsettes avidentifisert). Etter 15 år skal data slettes, såfremt det ikke er søkt om fortsatt lagring av data og det foreligger godkjenning for dette fra Datatilsynet.
Informasjonsskrivet er gjennomlest, og jeg/vi er kjent med at det er anledning til å trekke seg fra studien når som helst uten å måtte oppgi noen grunn. Hvis jeg trekker seg fra studien, kan mine foresatte be om at opplysningene i databasen blir slettet.

Sted_____ Dato_____

Navn_____

Foresatte_____
(underskrift)

Barn over 12 år _____
(underskrift)

Appendix 3

Samtykkeerklæring
(barn 15-18 år)

Jeg vil gjerne delta i prosjektet ”Skandinavisk ernæringsstudie hos pasienter med cystisk fibrose”. Jeg gir samtykke til å bruke opplysninger fra min pasientjournal. Jeg er innforstått med at data fra studien om forekomst av pseudomonas (såfremt jeg er deltaker i det prosjektet) vil bli benyttet som basisdata for det aktuelle prosjektet. Det gis tillatelse til at data fra prosjektet kan lagres i prosjektets database i 15 år fra innrulleringsdato, og kan benyttes som basisdata i fremtidig forskning om CF. Blodprøven min tillates lagret.
Data til felles skandinavisk bruk forutsettes avidentifisert. Etter 15 år skal alle data slettes, såfremt det ikke er søkt om fortsatt lagring og det foreligger godkjenning for dette fra Datatilsynet.
Jeg har lest informasjonsskrivet og er innforstått med at jeg når som helst kan trekke meg fra prosjektet uten å måtte oppgi noen grunn. Dersom jeg trekker meg, kan jeg kreve opplysningene om meg i databasen blir slettet.

Sted_____ Dato_____

Navn_____
(underskrift)

Samtykket bekreftes av en av de foresatte

_____
(underskrift)

Veiledning til KEF før gjennomgang av Dagboken med deltaker i kostholdsundersøkelsen

Det er kun pasienter som er fylt 4 år som skal registrere kostholdet. Kosten må registreres i tilknytning til årskontrollen hvor øvrige data samles inn.

Sjekk at alle får

- 7 sett kostdagbøker med innstemplet ENZYMER[1]
- 1 bildehefte,
- 7 hjelpeark,
- 1 frankert returkonvolutt.
- 7 ark for instruksjon og bruk hos dagmamma, barnehage og skole for dem det er aktuelt.

Identifikasjonnummer på dagbøkene

Identifikasjonsnummeret nederst til venstre på dagbøkene på hver side er viktig å bruke riktig ved utdeling av dagbøkene. Nummeret består egentlig av 3 felt og leses bakfra., f eks skal 20000101 oppfattes som 2000 0 101 der 101 er personnummeret, 0 er dagnummeret og 2000 viser til at heftet tilhører en serie på 7 dagbøker per person. ALLE 7 hefter som deles ut til en person MÅ HA samme personnummer. Heftet med 0 brukes til 1. dag , neste dag brukes hefte 1 osv.

Hold oversikt over hvem som har hvilke identifikasjonsnummer. Se eget skjema "Skjema for oversikt og reg ……"

Gjennomgang av dagboken

Forklar deltakerne at heftet med "0" som tall nr. 4 bakfra i identifikasjonsnummeret brukes første dag og neste dag brukes hefte med "1" som tall nr. 4 bakfra.

Presiser at det er det vanlige kostholdet som skal skrives inn. Dersom det i forbindelse med årskontrollen gis kostråd som innebærer endring, be om at disse ikke gjøres før etter at Dagbøkene er utfylt.

Gå gjennom Dagbokens oppbygging basert på matvaregrupper og ikke måltider.

Gå gjennom Råd for utfylling av Matdagboken sammen med pasienten.

- Hvordan fylle ut dagboken. Poengtere særskilt hvor sondeernæring, næringsdrikker, og berikning skal føres. Likeledes hvordan enzymer skal føres.

- Praktisk gjennomføring. Bruk Dagboken og bildeheftet for å illustrere.

Ta kontakt med pasienten per telefon 2-3 dager etter oppstart for å avklare evt. spørsmål.
Gå gjennom utfylt kostregistrering når den mottas og kontakt pasienten ved evt. uklarheter.
Menyboken sendes til UiO for beregning (nærmere avklaring nødvendig).
Pasienten får tilbakemelding på inntak ved neste konsultasjon eller via telefon.

NB! Husk å kopiere side 3 i alle matdagbøkene pga. oversikt over enzyminntak!

[1] Stemple inn ENZYMER til venstre nederst på side 3 i alle dagbøker.

Appendix 5

Informasjon til dagmamma/barnehage/SFO

:…… er med på en kostholdsundersøkelse.

Vennligst skriv opp:

- Alt barnet spiser (også halve kjeks, appelsinbåter, osv.) unntatt mat barnet har med hjemmefra.
- Alt barnet drikker (også vann) unntatt drikke barnet har med hjemmefra.
- Dersom barnet har med matpakke hjemmefra, send alle rester av matpakken med hjem.
- Skriv opp hvor mye pankreasenzymer barnet tar til måltider/mellommåltider
- Foreldrene tar med seg notatarket hjem hver dag.

Eks.

Kl.	**Matvarer – angi type så nøye som mulig**	**Mengde**	**Enzymmengde** **Antall kapsler/måleskjeer**
Kl.11	Tomatsuppe m/makaroni (pakke) Pannekaker Syltetøy Vann	Ca. 1 dl 2 stk 1 ss 1 glass	2 kapsler
Kl. 14	Litagoyoghurt Ryvita kenkkebrød Soft margarin i bordpakning/beger Gudbrandsdalsost (G35)	1 stk (125 ml) 1 stk Moderat lag 2 skiver	2 kapsler

Dato

Kl	**Matvare – angi type så nøye som mulig**	**Mengde**	**Enzymmengde** **Antall kapsler/måleskjeer**

Appendix 6

Veiledning i utfylling av Matdagbok

En viktig del av denne studien er å kartlegge hva personer som har cystisk fibrose, får i seg av mat og næringsstoffer. For å få et best mulig bilde av dette, vil vi be deg å skrive ned HVA og HVOR MYE du, eller barnet ditt, spiser og drikker i løpet av 7 dager. For å gjennomføre dette fås følgende utdelt:

- Veiledning vedr. utfylling av Matdagbok
- 7 Dagbøker for registrering av mat og drikke (en Dagbok for hver dag)
- 7 hjelpeark (et hjelpeark for hver dag)
- 7 ark med instruksjon til dagmamma, barnehage, evt. skole/SFO
- Bildehefte for porsjonsbestemmelse
- Frankert konvolutt for retur av 7 utfylte Dagbøker.

Kosten skal registreres fra ……dag til og med ……dag.

Skriv ned alt som du, eller barnet ditt, spiser og drikker fra oppvåkning om morgenen første dag til innsovning for natten siste dag i registreringsperioden. Det er viktig at ABSOLUTT alt tas med. Næringsdrikker, sondeernæring og berikningsprodukter må også skrives ned dersom det brukes. Vi ber også om at bruken av pankreasenzymer registreres nøyaktig.

Inntaket av mat og drikke skal være som vanlig. Det er viktig at vanene ikke endres i forbindelse med undersøkelsen!

Hvordan fylle ut Dagboken?

Bla igjennom Dagboken og bildeheftet for å bli kjent med innholdet før oppstart. På de siste sidene i denne informasjonen er det eksempler på hvordan Dagboken fylles ut.

Forsiden

På forsiden av hver Dagbok skal kjønn, alder, dato og hvilken ukedag det er, fylles inn. Det skal også noteres om det var en vanlig eller uvanlig dag. På forsiden finnes en oversikt over hvor de ulike matvarene finnes i heftet.

Tidsbolker

Legg merke til at en dag er delt inn i 5 tidsbolker (f eks kl. 6-10, kl. 10-14). Fire av disse er på 4 timer, mens den siste strekker seg fra kl. 22 om kvelden til kl. 06 neste morgen.
Skriv ned hvor mye du, eller barnet ditt, har spist eller drukket i de aktuelle tidsrommene. Begynner måltidet innenfor en tidsbolk og avsluttes i den neste, skrives alt i den tidsbolken måltidet starter.

Fyll tall i de svarte rutene

For hver matvare er det oppgitt en enhet. For eksempel skal drikke angis i antall glass, og brød oppgis i antall skiver. For alle matvarer må det angis hvor mange enheter som er spist/drukket. Det kan skrives som hele tall, f eks ”1, 2, 3,…” eller som deler, f eks ”1/4, ½ eller 1 ½” . Antall enheter skal fylles inn i de svarte rutene.

Appendix 6

Fyll bokstaver inn i de oransje rutene

For noen matvarer må bildeheftet brukes for å angi hvor mye som er spist. Det er da henvist til den bildeserien som skal brukes. Bildeseriene består av 4 alternativer merket A, B, C, D. Velg det alternativet som stemmer best med hvor mye som er spist. Bokstaven skrives i den oransje ruten. Enkelte matvarer skal sammenliknes med bilder som ikke ligner på det som er spist. Her skal bildene brukes til å se hvor stor plass matvaren som er spist tar på tallerkenen.

Spises flere porsjoner av ulik størrelse, så tenk på hvordan alle porsjonene ville sett ut til sammen. Har du f eks spist to porsjoner spagetti, en som ligner på B og en annen på A, kan du skrive 1 ½ B.

NB! Det skal ikke brukes kryss i Dagboken, bare tall og bokstaver

Når en matvare ikke er med i Dagboken
Når du eller baret ditt spiser matvarer/retter som ikke står oppført i Dagboken, må du beskrive nøye det som er spist, hvor mye og når i de åpne feltene for "Annet".

Næringsdrikker, sondeernæring føres under avsnitt om Drikker i feltet for "Annet" (type, mengde, tidspunkt). Dersom ekstra margarin, fløte, olje, glukosepolymer etc er tilsatt ekstra i enkelte retter, skrives det inn som "Annet" under den retten produktet er brukt i.

Margarin
Margarintyper må spesifiseres nærmere enn det skjemaet legger opp til: Skriv derfor eksakt navn og fabrikat på margarintypen som er brukt, rett under der det står Margarin i skjemaet. Du trenger ikke å gjøre dette dersom måltidet er spist utenfor hjemmet.

Pankreasenzymer
Pankreasenzymer må føres inn i Dagboken. Før inn inntaket av disse nederst på s. 3 under avsnitt Drikke. Rett ut for linjen som det er stemplet "Enzymer" her. Her skrives nøyaktig navn på enzymene til venstre. Antall kapsler (evt. måleskjeer) skrives rett under hver tidsbolk.

Praktisk gjennomføring

Om du vil skrive fortløpende i Dagboken rett etter maten er spist/drukket eller om du vil notere på hjelpearket og "føre inn" om kvelden, er opp til deg. Men du bør ikke vente til neste dag, da kan det være lett å glemme noe. Hjelpearket kan være greit å ha med seg på arbeid, i skole eller andre steder hvor det kan bli spist/drukket noe. Bruk eventuelt baksiden av hjelpearket om du vil gjøre mer detaljerte notater.

For barn som er hos dagmamma, i barnehage eller SFO er det laget et eget informasjonsskriv hvor barnets inntak kan føres inn. Det er viktig at dette arket tas med hjem hver dag for innføring i Dagboken.

- Det er viktig at du ikke bretter eller krøller Dagbøkene.
- Bruk myk blyant eller penn til å skrive i Dagbøkene med.

Eksempel (følg med i dagboka og bildeheftet under gjennomgangen)

Appendix 6

Åse begynner å spise middag kl. 17.45. Hun spiser **en porsjon med spagetti og tomatsaus med pølsebiter. I tillegg spiser hun en og en halv skive loff, en halv skie med soya soft margarin og en skive uten noe på. Hun drikker ett glass saft, og tar en halv mango til dessert**. Hun tar 4 Pankreon til måltidet.

Åse tar fram både dagboka og bildeheftet. Hun blar opp på siden for drikke og finner linjen "Saft med sukker". I kolonnen "kl 14-18" skiver hun 1 i en av de svarte rutene, og etter å ha sett bildeheftet skriver hun "B" i den oransje ruten, etter som glasset hun brukte ligner mest på B-glasset.
Du skal skrive tall og bokstaver som vist her:

	Antall	kl 6-10	kl 10-14	kl 14-18	kl 18-22	kl 22-6
Saft med sukker (eks. appelsin, solbær)	glass					

Deretter blar hun opp på siden med brød. Hun finner linjen med "loff/fint rundstykke" og skriver 1 ½ i de svarte rutene i kolonnen "kl. 14-18". Hun ser på tykkelsen i bildeheftet og finner at tegning C passer best til brødskivene hun spiste. Hun skriver C i den oransje ruten.

	Antall	kl 6-10	kl 10-14	kl 14-18	kl 18-22	kl 22-6
Loff/fint rundstykke	skiver					

Hun finner linjen med soya soft margarin og skriver ½ i kolonnen "kl 14-18".

	Antall	kl 6-10	kl 10-14	kl 14-18	kl 18-22	kl 22-6
Myk margarin (eks soya soft)	skiver					

I bildeheftet finner hun at hun brukte samme mengde margarin som på bilde B. Under "Hvor mye smurte du på brødet?" skriver hun B i den orange ruten.

	kl 6-10	kl 10-14	kl 14-18	kl 18-22	kl 22-6
Bildeserie 3					

Tilslutt blar hun opp på sidene med "andre retter". Det er flere pastaretter å velge mellom, og hun velger "pasta med tomatsaus". I bildeheftet finner hun at porsjonen ligner mest på bilde C. Hun skriver derfor 1 i den svarte ruta og C i den oransje.

		kl 6-10	kl 10-14	kl 14-18	kl 18-22	kl 22-6
Pasta med tomatsaus uten kjøtt	bildeserie 6					

I tillegg skriver hun hvor mye pølser hun hadde i tomatsausen. Hun finner "Grillpølse/wienerpølse vanlig" og skriver 1 i kolonnen "kl. 14-18".

Appendix 6

	Antall	kl 6-10	kl 10-14	kl 14-18	kl 18-22	kl 22-6
Grillpølse/wienerpølse vanlig	stk	☐☐	☐☐	☐☐	☐☐	☐☐

Hun finner ikke mango blant fruktene som er nevnt i dagboka. I boksen ”annet” etter frukt skriver hun ”Mango”, ½ stk., kl. 17.15.

Annet
Beskriv best mulig hva, hvor mye og når

Pankreasenzymer

Pankreasenzymer fører hun inn som Pankreon rett under innstemplet ”Pankreasenzymer” på s. 3 under avsnitt Drikke, og rett under tidsbolk kl. 14-18 skriver hun 4.

Spørsmål/problemer

Ved spørsmål, ring Norsk senter for cystisk fibrose v/Inger Elisabeth Moen, tlf. 23 0155 90. Du kan også sende e-post: ingerelisabeth.moen@ulleval.no

Inger Elisabeth Moen vil også ringe deg for å oppklare evt. spørsmål eller problemer 2 –3 dager etter oppstart av registrering.

Retur av utfylte Dagbøker

Send inn de 7 utfylte Dagbøkene så snart registreringsperioden er over. Bruk den ferdig frankerte svarkonvolutten. Hvis du har mistet konvolutten så sendes Dagbøkene til:

Norsk senter for cystisk fibrose v/Inger Elisabeth Moen
Bygning Q2,
Ullevål universitetssykehus
0407 OSLO

Annet pålegg

1 skive= 1/2 rundstykke= 1knekkebrød
=2 vaffelhjerter= 2 kjeks= 1/2 ciabatta

	Antall	kl. 6-10	kl. 10-14	kl. 14-18	kl. 18-22	kl. 22-6
Egg, kokt/stekt	til antall skiver					
Majonessalat (eks. italiensk salat, rekesalat)	til antall skiver					
Majonessalat, lett (eks. italiensk salat, lett)	til antall skiver					
Tomat som pålegg	til antall skiver					
Banan som pålegg	til antall skiver					

Annet
beskriv best mulig hva, hvor mye og når:

Pynt på brødskiver

	Antall	kl. 6-10	kl. 10-14	kl. 14-18	kl. 18-22	kl. 22-6
Majones/remulade, vanlig	til antall skiver					
Majones/remulade, lett	til antall skiver					
Agurk (frisk/syltet)	til antall skiver					
Rødbeter (syltet)	til antall skiver					
Paprika	til antall skiver					

Annet
beskriv best mulig hva, hvor mye og når:

Yoghurt

	Antall	kl. 6-10	kl.10-14	kl.14-18	kl.18-22	kl.22-6
Yoghurt med frukt	beger (175 ml)					
Yoghurt 0,1% fett	beger (125 ml)					
Yoplait frukt	beger (125 ml)					
Litago yoghurt	beger (125 ml)					
Litago yoghurt m/müsli	beger inkl. müsli					
Go'morgen yoghurt m/müsli	beger inkl.müsli					
Piano Duo Yoghurt	beger (125 ml)					

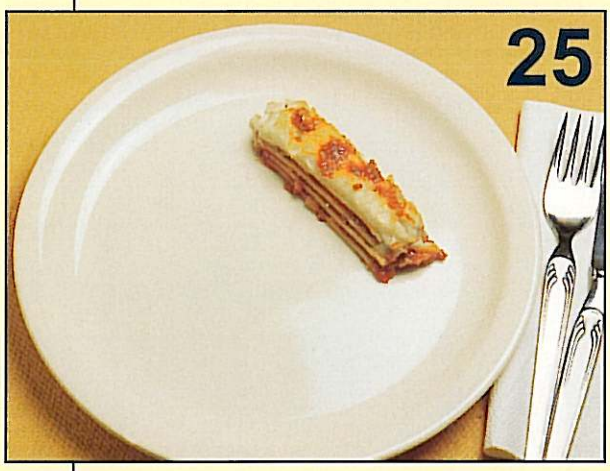
Appendix 8

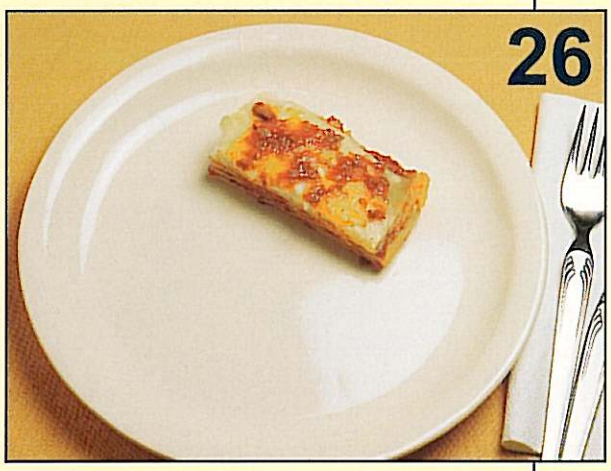
24. Wok

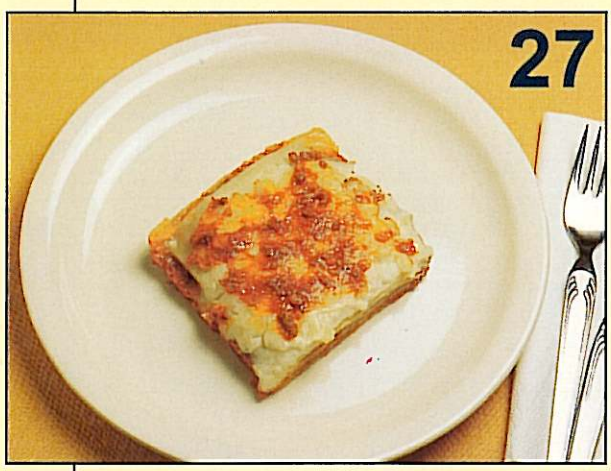
25. Gryterett

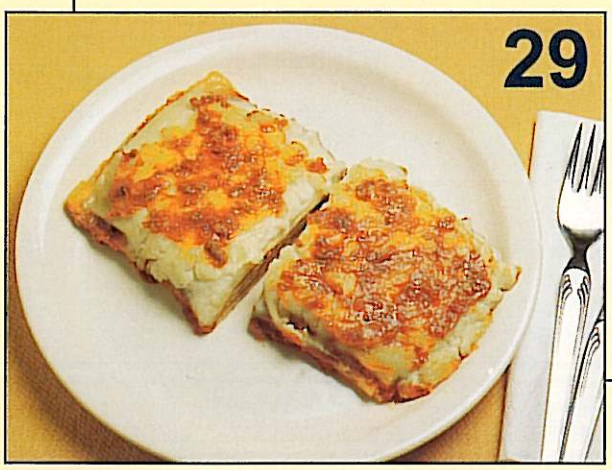
Appendix 9

LASAGNE









LASAGNE

Appendix 10

VARM AFTENSMAD

Jeg/mit barn spiste ikke varm aftensmad ☐ (sæt kryds) og gå til side 10

Husk evt. mellemmåltider side 12, 13.

Drikkevarer til varm aftensmad

	Antal
Kaffe	..... kop
Te	..... kop
Kakao-, chokolademælk	..... glas
Saftevand, limonade, læskedrik	..... glas
Saftevand/limonade/læskedrik (light, sukkerfri)	..... glas
Letmælk	..... glas
Sødmælk	..... glas
Skummet-, kærnemælk	..... glas
Sodavand, almindelig	..... glas
Sodavand (light, sukkerfri)	..... glas
Danskvand, mineralvand, apollinaris	..... glas
Postevand	..... glas
Øl, pilsner	..... flaske
Lys/let pilsner, alkoholfri øl	..... flaske
Stærkt øl	..... flaske
Vin	..... glas
Hedvin	..... glas
Juice	..... glas
Anden drik (notér hvilken) _____	..... glas

Kød, pølser og indmad

	Antal/portionsstørrelse
Hakket kød (f.eks. hakkebøf, frikadeller, medister, krebinetter, forloren hare)	..... stk/skiver
Okse/kalvekød (f.eks. bøf/kotelet med fedtkant, culotte, tykkam, højreb, tyndsteg, bryst, oksegrydesteg)	..... stk/skiver
Okse/kalvekød (f.eks. roastbeef, wienersnitzel, steak/bøf uden fedtkant, tyksteg, inderlår, mørbrad, filet, klump, skank)	..... stk/skiver
Svinekød (f.eks. kotelet, nakkekotelet, hamburgerryg, skinke, skinkeculotte)	..... stk/skiver
Svinekød (f.eks. skinkesnitzel, mørbrad, skinkemignon, bov, filet)	..... stk/skiver
Svinekød (f.eks. flæskesteg, ribbensteg, stegt flæsk, ribsteak, revelsben, rullesteg)	..... stk/skiver
Lammekød	..... stk
Pølser	..... skiver
Lever	..... stk/skiver
Andet kød (notér hvilket) _____	A B C D*
Gryderet/sammenkogt ret (f.eks. millionbøf, boller i karry, chili con carne, gullasch, osso buco)	... ...
Biksemad	..... portion

Fisk og skaldyr

	Antal/portionsstørrelse
Fiskefrikadelle	..... stk
Torsk, sej, rødspætte, skrubbe	..... portion
Sild, makrel, laks, ørred, ål	..... portion
Anden fisk (notér hvilken) _____	..... portion
Fiskegryde/sammenkogt fiskeret (f.eks. fisk i fad, bouillabaise)	A B C D*
	... ...

* Sammenlign din portion med billederne. Skriv antal portioner du har spist af den pågældende størrelse.

Appendix 11

Spørreskjemaet er utfylt av kef …….. og pasient …….. ….

Pasientnummer…….. …….....Pasient- ID ……..Dato....…….

Vitamin & mineraltilskudd, fiskeoljekapsler og tran

< betyr "mindre enn", ≥ betyr "mer enn"

Navn på tilskudd	**Mengde stk/ml**	**Daglig inntak ***	**Antall dager i uken ****	**Tar du enzymer til tilskuddet**		**Bruker du glemme å ta vitamin & mineraltilskudd, fiskeoljekapsler, tran**				
				Ja	**Nei**	**Ja <1 gang/uke**	**Ja 1-2 ganger/uke**	**Ja ≥3 ganger/uke**	**Nei**	**Vet ikke**

* fyll inn x om inntaket er daglig
** fyll inn antall dager om dersom færre enn 7 dager per uke

Appendix 12

Standardised height and weight measurements

Height:
Erect, heels together, no shoes, no stockings
Mean of three measurements in cm is recorded
(elevate the chin in between the measurements)

Weight:
In the morning fasting and having emptied the urinary bladder and bowel*
Wearing only undergarments**
The measurement is recorded in kg
Important!! The scale has to be calibrated regularly.

* If fasting not possible weight at least 2 h after meal
** If not possible the weight of the garments has to be deducted from the measured weight
jeans: 0.6 kg
T-shirt 0.1 kg

(Z-score) Swedish Standard deviation score probably all right also for Denmark and Norway – will be calculated in Gothenburg.