

# Refeeding syndrome in patients with Anorexia Nervosa

Procedures to detect and treat patients at risk of refeeding syndrome in regional departments of eating disorders in Norway and nutrient contents of the basic reference menu at Regional Department of Eating Disorders (RASP)



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# **Abstract**

## **Background**

Anorexia nervosa (AN) is a disorder recognized by underweight and psychiatric symptoms, and some patients are at risk of developing refeeding syndrome (RFS). AN patients may experience metabolic disturbances and severe symptoms during refeeding, and international guidelines in how to refeed AN patients at risk of RFS varies. The regional departments of eating disorders (EDs) in Norway treat about 100-200 patients every year with AN, and a survey investigating procedures have not been performed before.

## **Aim**

This master thesis has investigated how physicians and registered dietitians (RDs) in the departments of EDs in Norway consider RFS, and how they refeed and monitor patients with AN. Due to the complications and problems that may occur during refeeding in high-risk groups like AN, it was of interest to investigate if procedures, knowledge and awareness varied between the ED units and if the basic reference menu at RASP contain the energy and micronutrients that is recommended for AN patients during refeeding.

## **Method**

Procedures, questionnaires and analysis of the basic reference menu at RASP have been collected and analyzed. The procedures were collected by contacting the head physicians at the different regional departments of EDs by mail. The master student designed the questionnaire, with assistance from the RDs and supervisor at RASP. The four-week rollover dinner menu at RASP was weighed, photographed and nutritional content calculated. The average nutrient content of the dinners was analyzed together with the other meals (breakfast, lunch, and evening meal) in the basic menu/ and half of the basic menu to evaluate the yield of important nutrients trough one day.

## **Results**

Three out of six regional departments of EDs have a procedure to identify and/or treat patients at risk of RFS. Initial refeeding range of energy in the procedures varied between 10-30 kcal/kg/body weight, or half dietary lists (1000-1500 kcal). RFS is a rare syndrome in the ED

units. Only one clinician at one of the ED units had ever seen a patient with full-blown RFS. The basic reference menu at RASP covers the recommendations of most nutrients. Half basic reference menu contains more energy than most international guidelines recommended for patients at risk of RFS. The energy contents in dinner portions in the basic reference menu contain an average of about 480kcal.

### **Conclusion**

The procedures of RFS vary between the regional departments of EDs in Norway. A closer collaboration between the units may be favorable, and all units ought to have procedures to identify and treat patients at risk of RFS. The knowledge and awareness of RFS among physicians and RDs working at an ED unit in Norway are good. However, the questionnaire detected that there are some uncertainties both among the physicians and RDs about the definition of RFS.

The energy prescribed in “Halv grunnmeny” is higher than most of the international guidelines for initial refeeding of patients at risk of RFS. The basic reference menu makes an important frame for and is a good guidance for the milieu therapists that serve the patients during the nutritional rehabilitation at RASP. Supplementation of omega 3, vitamin D and iron should be assessed.

## **Foreword**

This master thesis is the final project to a master degree in Clinical Nutrition from the Department of Clinical Medicine at Faculty of Medicine and Dentistry at University of Bergen. The thesis has been written in collaboration with Regional Department of Eating Disorders (RASP) at Oslo University Hospital, Ullevål.

First, I wish to thank my supervisors that have guided me through the work with this thesis. From the planning phase, during the implementation and completing phase, they have assisted with advice, encouragement and knowledge I could not have been without.

I also want to thank the Research team at the Competence Center at RASP and the registered dieticians that have contributed during the development of the questionnaire and with advice and encouragement during the writing process.

## Abbreviations

<b>2.3 DPG</b>	2.3 diphosphoglycerate
<b>AN</b>	Anorexia nervosa
<b>APA</b>	American Psychiatric Association
<b>ATP</b>	Adenosine triphosphate
<b>BMI</b>	Body mass index, kg/m <sup>2</sup>
<b>BMR</b>	Basal metabolic rate
<b>BN</b>	Bulimia nervosa
<b>Cl<sup>-</sup></b>	Chloride
<b>ED</b>	Eating disorder
<b>EN</b>	Enteral nutrition
<b>ESPEN</b>	European Society for Clinical Nutrition and Metabolism
<b>IBW</b>	Ideal body weight
<b>IrSPEN</b>	The Irish Society for Clinical Nutrition and Metabolism
<b>IM</b>	Intramuscular
<b>K<sup>+</sup></b>	Potassium
<b>Kcal</b>	Kilocalorie
<b>Na<sup>+</sup></b>	Sodium
<b>NICE</b>	The National Institute for Health and Clinical Excellence
<b>Mg<sup>2+</sup></b>	Magnesium
<b>MARSIPAN</b>	Management of Really Sick Patients with Anorexia Nervosa
<b>PN</b>	Parenteral nutrition
<b>RASP</b>	Regional seksjon spiseforstyrrelser (Oslo) (English: Regional Department of Eating Disorders)
<b>RD</b>	Registered dietician
<b>RESSP</b>	Regionalt senter for spiseforstyrrelser (Bodø)
<b>RFS</b>	Refeeding syndrome
<b>RKSF</b>	Regionalt kompetansesenter for spiseforstyrrelser (Stjørdal/Levanger)
<b>RSS</b>	Regionalt senter for spiseforstyrrelser (Tromsø)

## **Descriptions**

<b>Anabolic</b>	Energy requiring processes
<b>Catabolic</b>	Energy releasing processes
<b>Enteral nutrition</b>	In this thesis, enteral nutrition is used to describe tube feeding exclusively (not food or nutritional drinks).
<b>“Grunnmeny”</b>	The basic reference menu at RASP (2650 kcal)
<b>Incidence</b>	Number of new cases in a population over a specific period
<b>“Halv grunnmeny”</b>	About half the basic reference menu at RASP (1350/1400 kcal).
<b>Parenteral nutrition</b>	Nutrition given intravenously
<b>Prevalence</b>	Total number of cases in a population
<b>Semi-starvation</b>	Partial absence of food

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# 1 Introduction

Eating disorders (EDs) is a group of disorders that is characterized by disturbed eating and body image. The most well-known diagnoses are anorexia nervosa (AN) and bulimia nervosa (BN), but the largest group of patients with EDs is found in the diagnosis eating disorders not otherwise specified (EDNOS) (Smink, van Hoeken, & Hoek, 2012). Only a description of AN will be given in this thesis. AN is an ED with severe psychiatric symptoms, as well as a disturbed body image, underweight and malnourishment (Gentile, Pastorelli, Ciceri, Manna, & Collimedaglia, 2010; Zipfel, Giel, Bulik, Hay, & Schmidt, 2015). A further description of AN is given in chapter 2.2.

Refeeding syndrome (RFS), a condition recognised by metabolic disturbances during refeeding of severely underweight or starved patients, has been known for decades (H. Mehanna, Nankivell, Moledina, & Travis, 2009). Even though RFS is well known, a common global definition is lacking, and the awareness of this syndrome in patients with AN among health personnel varies (M. A. Crook, 2014). There is also a lack of information about how the health personnel judge the severity of this condition. A question that has been raised is whether the concern or awareness of RFS is appropriate during treatment of patients with AN or whether the concern in patients with AN is exaggerated.

The different regional departments of EDs in Norway treat about 100-200 patients each year with AN (personal communication Rø, Ø 2016), and AN patients is the most common patient group at the regional department of ED in Norway. A key component in the treatment of these patients is nutritional rehabilitation and reduction of underweight (Gentile et al., 2010). Treatment of AN and other EDs and the severity of EDs have lately generated a surge of interest in the media. How these patients are treated in Norway and what the procedures of the treatment given due to the concern of RFS are topics that have not been evaluated before.

## 1.1 Objectives/aims

Due to the severity of AN and risk of developing RFS it seems important to figure out whether a common practice exists among the regional departments of EDs in Norway to detect and prevent development of RFS. Due to the complications and problems that may occur during refeeding in

high-risk groups like AN, it has been of interest to investigate if procedures, knowledge and awareness varies between the regional departments of EDs, and if the basic reference menu at RASP contains the energy and micronutrients that is recommended for this patient group during the refeeding phase of the treatment.

## **1.2 Research questions**

1. Do procedures exist to identify, treat and monitor patients in risk of developing RFS in regional departments of EDs in Norway? Do the procedures correspond to international guidelines?
2. How is the experience and knowledge about RFS among physicians and RDs working at the departments of EDs in Norway?
3. Does the half basic reference menu (“Halv grunnmeny”) developed by RDs at RASP cover the electrolyte and energy recommendations given for the refeeding phase (first 2-3 weeks) in severely malnourished patients?

## **2 Background**

In the following chapters, background information about RFS and AN will be given. Regarding RFS, a historical background will be presented, as well as a short description of the mechanism, definitions, incidences and risk groups. The background information about AN includes diagnostic criteria, incidence and prevalence, pathogenesis, health consequences and treatment. Guidelines for refeeding AN patients and patients at risk of RFS are then described.

Considering risk and treatment of RFS, both procedures for AN adolescents and adults have been investigated. When available, guidelines for both groups are presented and discussed, but unfortunately, the literature in this field does not always distinguish between the age groups. If possible, recommendations and information about the age groups are kept separate.

## **2.1 Refeeding syndrome**

### **2.1.1 History**

Refeeding syndrome was first observed during and after World War 2 (Fuentebella & Kerner, 2009). Observations in Leningrad, the famine in Netherlands, the Minnesota semi-starvation experiment and refeeding of starved prisoners in Japan, are all examples of situations where they observed cardiac insufficiency, oedema, high blood pressure and neurological complications during refeeding (Fuentebella & Kerner, 2009; Kraft, Btaiche, & Sacks, 2005; Miller, 2008).

In the Minnesota semi-starvation experiment from 1944-45 the patients experienced early signs and symptoms of heart failure after intake of high calorie diets after six months of semi-starvation (Brozek, Chapman, & Keys, 1948). In the semi-starvation period, they were given 1600 kcal and 49 grams of protein for six months after a three-month long observation, resulting in an average weight loss of 23.9 %. When they started refeeding after six months, complications that may be known as symptoms of RFS today occurred (Brozek et al., 1948).

In a Japanese study from 1945, previously starved prisoners were refeed and developed severe symptoms (M. A. Crook, 2014). They were given high calorie diets, and were supplemented with yeast, thiamine chloride and ferrous sulphate (Maurice A. Schnitker, Paul E. Mattman, & Theodore L. Bliss, 1951). It was estimated that the patients' diets consisted of 800-1000 kcal during semi-starvation, and the prisoners had lost 40 % of their normal body weight. They developed severe symptoms like neuropathy and oedemas; symptoms associated with RFS, and 21 % of them died (M. A. Schnitker, P. E. Mattman, & T. L. Bliss, 1951).

Even though the knowledge about the possible consequences of refeeding has been known since the World War 2, the term RFS was first used by Weinsier and Krumdieck in 1981 (Boateng, Sriram, Meguid, & Crook, 2010). Two severely malnourished patients (40 and 70 % of ideal body weight (IBW)) died after they were given carbohydrates 21-23 g/kg/day and protein 3.5 g/kg/day in total parenteral nutrition (PN) (Weinsier & Krumdieck, 1981).

The introduction of enteral nutrition (EN) and PN have given health personnel the opportunity to refeed patients more aggressively (Kraft et al., 2005), but the risk of developing RFS may be even higher with these feeding methods.

## **2.1.2 Mechanisms of refeeding syndrome**

RFS, also called nutritional recovery syndrome (Klein, Stanek, & Wiles, 1998), is recognized by shifts in electrolytes and fluids due to changes in hormonal and metabolic systems during starvation and refeeding (H. M. Mehanna, Moledina, & Travis, 2008). The main finding is hypophosphatemia, but also levels of other electrolytes, especially potassium and magnesium (Golden, Keane-Miller, Sainani, & Kapphahn, 2013), vitamins (especially thiamine) and trace elements may be low (Boateng et al., 2010; Golden et al., 2013; Sobotka, 2010). The symptoms of RFS are generally expected to be observed within 3-10 days after refeeding has started (Hofer et al., 2014). A summary of deficiencies, organ systems and symptoms involved in RFS are presented in table 1. The following chapters describe the physiology of RFS, and important electrolytes involved.

### **Starvation**

During starvation, or semi-starvation, the body has to use already stored energy. The body tries to compensate for the lack of ingested energy by means of changes in metabolism from an anabolic state to a catabolic state (M. A. Crook, 2014). Due to the depletion of glycogen stores during starvation (within 24-72 hours) (Kraft et al., 2005), the muscles release amino acids and the adipose tissue release free fatty acids and glycerol to compensate for the low calorie intake. This utilization of fat and protein provides glucose through gluconeogenesis and ketones, which will make a decrease in lean body mass if starvation is persistent (M. A. Crook, 2014).

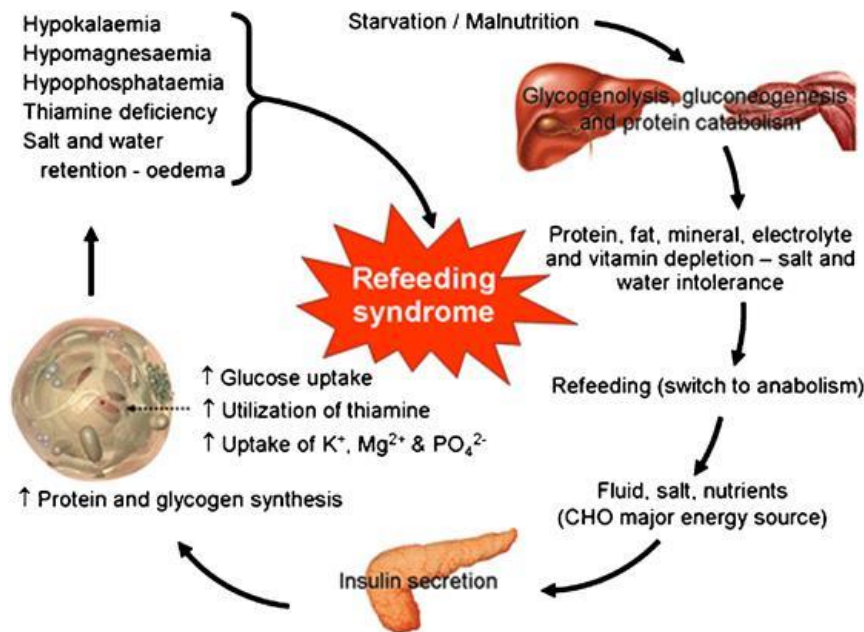
Insulin levels decrease, while glucagon levels increase during starvation. Muscles and other tissues decrease their use of ketone bodies, resulting in an increase of ketone levels in blood. This increase result in an increased use of ketone bodies compared to glucose in the brain (H. M. Mehanna et al., 2008). In this way, the body reduces the mobilization of proteins from other tissues, and save the body stores. The liver decreases its gluconeogenesis when the body adapt to ketone production, and the metabolism decreases due to decreased oxygen consumption, reduced muscle activity and reduced body temperature in a fasting state (Kraft et al., 2005).

Macromolecules, as well as the body's storage of electrolytes, are depleted during starvation, and cell volumes decrease in the brain, liver, muscle and heart. Homeostatic changes ensure that the

plasma levels of ions, as expressed through blood samples, are surprisingly normal even though intracellular body stores are markedly decreased (H. M. Mehanna et al., 2008). Physiological adaptations to ensure satisfying plasma levels include increased renal tubular reabsorption of phosphate, potassium and calcium, tissue and bone breakdown, and dehydration, which may cover up low serum electrolyte levels (O'Connor & Nicholls, 2013).

## Refeeding

**Figure 1** Mechanisms of possible consequences of refeeding after starvation



Retrieved from “Nutrition in clinical practice-the refeeding syndrome: illustrative cases and guidelines for prevention and treatment” Stanga et al (2008).

When refeeding is started after a starvation period, the body shifts from a catabolic state back to an anabolic state (H. Mehanna et al., 2009). Carbohydrates, or glucose, become the primary source of energy, resulting in a shift in insulin and glucagon secretion. This shift causes a high demand of intermediates in glycolysis, like phosphate and thiamine, due to the production of phosphorylated adenosine triphosphate (ATP) and 2.3 diphosphoglycerate (2.3 DPG) (Fuentebella & Kerner, 2009; Kraft et al., 2005). ATP is a coenzyme used by the cells in our body, and 2.3DPG have an important role in promoting release of oxygen from haemoglobin (Solomon & Kirby, 1990). The shift in metabolism increase the usage and production of these intermediates, and cellular uptake of glucose, phosphate, potassium and magnesium ions are

increased, and plasma levels of these electrolytes could drop rapidly (M. Crook, Hally, & Panteli, 2001; M. A. Crook, 2014).

## Electrolytes, vitamins and fluid

To make a proper understanding of what may happen in RFS, a description of the main ions that are involved and which role they have in the body is given below.

**Table 1** Deficiencies, organ systems and symptoms that may be involved in RFS

	Cardiac	Respiratory	Hematologic	Neurologic	Gastrointestinal	Muscular	Other
<b>Hypophosphatemia</b>	Hypotension Decreased stroke volume	Impaired diaphragm contractility Dyspnoea Respiratory failure	Leukocyte dysfunction Haemolysis Thrombocytopenia	Paraesthesia Weakness Confusion Disorientation Lethargy Paralysis Seizures Coma			Death
<b>Hypokalaemia</b>	Arrhythmias	Failure		Weakness Paralysis	Nausea Vomiting Constipation	Rhabdomyolysis Muscle necrosis	Death
<b>Hypomagnesaemia</b>	Arrhythmias			Weakness Tremor Tetany Seizures Altered mental status Coma	Nausea Vomiting Diarrhoea		Refractory hypokalaemia and hypocalcaemia Death
<b>Vitamin/Thiamine Deficiency</b>			Lactic acidosis	Encephalopathy			Death
<b>Sodium Retention</b>	Fluid overload Pulmonary oedema Cardiac compromise						
<b>Hyperglycaemia</b>	Hypotension	Hypercapnia Failure					Ketoacidosis Coma Dehydration Impaired immune function

(Kraft et al., 2005)

**Hypophosphatemia** Phosphorus is the major intracellular anion in our body, and 85 % of phosphorus in humans is found in bone, and 15 % circulating in soft tissues like blood and extracellular fluid (Skipper, 2012). During starvation the body stores of this electrolyte is decreased. Fat metabolism during starvation does not utilize ATP (Ornstein, Golden, Jacobson, & Shenker, 2003), so once the body shifts to an anabolic state the requirements of phosphorus

increase rapidly, as described in the paragraph above. The resulting low phosphorus levels are mainly a consequence of increased insulin excretion due to elevated glucose content of the food during refeeding (Mehler, Winkelman, Andersen, & Gaudiani, 2010). The electrolyte abnormalities are most often observed during the first five days of refeeding (M. Crook et al., 2001). The clinical signs of hypophosphatemia are listed in table 1.

The normal range of serum phosphate is 0.85-1.4 mmol/L. Hypophosphatemia is normally asymptomatic for levels > 0.64 mmol/L (Elektrolyttveilederen, 2014). Low serum levels of phosphorus are in most of the literature defined as < 0.80 mmol/L, mild hypophosphatemia as 0.50 mmol/L and severe hypophosphatemia as < 0.30 mmol/L (M. A. Crook, 2014), but the cut-offs may vary.

**Table 2** Cut-off values for hypophosphatemia in different sexes and ages

Cut-off values, hypophosphatemia, mmol/L	Women	Men	Adolescents 13-17
	0.89	0.79	0.90

(Elektrolyttveilederen, 2014; Unilabs Laboratoriemedisin, 2016).

**Hypokalaemia** Potassium is the major intracellular cation (98 % of the potassium in our body is in the intracellular space, but there are also some in bones and cartilage) (Kraft et al., 2005). Potassium is essential for maintaining cell membrane action potential. This membrane action potential is disturbed when the body's potassium stores are depleted, which in turn may result in symptoms as presented in table 1. Severe hypokalaemia is defined as serum levels < 3 mmol/L, and at this level, symptoms normally will occur (Elektrolyttveilederen, 2014).

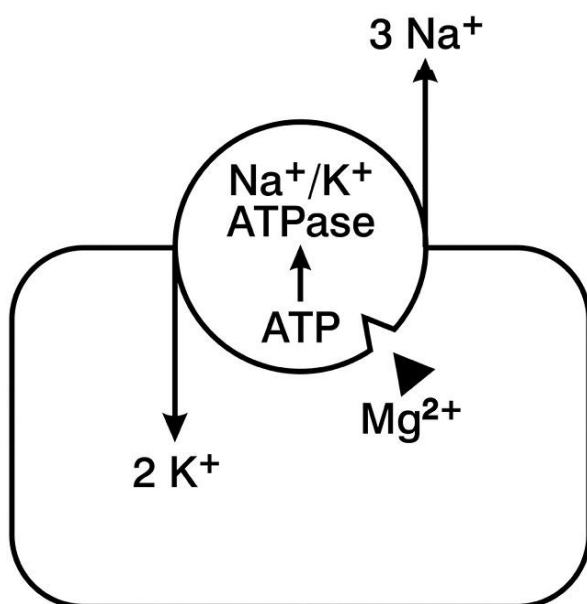
Potassium levels are often decreased in patients with BN and purging type of AN (described further in chapter 3.2), due to vomiting and use of diuretics and laxatives (Mehler & Rylander, 2015). There is an up regulation of the rennin-angiotensin-aldosterone steroid hormone system if laxative abuse or vomiting is present due to dehydration (Mehler & Rylander, 2015). The up regulation will increase renal absorption of sodium, water and bicarbonate, and at the same time increase the excretion of potassium to maintain electrochemical balance (Mehler & Rylander, 2015). A further description of this mechanism will not be given here, but when dealing with this patient group, the severity of the disease and potassium levels should be taken into consideration when evaluating these patients.



**Hypomagnesaemia** Magnesium is mostly found in bone, muscle and soft tissue, and is the second most abundant cation in our body. Only 1 % of the magnesium is stored in the extra cellular fluid (Kraft et al., 2005). Serum levels of  $< 0.5$  mmol is defined as hypophosphatemia (Elektrolyttveilederen, 2014). Magnesium is important for optimal cell function, and is a cofactor in many enzymes. Magnesium is an important structure of DNA, RNA and ribosomes, and the demand for magnesium increases when metabolism increases (Fuentebella & Kerner, 2009). Symptoms of hypomagnesaemia are presented in table 1.

Magnesium and potassium levels are linked, because they in many cases act as antagonists. Hypomagnesaemia could cause hypokalaemia because of this linkage (Kraft et al., 2005; H. Mehanna et al., 2009). Magnesium is also an important component of the  $\text{Na}^+/\text{K}^+$ -pump, as a cofactor of the enzyme ATPase in the cells, and therefore a depletion of magnesium could affect potassium repletion (Fuentebella & Kerner, 2009; Kraft et al., 2005).

**Figure 2** Magnesium's contribution as a co-factor in ATPase



Retrieved from "Cation dyshomeostasis and cardiomyocyte necrosis: the Fleckenstein hypothesis revisited"  
Borkowski, Cheema, Shahbaz, Bhattacharya, & Weber (2011)

Hypomagnesaemia could contribute to hypocalcaemia due to decreased release or activity of parathyroid hormones (Kraft et al., 2005). Adequate magnesium levels are also required for the active form of thiamine, because of magnesium's role as a co-factor in the enzyme transketolase (Fuentebella & Kerner, 2009).

**Thiamine** Vitamin B1 is an important vitamin and coenzyme in carbohydrate metabolism (H. Mehanna et al., 2009), so if refeeding (of carbohydrates) is started too rapid, the enzyme will be depleted and Korsakoff's syndrome and Wernicke's encephalopathy may occur. It is important to remember that water retention during refeeding is not always caused by vitamin B1 deficiency, but could be due to increased insulin secretion and fluctuation of water into the cells. Korsakoff's syndrome is recognised by amnesia and confabulation while Wernicke's encephalopathy is characterized by ataxia, confusion, hypothermia, ocular abnormalities and coma (Fuentebella & Kerner, 2009). Thiamine is rapidly used during glycolysis, and low levels impair glucose metabolism and may lead to lactic acidosis (Fuentebella & Kerner, 2009).

Depletion of thiamine is one of the symptoms of RFS (Gentile et al., 2010), and the body stores could be depleted quickly with malnutrition and underweight. The half-life of thiamine is approximately 9.5 to 18.5 days (McCray, Walker, & Parrish, 2005). Deficiency could occur after less than 28 days of malnutrition (Fuentebella & Kerner, 2009). The requirements of thiamine are related to energy and carbohydrate intake, due to thiamine's role in thiamine pyrophosphate, which is essential in metabolism of glucose (McCray et al., 2005). The table below shows recommended intake for women, men and children.

**Table 3** Recommended intake of thiamine, mg/d

	<b>Women</b>	<b>Men</b>	<b>Children 10-13y girls/boys</b>
<b>Recommended intake, mg/day</b>	1.1	1.4	1.0/1.2
<b>Average requirement, mg/day</b>	0.9	1.2	

(Nordic Nutrition Recommendations, 2012)

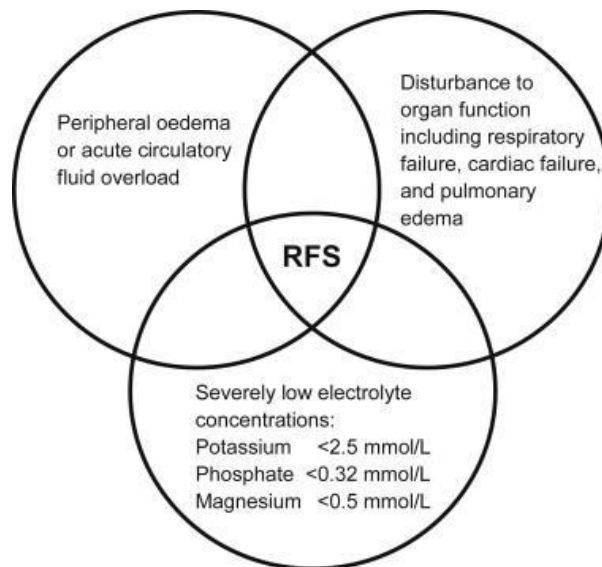
**Salt and water** Rapid carbohydrate refeeding decrease the excretion of sodium and water by the kidneys (H. Mehanna et al., 2009) due to increased insulin excretion. This results in expanded extra cellular fluid and weight gain (due to fluids), and fluid levels should be monitored closely when refeeding malnourished patients. Fluid and sodium overload may be shown as oedemas, congestive cardiac failure and fluid overload (Fuentebella & Kerner, 2009). A low sodium diet is recommended in feeding of patients at risk of RFS (M. A. Crook, 2014).

High protein diets may result in high sodium levels, due to metabolic acidosis, azotaemia or dehydration (M. Crook et al., 2001). Patients at risk of RFS are at risk of renal abnormalities, and should be monitored regarding renal function during refeeding, especially if protein intake is high or the patient struggle to meet the fluid requirements (M. A. Crook, 2014).

### 2.1.3 Diagnostic criteria

Some authors have tried to define the diagnostic criteria for RFS and to explain the syndrome (Solomon & Kirby, 1990). Hofer et.al (2014) have three facets that have to be met to diagnose a patient with RFS (figure 3).

**Figure 3** Diagnostic criteria of RFS



Retrieved from “Safe refeeding management of anorexia nervosa inpatients: an evidence-based protocol” Hofer et al. (2014).

The authors point out that symptoms may be non-specific and difficult to assess, thus making a common definition problematic (M. A. Crook, 2014; Fuentebella & Kerner, 2009; H. Mehanna et al., 2009). Well-nourished patients may also experience a minor fall in electrolytes with refeeding only after a few days of starvation, but not have any clinical symptoms (Stanga et al., 2008). This complicates the diagnosis, and confirms that unusual lab-values itself is not synonymous with RFS (Stanga et al., 2008). The word syndrome implies multiple symptoms and abnormalities, but the term RFS may in the literature be used about single findings like hypophosphatemia

(Skipper, 2012). The duration of the starvation period before RFS may occur is varying, but hypophosphatemia induced symptoms, which is a contributor of RFS, may be developed only after 48 hours of starvation (Marik & Bedigian, 1996).

The ICD-10 diagnosis classification does not have a specific diagnose for RFS (World Health Organization, 1992), making this syndrome both difficult to detect and to research.

The true incidence of RFS is unknown and the studies investigating the incidence have different numbers of cases dependent on wards and diseases (Owers et al., 2015), and due to different diagnostic criteria used. The estimated incidence varies between 0.43 % to 34 % in different hospital populations (M. A. Crook, 2014). Hofer et al. (2014) investigated complications during refeeding in a retrospective observational study of AN patients, and found that 10.5 % developed symptoms like oedemas, organ dysfunction and hypokalaemia, but none of them developed RFS. A similar result was found by Vignaud et al. (2010) were 10 % of AN patients admitted to an intensive care unit developed metabolic, haematological, hepatic, and infectious events, but not RFS.

The incidence of refeeding hypophosphatemia, often used as a surrogate for RFS, in AN patients vary from 0 % to 45 % in different studies (Kameoka et al., 2015).

#### **2.1.4 Patients at risk**

The National Institute for Health and Clinical Excellence (NICE) have developed some criteria to identify patients at risk of RFS (table 4). The NICE-guidelines are only level D recommendations, which means that the recommendations are based on evidence from expert committees, case reports and clinical experience from respected authorities, and are not necessarily rooted in research, but are still the recommendation that is found in most literature (H. M. Mehanna et al., 2008; Shekelle, Woolf, Eccles, & Grimshaw, 1999).

**Table 4** NICE guidelines to identify patients at risk of RFS

<b>The patient has either one or more of the following</b>
<ul style="list-style-type: none"><li>- Body mass index (kg/m<sup>2</sup>) &lt; 16</li><li>- Unintentional weight loss &gt; 15 % in the past three to six months</li><li>- Little or no nutritional intake for &gt; 10 days</li><li>- Low levels of potassium, phosphate, or magnesium before feeding</li></ul>
<b>Or the patient has two or more of the following:</b>
<ul style="list-style-type: none"><li>- Body mass index &lt; 18.5</li><li>- Unintentional weight loss &gt; 10 % in the past three to six months</li><li>- Little or no nutritional intake for &gt; 5 days</li><li>- History of alcohol misuse or drugs, including insulin, chemotherapy, antacids, or diuretics</li></ul>

(National Institute for Health and Clinical Excellence, 2006)

What the guideline define as “little nutritional intake” is not described. In addition to the NICE guidelines, other authors have made guidelines or suggestions to identify patients at risk of RFS (Stanga et al., 2008).

**Table 5** Patients at risk of developing RFS

<b>Low nutrient intake</b>
<ul style="list-style-type: none"><li>- Patients starved for &gt; 7 days</li><li>- Prolonged hypocaloric feeding and fasting</li><li>- Chronic swallowing problems and other neurological disorders</li><li>- Anorexia nervosa</li><li>- Chronic alcoholism</li><li>- Depression in the elderly</li><li>- Patients with cancer</li><li>- Chronic infectious diseases</li><li>- During convalescence from catabolic illness</li><li>- Postoperative patients</li><li>- Diabetic hyperosmolar states</li><li>- Morbid obesity with profound weight loss</li></ul>

- Homelessness, social deprivation
- Idiosyncratic/eccentric diets
- Hunger strikes

**Increased nutrient losses/decreased nutrient absorption**

- Significant vomiting and/or diarrhoea
- Dysfunction or inflammation of the gastrointestinal tract
- Chronic pancreatitis
- Chronic antacid users (these bind minerals)
- Chronic high-dose diuretic diets
- After bariatric surgery

(Stanga et al., 2008)

## 2.2 Anorexia nervosa

AN can be divided into two distinct sub-types; restrictive and binge-purge subtype (Hofer et al., 2014). The restrictive type is characterized by an extreme reduction of food intake, while the binge-purging subtype also includes episodes of bingeing and purging (Meczekalski, Podfigurna-Stopa, & Katulski, 2013), like vomiting, diuretic or laxative abuse (Mehler & Rylander, 2015).

### 2.2.1 Diagnostic criteria

The official diagnostic system in Norway is ICD-10 (ICD-10 diagnostic criteria for AN are presented in table 7, but there are also other diagnostic criteria that are used in the literature (Diagnostic and Statistical Manual of Mental Disorders (DSM) IV and 5 (Zipfel et al., 2015)).

The ICD-10 criteria are currently under revision, and an updated version (ICD-11) is in progress (Zipfel et al., 2015). ICD-10 has both a version used in research and a version used by clinicians, and the one used in research are presented below.

**Table 7** ICD-10 criteria to diagnose patients with AN

A. Weight loss, or in children a lack of weight gain, leading to a body weight of at least 15 % below the normal or expected weight for age and height.
B. The weight loss is self-induced by avoidance of “fattening foods”.
C. A self-perception of being too fat, with an intrusive dread of fatness, which leads to a self-imposed low weight threshold.
D. A widespread endocrine disorder involving the hypothalamic-pituitary-gonadal axis, manifest in the female as amenorrhoea and in the male as a loss of sexual interest and potency (an apparent exception is the persistence of vaginal bleeds in anorexic women who are on replacement hormonal therapy, most commonly taken as a contraceptive pill).
E. Does not meet criteria A and B of bulimia nervosa.

(World Health Organization, 1992)

## 2.2.2 Incidence and prevalence

Hoek (2006) found that incidence rates of AN in different studies varied from 4.2-8.3 per 100 000 person, and that 40 % of all AN cases are in the age group 15-19 years. The incidence rate in this group has also increased in the last decades (Smink et al., 2012), but it is unclear if this is due to earlier detection, earlier onset of the disease, or due to earlier menarche and puberty (Favaro, Caregaro, Tenconi, Bosello, & Santonastaso, 2009).

The lifetime prevalence of AN in females is estimated to be between 0.3-2.2 % (Smink et al., 2012). The lifetime prevalence in men is lower, about 0.24 %, but may be underestimated (Meczekalski et al., 2013). The prevalence of the other EDs is higher than for AN (Hoek, 2006). In Norway, this estimate means that about 50 000 women are affected by an ED, and of these 2700 women have AN, 18 000 women have BN and 28 000 women have BED (Rosenvinge JH, 2002). These numbers are only an estimate based on numbers from other countries.

The average age of onset for AN is 17.4 years in females and 18.1 years in males (Favaro et al., 2009), and few new cases occur after age 25 (Favaro et al., 2009). It is also noteworthy that less than 50 % of those having an ED are identified in primary care (Bjørnelv, 2004), and less than 50 % of AN patients access treatment (Zipfel et al., 2015).

## 2.2.3 Pathogenesis

The pathogenesis of AN is complex and will differ between every patient, but there are certain factors that often are present. AN seems to be more common in some families, which are due to both genetic (28-74 %) and social factors (Zipfel et al., 2015). Developmental and personal factors that may contribute are prematurity, sleeping and feeding difficulties in infancy, depression, perfectionism, emotional liability, autism and anxiety (Zipfel et al. 2015). The onset commonly observed in puberty may be due to hormonal changes and dysregulations that interact with neurotransmitter functioning (Zipfel et al., 2015). Strict dieting and excessive exercise are risk factors for AN. Female gender is by itself a risk factor of developing AN. Sexual or physical abuse are also commonly reported in this patient group (Meczekalski et al., 2013).



It has been investigated whether neurological abnormalities could be a predictor of AN, but most studies have looked at already ill or recovered patients, and these abnormalities could be changes due to malnourishment (Zipfel et al., 2015).

There is also a socio-cultural risk factor for developing EDs. AN is found across different cultures, but studies have found higher prevalence in western cultures (Pilecki, Salapa, & Jozefik, 2016). There is a perceived pressure to be thin and to have a body applicable to the standards set in a western society, which again is a causal risk factor for dieting, body dissatisfaction and fear of weight gain, all factors that can trigger an ED. The drive for thinness is amplified by mass media, which idealizes certain body types and influences the attention to our own body negatively (Pilecki et al., 2016).

#### **2.2.4 Adverse health effects**

A disturbed body image, an intense fear of weight gain and restricted food intake are all symptoms that are present in a patient with AN, as well as extreme underweight (< 85 % of IBW). Excessive physical activity and purging are also common (Zipfel et al., 2015). Very often, these patients have medical and psychiatric comorbidities (Meczekalski et al., 2013), and emotional and cognitive functioning is disturbed. Depression is the most common psychiatric comorbidity, with a rate of 40-45 % (Meczekalski et al., 2013); highest among adults and higher among the binge-purging type of AN than the restricted type (Halmi, 2003). Other common comorbidities are anxiety disorders, substance use, social phobia and post-traumatic stress disorder (Meczekalski et al., 2013).

Somatic complications are common, and all organ systems may be affected. Cardiac problems may occur because of the structural, functional and electrocardiological changes, and the incidence may be as high as 87 % in the most severe cases (BMI < 15) of AN patients (Meczekalski et al., 2013; Norrington, Stanley, Tremlett, & Birrell, 2012). The gastric wall circulation is disturbed, and necrosis may occur (Meczekalski et al., 2013). Gastric emptying is significantly delayed in patients with AN (Norris et al., 2015), and many patients complain about feeling of fullness after ingested meals. The situation is worsened with longer time span of the disorder and severity of malnutrition. Haematological changes could be changes in red blood

cells, white blood cells and platelets (Mehler & Brown, 2015). Reductions in grey and white matter have been observed in underweight AN patients, but these changes will probably recover with weight gain (Boateng et al., 2010; Zipfel et al., 2015). A summary of signs and symptoms are presented in table 6.

**Table 6** Signs and symptoms that may occur in patients with AN

<b>Cardiac</b>	<b>Endocrine</b>	<b>Fluid and electrolytes</b>
<ul style="list-style-type: none"> <li>- Bradycardia</li> <li>- Hypotension</li> <li>- Tachycardia</li> <li>- Prolonged Qt-interval</li> <li>- Arrhythmias</li> </ul>	<ul style="list-style-type: none"> <li>- Hypoglycaemia</li> <li>- Poor metabolic control in co-existent type 1 diabetes</li> <li>- Amenorrhea</li> <li>- Secondary hyperaldosteronism</li> </ul>	<ul style="list-style-type: none"> <li>- Hypokalaemia, hypochloremia, metabolic alkalosis</li> <li>- Hypophosphatemia (during refeeding)</li> <li>- Hypomagnesaemia</li> <li>- Hyponatremia</li> </ul>
<b>Gastrointestinal</b>	<b>Skin/bone</b>	<b>Others</b>
<ul style="list-style-type: none"> <li>- Severe acute pancreatitis</li> <li>- Parotid and salivary gland hypertrophy</li> <li>- Reduced gastric motility and early satiety</li> <li>- Mallory-weiss tears, ruptures</li> <li>- Esophagitis</li> <li>- Raised liver enzymes and low albumin</li> </ul>	<ul style="list-style-type: none"> <li>- Osteopenia/osteoporosis, stress fractures</li> <li>- Reduced height growth</li> <li>- Brittle hair, hair loss, lanugo hair</li> <li>- Dorsal hand abrasions, facial purpura, conjunctival haemorrhage</li> </ul>	<ul style="list-style-type: none"> <li>- Hypothermia</li> <li>- Anaemia</li> <li>- Neutropenia</li> <li>- Erosions and perimyolysis (if vomiting)</li> </ul>

(Meczekalski et al., 2013; Mehler & Brown, 2015)

The basal metabolic rate (BMR) may be reduced with as much as 20-25 % (H. Mehanna et al., 2009; H. M. Mehanna et al., 2008). Most studies find that this is due to both the lower fat mass and fat free mass in AN patients than controls, while a few studies also find that the decrease in BMR is even lower than expected when looking at body mass in AN patients (de Zwaan, Aslam, & Mitchell, 2002).

Patients in this group have an increased mortality rate (six times higher) compared to a healthy population (Meczekalski et al., 2013) and have the highest mortality rate compared to other psychiatric disorders (Davenport, Rushford, Soon, & McDermott, 2015; Meczekalski et al., 2013). The mortality rate is higher in older patients, which could be explained by that older patients have a longer duration of illness, and hence an advanced stage of comorbidities and somatic complications (Ackard, Richter, Egan, & Cronemeyer, 2014). The longer patients have had AN, the less effective the treatment will be due to the chronicity of the disease (Davenport et al., 2015).

One in 5 deaths, or 20 %, is due to suicide in this patient group, independent of age (Meczekalski et al., 2013). Most of deaths are caused by medical complications due to starvation and malnutrition (Zipfel et al., 2015). Due to these complications mentioned, patients with a weight less than 30 % of ideal body weight (IBW) are normally encouraged to be treated in a hospital (Mehler et al., 2010).

## **2.2.5 Treatment**

Weight gain is crucial in the treatment of patients with AN. Weight gain through regular meals sufficient in energy cause positive changes to the brain and hormonal system that make the patient receptive to other treatments (Mehler et al., 2010; Ornstein et al., 2003). Most of the medical complications will also be reversed when weight are recovered (Ornstein et al., 2003). However, osteoporosis may be persistent after recovery and reduced height growth (due to AN in adolescents) may not be fully caught-up. On the other hand, weight restoration and food intake is challenging in the recovery phase in patients with AN (Mehler et al., 2010).

A relapsing or protracted course of the disease are common in adults and older adolescents (Zipfel et al., 2015), and the fully recovery rate of AN is as low as 33 %, but higher in adolescents than adults (Meczekalski et al., 2013). In adult patients, the average course of treatment before remission of the disease is 5 to 6 years (Zipfel et al., 2015). The definitions for complete recovery from this disease vary (in the literature), and a healthy weight within the normal ranges does not necessarily correspond to healthy attitudes concerning food, body, exercise and meals. The best definition evaluating recovery from EDs may be that the weight is

within normal limits and the concern for food, appearance and meals do not affect the social functioning, work or family life (Skårderud, 2000).

Several psychological and pharmacological treatments are used in AN patients (family based treatment, cognitive behaviour therapy and others (Zipfel et al., 2015)), but will not be described further in this thesis. The physiological treatment with refeeding of these patients is described below.

## 2.2.6 Refeeding of AN patients – guidelines and recommendations

The guidelines in how to identify AN patients are presented in chapter 2.1.5. The following chapter will look at the different recommendations for how to refeed AN patients in an inpatient setting. In the guidelines presented in table 8 and 9, the refeeding range vary between 5-40 kcal/kg/day, which means that an initial feeding range of a 30 kg patient diagnosed with AN, vary between 150-1200 kcal/day. The European and Australian guidelines are more restrictive and conservative than the American guidelines, but all guidelines are based on clinical practice, and not scientific evidence (O'Connor & Nicholls, 2013). The guidelines may differ somehow regarding if the guideline are made for all patient at risk of RFS (table 8), or is a guideline in how to refeed AN patients (table 9).

**Table 8** Recommended refeeding guidelines for malnourished patients at risk of RFS

<b>Guideline/ recommendation</b>	<b>Age</b>	<b>Kcal/kg</b>	<b>Kcal/day</b>	<b>Energy increase</b>	<b>Supplementation</b>
<b>NICE</b> <sup>1</sup>	Adult	5-20	*	Slowly increase over 4-7 days.	See table 10
<b>Europe (Stanga et al., 2008)</b>	Adult	10-15	*	Up to 30 kcal/kg by day 10	See table 10
<b>IrSPEN</b> <sup>2</sup>	Adult	5-10	*	*	50 mmol phosphate in a 500 ml solution

\*not specified

(National Institute for Health and Clinical Excellence, 2006; IrSPEN, 2015; O'Connor & Nicholls, 2013; Stanga et al., 2008)

<sup>1</sup> National Institute for Health and Care Excellence

**Table 9** Recommended refeeding guidelines for malnourished patients with AN

<b>Guideline/ recommendation</b>	<b>Age</b>	<b>Kcal/kg</b>	<b>Kcal/day</b>	<b>Energy increase</b>	<b>Supplementation</b>
<b>NICE</b>	*	*	*	3500-7000 kcal extra/week	Multivitamin/mineral
<b>RANZCP<sup>3</sup></b>	Adult	15-20	600-800	Increase with 300kcal every 3.day	Phosphate 500 mg twice daily and thiamine 100 mg daily first week
<b>Academy of Nutrition and Dietetics/APA<sup>4</sup></b>	Adult	30-40	1000-1600 (1200)	Increase with 100-200 kcal/day. Up to 70-100 kcal/kg	*
<b>MARSIPAN<sup>5</sup></b>	Adult	5-20	*	Increase to 15-20 kcal/kg within 48hours	Reduced carbohydrates and phosphorus rich foods
<b>JuniorMARSIPAN<sup>6</sup></b>	< 18	5-20	1000	Increase with 200 kcal/day	Reduced carbohydrates and phosphorus rich foods
<b>America (Sylvester &amp; Forman, 2008)</b>	< 18	*	1250–1750	Increase with 250 kcal/day	*

\*not specified

(Beumont et al., 2004; National Institute for Health and Care Excellence, 2004; O'Connor & Nicholls, 2013; Royal College of Psychiatrists, 2012, 2014; Sylvester & Forman, 2008)

The American guidelines point out that some patients should start feeding at lower levels than 30-40 kcal/kg because of the risk of RFS, but do not specify what that amount should be (Ozier & Henry, 2011). A variety of recommendations in the literature made to reduce the risk of RFS during refeeding ranges between 25-75 % of estimated energy needs (Fuentebella & Kerner, 2009).

“Kosthåndboken” (Helsedirektoratet, 2015), recommend starting refeeding of patients at risk of RFS (not exclusively AN patients) at 15 kcal/kg/day and closely monitor electrolytes like potassium, magnesium and phosphate. They recommend thiamine supplementation

<sup>2</sup> Irish Society for Clinical Nutrition and Metabolism

<sup>3</sup> The Royal Australian and New Zealand College of Psychiatrists

<sup>4</sup> American Psychiatric Association

<sup>5</sup> Management of Really Sick Patients with Anorexia Nervosa, working group from the Royal Colleges of Psychiatrists, Physicians and Pathologists

<sup>6</sup> Management of Really Sick Patients under 18 with Anorexia Nervosa

prophylactically before intravenous treatment with glucose starts. NICE-guidelines recommend correcting all electrolyte deficiencies before refeeding starts (Fuentebella & Kerner, 2009).

Only two guidelines found are made specifically for adolescents, but these guidelines do not differ noteworthy from the others, except from a bit higher recommendation in the upper range of refeeding by Sylvester and Forman (2008) compared to the other guidelines.

The table 10 below is taken from Stanga Z (2011), and is a summary of the guidelines from ESPEN<sup>7</sup>, which also cover the guidelines from NICE. These guidelines are made regarding all patients at risk of RFS, and not AN patients only.

**Table 10** Recommendations of refeeding, supplementing and monitoring patients at risk of RFS

<i>General recommendations</i>
Raise awareness within all health care personnel
● Be aware of patients at risk
● Provide adequate assessment, interdisciplinary care plans, and follow up
● Appreciate that risks apply whether patients are fed by the oral, enteral or parenteral route
● Carefully restore circulatory volume: monitor pulse rate and fluid balance
● Energy intake should be instituted carefully and gradually increased over 4–10 days
● Empirical supplementation of the electrolytes and vitamins can be started before feeding is initiated
<i>Days 1–3</i>
1. Energy (by all routes): start at 42 kJ/kg/day (10 kcal/kg/day) and slow increase to 63 kJ/kg/day (15 kcal/kg/day); 50–60% carbohydrates, 30–40% fat, and 15–20% protein.
2. Electrolytes: measure serum concentrations basally, 4–6 h later, and daily during feeding (see below). Supplement prophylactically (unless pre-feeding plasma levels are high), in most cases by the intravenous route initially. Amounts depend on patient size and plasma concentrations, but usual daily requirements are:
● Phosphate 0.5–0.8 mmol/kg/day
● Potassium 1–3 mmol/kg/day
● Magnesium 0.3–0.4 mmol/kg/day. Levels should be monitored frequently and supplements increased if necessary.
3. Fluid: restrict to sufficient to maintain renal function, to replace deficits or losses, and avoid weight gain, that is achieve zero balance. Patients usually need 20–30 ml/kg/day.
4. Salt: restrict sodium to <1 mmol/kg/day. If oedema develops, restrict further.
5. Minerals and trace elements: 100% DRI. Iron should not be supplemented in the first week.
6. Vitamins 200% DRI. Give 200–300 mg thiamine i.v. at least 30 min before feeding, and 200–

<sup>7</sup> European Society for Clinical Nutrition and Metabolism

300 mg daily i.v. or orally till day 3.

#### 7. Monitor daily

- Body weight (fluid balance).
- Clinical examination: oedema, blood pressure, pulse rate, cardiovascular and respiratory systems.
- Biochemistry: phosphate, magnesium, potassium, sodium, calcium, glucose, urea, creatinine, (thiamine).
- Preferably ECG-monitoring in severe cases.

#### *Days 4–6*

1. Energy (by all routes): 63–84 kJ/kg/day (15–20 kcal/kg/day); 50–60% carbohydrates, 30–40% fat, and 15–20% protein.

2. Electrolytes: continue supplementation as above, giving more or less according to plasma concentrations. If the refeeding syndrome is already established, aim to restore normal levels. If

●  $\text{PO}_4^{2-}$  <0.6 mmol/l—give 30–50 mmol phosphate (eg. Phosphates Polyfusor) i.v. over 12 h.

●  $\text{Mg}^{2+}$  <0.5 mmol/l—give 24 mmol  $\text{MgSO}_4$  i.v. over 12 h.

●  $\text{K}^+$  <3.5 mmol/l—give >20–40 mmol KCl i.v. over 4 h. Remeasure and repeat if necessary.

3. Minerals and vitamins: as for days 1–3.

4. Fluid: depending on hydration, weight change and losses. Patients usually need 25–30 ml/kg/day.

5. Monitor daily: as for days 1–3.

#### *Days 7–10*

1. Energy (by all routes): 84–132 kJ/kg/day (20–30 kcal/kg/day); 50–60% carbohydrates, 30–40% fat, and 15–20% protein.

2. Electrolytes, minerals and vitamins: as above. Iron should be supplemented from day 7 onwards

3. Fluid: to maintain zero balance. Approximately 30 ml/kg/day

4. Monitor

● Body weight and biochemistry: twice weekly

● Clinical examination: daily

(Stanga et al., 2008; Stanga Z, 2011)

## 3 Methods

To answer the three research questions, three different data collections have been required.

### 3.1 Procedure collection

The regional departments with hospitalized patients with EDs in Norway are located in Oslo, Bergen, Stjørdal, Levanger, Bodø and Tromsø. The names of the departments (in Norwegian) are listed below:

- Oslo: “Regional seksjon spiseforstyrrelser” (RASP)
- Bergen: “Seksjon for spiseforstyrrelser”
- Levanger/Stjørdal: “Regionalt kompetansesenter for spiseforstyrrelser” (RKSF)
- Bodø: “Regionalt senter for spiseforstyrrelser” (RESSP)
- Tromsø: “Regionalt senter for spiseforstyrrelser” (RSS)

The procedures in the six regional departments of EDs in Norway were collected by contacting the head physicians in each regional department by e-mail, and the procedures were sent back by mail to the master student. If lack of information of their procedures was given, up to four reminder e-mails were sent. The procedures were collected between September 2015 and April 2016.



**Table 11** The regional departments of EDs in Norway and two additional units. Number physicians and RDs working there and number of available beds for inpatient treatment per 01.01.16.

Regional department/ ED unit	Age group	Number of beds	Number of physicians/ number of RDs	Other information
RASP (Oslo)	Intensive, all age groups	8	11/3	Some rooms also available for families No acute admissions, only planned
	Adults	12		
	< 21	4-5		
“Seksjon for spiseforstyringer” (Bergen)	> 16	5	1/0	Planning 3 new beds next winter (2017) (total of 8 beds)
RKSF (Stjørdal)	> 25	8	1/0	Patients with > 10y history of ED prioritized
RKSF (Levanger)	> 16	10	2/0	
RESSP (Bodø)	> 18	12	2/1	4 beds reserved acute patients
RSS (Tromsø)	< 18	5	1/0	5 from 01.01.16, previously 4
<b>Total regional departments</b>		55-56	17/4	
Modum bad (Modum)	> 18	20	2/1	
Capio (Fredrikstad)	13-18	13	1/0	12 beds reserved adolescent belonging to “South-Eastern Norway Regional Health Authority”
<b>Total all</b>		88-89	20/5	

In these divisions, the number of physicians varied between 1-11 and number of RDs varied from 0-3. Some of the units mentioned in table 11 use RDs from the local hospital in special cases when needed, but only 3 out of 8 units investigated have a RD. Numbers of other health personnel was not counted. The number of physicians, RDs and available beds are collected by asking the head physicians in each department.

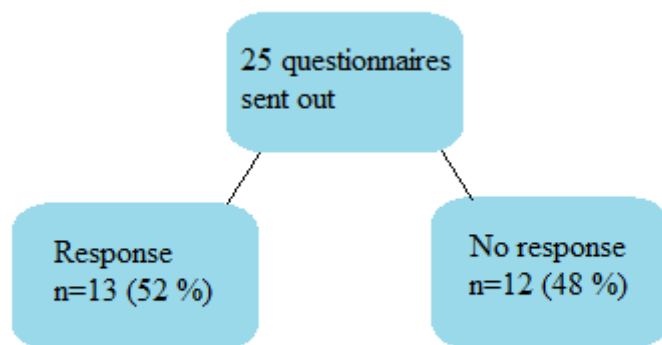
## 3.2 Questionnaire

A questionnaire was developed and sent to physicians and RDs at the different ED units in Norway. Unlike the procedure collection, the questionnaire was also sent out to two other divisions that have inpatient treatment of EDs; Modum Bad (Modum) and Capiro (Fredrikstad). This was to get a higher number of informants and to increase the strength of the survey.

The master student made the questionnaire, with support from the supervisor and RDs at RASP. The questionnaire was made during the autumn, and during the process, the RDs and supervisor at RASP filled out the questionnaire as a pilot study. The questionnaire is located in Appendix 1.

To identify all physicians and RDs working at the ED units, the student collected e-mail addresses to the leaders of each unit by calling them or contacting the supervisor at RASP that could assist with some of the addresses. In the mail sent to the leaders of each unit, the purpose of the questionnaire was described, and the e-mail addresses for all physicians and RDs working at their unit were requested. The e-mail addresses were sent back to the student by the leaders of each unit, or by the physicians or RDs working there themselves. As soon as the e-mail addresses were received, the questionnaire was sent back to the participants. This envoy starting at 16<sup>th</sup> of December until 18<sup>th</sup> of January. A reminder e-mail was sent up to four times if the participants of the survey did not answer. No questionnaires were received after first of March.

**Figure 4** Responders and no responders to the questionnaire



A total of 25 physicians and RDs received the questionnaire; of which 20 physicians and 5 RDs. Of those receiving the questionnaire, 22 were women, only 3 men.

The student plotted in the variable sets and data sets from the questionnaires and did a descriptive analyse of the results using Statistical package for the social sciences (SPSS) analysis program (*IBM SPSS Statistics Version 21, Release 21.0.0.2, 32-bit edition*). Microsoft Excel 2010 was used to make the graphs and figures in this thesis.

### **3.3 The basic reference menu**

The basic reference menu (“Grunnmeny”) at RASP is made in order to meet energy needs to maintain a stable weight when the weight have normalized in AN patients. The calculated energy content in “Grunnmeny” is 2650 kcal, which is higher than the recommendations from “The Norwegian Directorate of Health” (Helsedirektoratet, 2015) of 2300 kcal for women aged 18-30 with moderate activity levels. Some patients maintain weight with lower energy intake. The basic menu for boys and men have a higher energy content.

At RASP, most patients follow “Grunnmeny” or “Halv grunnmeny”, often after an escalation period over a few days/weeks. However, all patients get individual food lists, and the amount of energy they are prescribed, depends upon the patients’ energy intake at admission. Most patients also need a higher energy intake during the weight restoration period, but those menus are individual and are not analysed here. It is worth noticing that “Halv grunnmeny” is not the true half of the “Grunnmeny” meal content, but it reflects almost the true half energy content (about 1400 kcal) and is set up to specifically cover the recommendations of micronutrients (first and foremost phosphorus) and protein. Individual customization is made by RDs in individual food lists based upon the food choices or possibilities given in “Grunnmeny”. The meals are normally served to the patients the first two weeks by “milieu therapists” or parents. The patients have to serve themselves to each meal later on during the treatment period. For breakfast (cereals and porridge) and dinner, a demo plate is placed next to the dinner table so they know how much to serve themselves with.

RASP has a four week rollover dinner menu made and calculated by the RDs at RASP. The dinner is the same for all patients in the weekdays and Sundays, but on Saturdays, the patients can choose between rice pudding and beta soup. The dinner menu has been set up to provide different challenges for the patients in order to make the patients more used to normal dinners

and food choices before discharge. The RDs have the responsibility of making the recipes and portion indications to all dinners, as well as all other meals (breakfast, lunch, evening meals and snack meals) during the day, to secure adequate energy and nutrients for the patients to reduce their underweight.

To get an accurate estimate of the content of the dinner portions, portion sizes from the demonstration plates that were used in the meal session for the patients through four weeks were collected, weighted and photographed by the master student. The aim was to check if the recommended content of the dinner portions by the RDs matched the actual portion sizes served, or if there were major deviations in nutrient content. Other meals (breakfast, lunch, evening meal and snacks) were not weighed. In total, 25 dinner portions were weighed and photographed, of them seven at the master student's home. On Saturdays, the patients can choose between two options, and these options are the same every week, and were therefore only weighed once.

Ordinary kitchen scales located at the kitchen at RASP was used to weigh the dinner portions (OBH Nordic, "Balance", maximum capacity 5 kg, accuracy 1 gram). Most of the weighing was done at RASP the same day, or the day after the dinner was served. If the weighing was done the day after, the dinner plate was stored in the fridge, covered by cling film. If the demonstration plate was thrown away before the student had measured the weight, the student made the dinner at home by following the recipes and measures used at RASP, and followed the same procedure of taking picture of and weighing the food. A different scale was used at home (ELDOM, maximum capacity 5000 g, accuracy 1 gram).

In addition to the weighing of the dinner plates, a variety of meal options from the "Grunnmeny" (Appendix 4) and "Halv grunnmeny" (Appendix 5) was plotted into "Kostholdsplanleggeren". The contents of these lists was analysed with the intention of comparing them with the recommended energy and nutrient prescription for patients at risk of RFS. The most probable eaten food and drinks, in addition to the dinner portions, in order to quantify average micronutrients and energy during a 7-day period were analysed. Different possible weekly food lists were analysed, 4 based on "Grunnmeny" and 4 based on "Halv grunnmeny". The software system "Kostholdsplanleggeren" (Version KP-2014) was used to analyse the nutrient contents of the food. "Kostholdsplanleggeren" is a diet tool from the Norwegian

Directorate of Health and the Norwegian Food Safety Authority (Matportalen, 2016), that is available for free online.

## 4 Results

The results are presented in three different chapters. These are divided into the results from the procedure collection, the results from the questionnaire and the results from the review of the basic reference menu (“Grunnmeny” and “Halv grunnmeny”) at RASP. An overview of the regional departments and the two other ED units included in the results are presented in table 11.

### 4.1 Procedure collection

From the six regional departments of EDs investigated, three of them (50 %) had developed their own procedures regarding RFS. RESSP (Bodø) and RKSF (Levanger) had a procedure that includes both how to identify patients at risk, and a procedure in how to treat and monitor these patients. RASP had a procedure, but only for which blood tests and medical examination that these patients should have, not a procedure in how to identify or refeed these patients.

To identify patients at risk of RFS, there were some differences between RESSP and RKSF. RESSP follow the NICE-guidelines in how to identify patients at risk (table 3). RKSF had made their own procedure, and defined patients at risk as:

- Patients with BMI < 11
- Patients with a BMI 9.5-11 and a nutritional intake of 10-15 kcal/kg the last 10 days are characterized as in high risk
- Patients with a BMI from 7.0-9.5 and nutritional intake of < 10 kcal/kg the last 10 days are characterized as in extremely high risk.

Blood test and supplements that all hospitalized patients at a regional department of EDs receive are located in Appendix 2. The following tables describe additional supplementations, medical examinations and nutritional recommendations of patients at risk of RFS and procedures to treat

and monitor these patients. Only the Norwegian departments that have such procedures are included in the tables. The routines at the other departments that do not have specific procedures regarding RFS are described afterwards.

**Table 12** Procedures for medical and biochemical evaluation, nutritional- and fluid recommendations for patients at risk of RFS

	<b>RASP (Oslo)</b>	<b>RKSF (Levanger)</b>	<b>RESSP (Bodø)</b>
<b>Daily medical examination</b>	Pulse, blood pressure, temperature. Body weight 1-2 times a week.	*	ECG <sup>8</sup> , pulse, blood pressure, dyspnoea, oedema, relative tachycardia Body weight daily in severe cases
<b>Daily blood tests</b>	Na <sup>+9</sup> , K <sup>+10</sup> , Cl <sup>-11</sup> , phosphate, calcium total, calcium ionized, Mg <sup>2+12</sup> for 7-10 days (2x/week moderate risk)	Continuous evaluation, electrolytes daily the first week, weekly when stable	Na <sup>+</sup> , K <sup>+</sup> , Mg <sup>2+</sup> , phosphate until the patient is following A-menu <sup>13</sup> . Later 3x/week for 21 days or when the patient have stable body weight
<b>Nutrition</b>	”Halv grunnmeny” (about 1350/1400 kcal), or less than ”Halv grunnmeny”	<u>High risk</u> : Half or less than half of dietary lists  <u>Extremely high risk</u> : ND <sup>14</sup> or EN <sup>15</sup> 10-20 kcal/kg.  <u>If electrolyte disturbances</u> : 10 kcal/kg/day, 8-12 meals/day (including one at 2am)	20-30 kcal/kg/day Gradually increase for 4-7 (10) days. <u>Extremely high risk</u> : Even lower energy is recommended  No use of brown goat cheese, jam or dessert before the patient is stable and following A-menu.

<sup>8</sup> Electrocardiogram

<sup>8</sup> Sodium

<sup>9</sup> Potassium

<sup>10</sup> Chloride

<sup>11</sup> Magnesium

<sup>12</sup> Dietary list at RESSP (approximately 2200kcal)

<sup>14</sup> Nutritional drinks

<sup>15</sup> Enteral nutrition

<b>Fluid</b>	*	20-30 ml/day, 25-30 ml/day by day 4.  “Farris” until salt requirements are clarified. Continuous evaluation.	1-1.5 liters/day.  No sugar containing drinks (juice, soda, and sugar/honey in tea/coffee) before the patient is stable and following A-menu. Biola and milk are ok.
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\* not specified in procedures

The procedures at RASP do not specify the fluid recommendations of a patient at risk of RFS, but the RDs use fluid restrictions and assess fluid intake depending on what the patients are able to drink and due to probable risk of RFS but also risk of oedema formation especially at the first 1-2 weeks of refeeding. Normally, the patients are given 1000-1400 ml in the refeeding phase, and in “Grunnmeny”, they recommend 1900-2100 ml. If patients at RASP (Oslo), RKSF (Levanger) and RESSP (Bodø) are identified by the procedures as at risk of developing RFS, they are given supplements prophylactically (table 13) before, refeeding is started to reduce the risk of developing deficiencies and complications during the initial refeeding.

**Table 13** Prophylactically supplementation of patients at risk of RFS

	<b>Oslo</b>	<b>Levanger</b>	<b>Bodø</b>
<b>Thiamine</b>	50 mg x 1 for 5 days (IM <sup>16</sup> )	Individual evaluation	100 mg x 1 for 3 days or 50 mg x 1 for 5 days (IM). Always first injection before refeeding
<b>Phosphate</b>	<u>Preventive:</u> Monokaliumphosphate 15mmol x 2 or phosphate-Sandoz 500 mg x 2 <u>If identified hypophosphatemia:</u> As preventive x 3	Individual evaluation	Individual evaluation
<b>Calcium</b>	500 mg with vitamin D*	Individual evaluation	Individual evaluation
<b>Potassium</b>	**	Individual evaluation	Individual evaluation
<b>Magnesium</b>	**	Individual evaluation	**

\*all patients, not exclusively for at risk patients

\*\*no supplementation according to procedure

<sup>16</sup> intramuscular

The procedures collected are located in Appendix 3 (chapter 7.3.1-7.3.3).

All six head physicians that were contacted regarding the procedures pointed out that they always do a detailed medical and biochemical examination of each patient. This included tests like electrocardiography (ECG), blood pressure, weight and height, pulse, respiration, coordination, skin (dryness/lanugo hair), urine etcetera. However, the impression during the procedure collection was also that RFS is something the head physicians are aware of, but a condition they rarely or never experience.

Those departments that did not have a procedure in how to refeed and monitor patients at risk of RFS still had procedures or routines in how to refeed AN patients in general, and during the procedure collection some comments were provided as to how these departments deal with AN patients at risk of RFS.

**“Seksjon for spiseforstyringer (Bergen)** give at risk patients half „Basiskost“ which have about 1000 kcal (“Basiskost” have approximately 2000 kcal). At risk patients are all that have eating little or nothing the last two weeks. If a patient is identified as at high risk of developing RFS, they give nutritional drinks in several small meals during the day. They start with 15-30 kcal/kg/day, and increase up to 30 kcal/kg/day. If the patients tolerate this increase of energy, additional 200 kcal (in terms of food or nutritional drinks) are added to the energy requirements every other day, until an increase in body weight of 1-1.5 kg/week are reached.

They give supplements of multivitamin, omega 3 and calcium 500 mg/day. Electrolytes are monitored, and if s-phosphate drops below 0.85 mmol/L, the nutritional support is decreased or stopped until s-phosphate are stable. If phosphate levels are > 0.7 mmol/L it is sufficient to give the patients food choices high in phosphorus or phosphate mixture. If phosphate levels drop to < 0.5 mmol/L, the patient should be transferred to the medical department to get phosphate intravenously.

**RKSF (Stjørdal)** have dietary lists for all patients, which consist of about 2000 kcal. At risk patients could start with half or reduced dietary list, and gradually increase up to full dietary list. They further increase or decrease the amount of food on the lists after results of a weighing of the



patient done twice a week. If the patient has a BMI < 14, nutritional drinks are recommended as a supplementation to the dietary list.

**RSS (Tromsø)** monitor phosphate and hydration in at risk patients. What is defined as at risk patients are not mentioned. If a patient is designated as at risk of developing RFS, refeeding is started at 1500 kcal, and increased with 250-300 kcal every third day up to a dietary list at 2400 kcal (or even more energy in terms of food or nutritional drinks if necessary). If patients are designated as in high risk, an additional dietary lists starting at 1200 kcal may be used. They report that only one patient have received phosphate supplements during the last six years.

## 4.2 Questionnaire

Answers were received from physicians and RDs that worked at four out of eight of the ED units from which the questionnaire were sent out to. In total 13 responded, of which five RDs (100 %) and eight physicians (40 %) responded. There was a wide range (0.5 to 34 years) between the responders who had worked with this patient group for a long time and those who had just started. The mean working years were 7.8 years and the median was 2.5 years. The mean working years for RDs was 4.6 years and physicians 9.8 years.

The answers do not concern any specific patients, but are opinions and perceptions given from the physicians and RDs working with this patient group (AN). Their subjective opinion and experiences are collected and analysed to give an overview of the knowledge, opinions and awareness of RFS considering AN patients hospitalized at an ED unit with inpatient treatment. This section do not only concern with physicians and RDs at the regional departments of EDs, but physicians and RDs at two additional units.

The questionnaire is located in Appendix 1.

## 4.2.1 Procedures to prevent refeeding syndrome

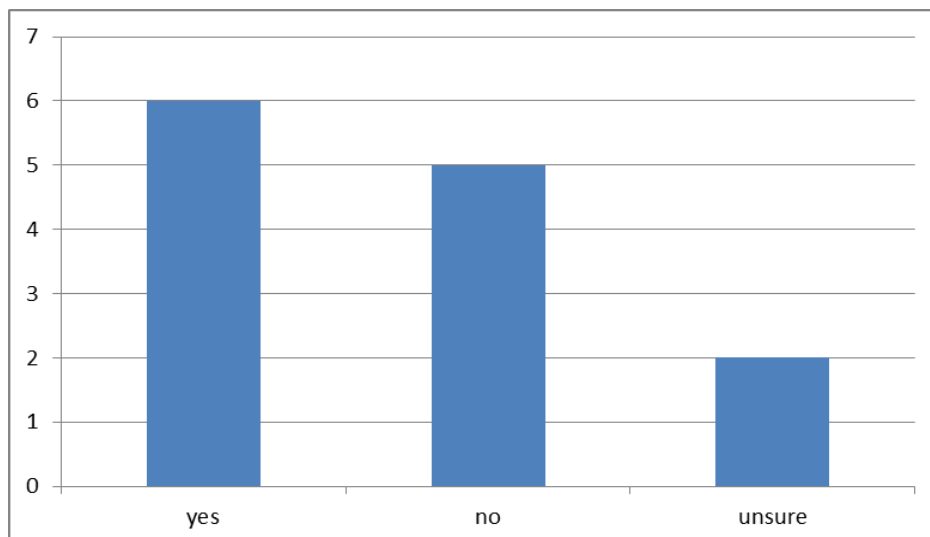
Ten responders (77 %) answered that their department had specific procedures made by the unit to detect and treat patients at risk of RFS. Eleven (85 %) answered that their ED unit on the other hand had a procedure that would detect patients at risk of RFS anyway, even if the procedures were not made exclusively for AN patients at risk of RFS.

## 4.2.2 Knowledge about refeeding syndrome

Four out of thirteen (31 %) of the physicians and RDs thought they had satisfying knowledge about the RFS, and that they were able to start treatment without obtaining more knowledge. Out of these four, one was RD and three were physicians. However, the rest of the responders felt that they knew enough about RFS, but they that would confer with other health personnel before they would start treatment to ensure that the treatment and monitoring was proceeding right.

Regarding education about RFS, all RDs answered that they had learned about the RFS during their education. The physicians had variable answers, with only one reporting to have learned about RFS during education. The physician who reported to have learned about the RFS during education was the youngest of the physicians.

**Figure 5** Number of responders who have learned about the RFS during their education



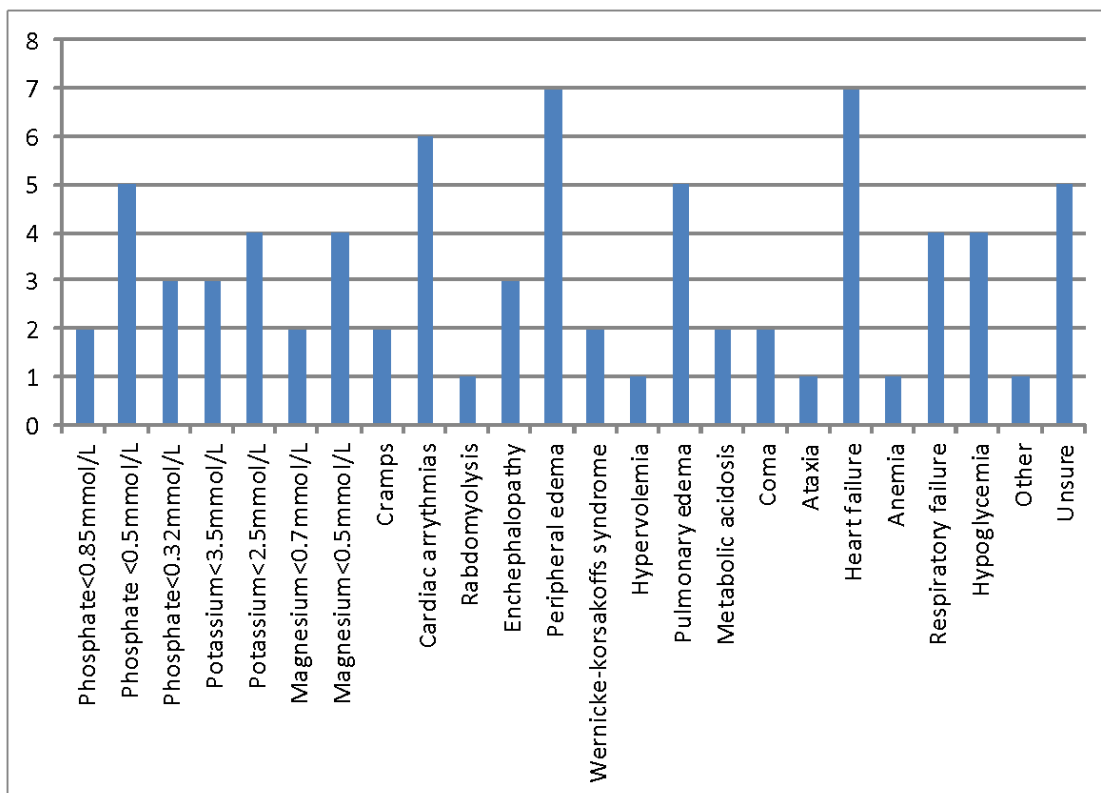
### 4.2.3 Definition of refeeding syndrome

Five responders (38 %) reported that they were unsure of the diagnostic criteria of RFS, but still listed what they thought should be present to diagnose a patient with RFS. Some of the signs and symptoms were reported as should be present more than others, but all the alternatives used in the questionnaire were marked. There was no clear differences between the answers from physicians and RDs. Overall, the answers received were divided, indicating uncertainty or disagreements.

The five most common factors reported that should be present to diagnose a patient with RFS were:

- Phosphate < 0.5 mmol/L
- Cardiac arrhythmias
- Peripheral oedemas
- Pulmonary oedemas
- Heart failure

**Figure 6** Number of responders reporting which signs and symptoms should be present with a full blown RFS



To this question, the responders could also comment their answers. Corrections of declines in hypophosphatemia, hypokalaemia, hypomagnesaemia and hyperglycaemia were pointed out as important. One reported that Ca levels < 1.9 mmol/L is a sign of RFS or beginning RFS. Tachycardia, circulatory failure and cerebral symptoms were also listed as symptom of RFS. Some of the responders pointed out that even if they listed some signs and symptoms that should be present to define something as a full-blown RFS, they were not sure if these symptoms themselves were enough to diagnose a patient. These symptoms could be observed, but the patients may still not have RFS.

#### **4.2.4 Patients at risk of refeeding syndrome**

Of the responders, 12 (92 %) answered that they have been in contact with patients at risk of developing RFS. Only one responder (8 %) answered no to this question.

#### **4.2.5 Patients with abnormal values or symptoms**

Nine responders (69 %) had seen patients with declines in electrolytes or symptoms indicating that the patients were developing RFS. The number of patients observed with such abnormalities during the last year varied between 0 to 10, with a median of three patients.

The electrolytes observed were (number of responders answered in parenthesis):

- hypophosphatemia (6)
- hypokalaemia (5)
- hyponatremia (3)
- hypocalcaemia (2)

or signs;

- oedemas (3)
- hypoglycaemia (2)
- muscle weakness (1)
- dyspnoea (1)
- liver failure (1)

All patients reported by the responders were refed with food only, or in combination of EN or nutritional drinks. No patients experienced these abnormalities received PN.

#### **4.2.6 Patients with refeeding syndrome**

Only one (8 %) of the responders to the questionnaire had seen a patient with full-blown RFS. This patient was refed with food and nutritional drinks, with no use of EN or PN support. Why this patient developed the syndrome, what criteria that were fulfilled to diagnose the patient with RFS or other relevant factors is not described.

#### **4.2.7 Initial weight loss**

One of the responders answered that patients that follow prescribed food lists and recommended energy intake initially lose weight often, 7 answered that this happens occasionally, 4 answered this is a rare problem and 1 answered that this never happens.

## CASE

The following three sections (4.2.8-4.2.10) are linked to the patient case in the questionnaire:

*«Kvinne 19 år, spiseforstyrrelser siden 14- års alder. Restriktiv anoreksi med oppkast, aktivitetstrang og misbruk av laksativer. Løs avføring/diare. Veier 28 kg og har en BMI på 12,6 kg/m<sup>2</sup> ved innkomst. Får i seg ca 1000 kcal/dag via sonde og mat.»*

### 4.2.8 Blood samples

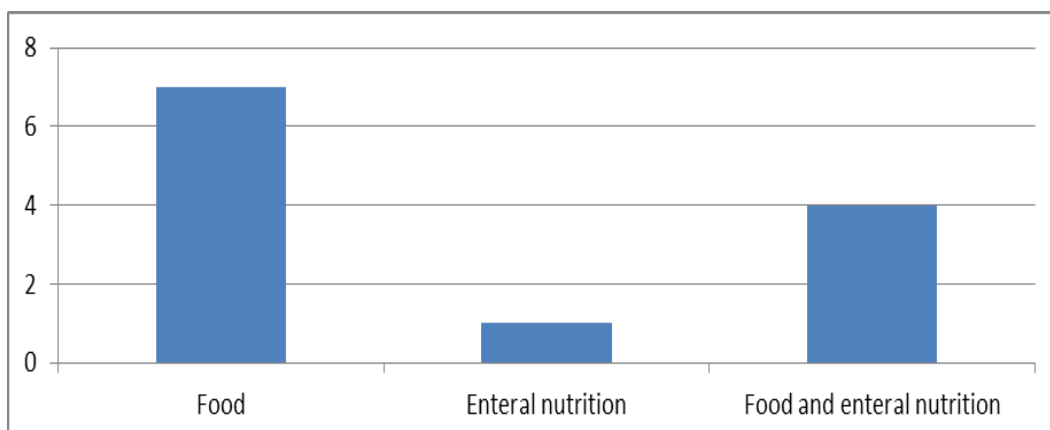
The responders were asked what they thought was the most important blood tests to take regarding detecting and monitoring the risk of RFS in this patient. One answer was taken out of the analysis due to misunderstanding of the question.

Five blood tests stood out (percent of responders answering this in parenthesis), and that were sodium (83.3 %), phosphate (100 %), glucose (66.7 %), potassium (100 %) and magnesium (75 %).

### 4.2.9 Initial feeding of one patient at risk of RFS – an example

The amount of energy or kilocalories the responders would recommend initially in the case given, varied from 1000-1400 kcal/day, with a median of 1100 kcal. Six (46 %) out of 13 would have started with 1000 kcal. All of them suggested food or a combination of food, nutritional drinks and EN. The preferred feeding in RFS methods are presented in the figure below. No one would use PN as a feeding method if not necessary.

**Figure 7** Number of responders answering that they will give the patient from the case food only, EN only or a combination of food and EN



In the question about energy distribution between proteins, carbohydrates and fats, three of the RDs pointed out that carbohydrates, and especially added sugar, should be limited in the first weeks of refeeding. Other than that, responders pointed out that the national guidelines should be followed. Some also pointed out that the protein content should be in the higher range of the recommendations to get enough protein/nitrogen compared with lean body mass and muscular growth.

#### 4.2.10 Supplements and monitoring

The responders were asked about which supplements they would recommend and if they wanted to give the supplement prophylactically or only when levels dropped or was low.

**Table 14** Number of responders answering that they will give supplements to patients at risk of RFS prophylactically

	<b>Intramuscular</b>	<b>Per os</b>
<b>Thiamine</b>	10 (76.9 %)	
<b>Phosphate</b>		8 (61.5 %)
<b>Magnesium</b>	1 (7.7 %)	7 (53.8 %)
<b>Omega 3</b>		9 (69.2 %)
<b>Multivitamin</b>		8 (61.5 %)
<b>Vitamin D</b>		5 (38.5 %)
<b>Calcium</b>		6 (46.2 %)

The last question in the questionnaire was about monitoring of the patient. Ten out of 13 would have monitored the patient once daily during the first two weeks of refeeding. One would have done the monitoring every other day, and 1 twice a week. One responder did not answer this question. On the question of how long the physicians and RDs would have monitored the patient beyond these two weeks, 6 responded that they would monitor until the patients electrolytes are stable, 2 responded they would monitor for another two weeks, and 5 responded that they would monitor the patient even longer than additional two weeks. How often the monitoring should be done after the two first weeks was not asked.

### 4.3 Basic reference menu

Only the basic reference menu at RASP is analysed, and the menus used at the other ED units are not investigated in this thesis.

**Table 15** An example of a daily food list for a patient hospitalized at RASP

<b>Breakfast</b>	1 portion of porridge (4 dl) 1 glass (200 ml) Biola 1 apple 2 capsules omega 3
<b>Lunch</b>	3 slices whole wheat bread 1 slice of crisp bread 2 pk Soft flora (margarine) 1 egg (boiled) 1 portion of “Prim” 1 portion cream cheese 2 slices of cucumber 2 slices of tomato 1 glass (200 ml) of milk (1.2 % fat) 1 apple
<b>Dinner</b>	1 slice of pie with ham, egg and cheese Salad: raisins, lettuce, apple, carrot 1 glass (200 ml) juice 1 yoghurt (dessert)
<b>Evening meal</b>	Cereals (1.75 dl) and milk (2.5 dl) 1 glass (200 ml) of milk (1.2 % fat) 1 orange

The table above is only an example of how one day with “Grunnmeny” may look like, and the patients have different options for each meal (Appendix 3). The results of the master students weighing of the dinner portions in “Grunnmeny” are presented in table 16. The amount of kilocalories in each dinner portion measured varied from 234-662 kcal, which is a difference of



428 kcal. The mean energy content was 482 kcal (SD 100). The dinner portion with the lowest calorie content was the vegetarian pizza, with only 234 kcal. In the recipe of this dish, there is no guideline in what the weight and thickness of the slice should be but only a reference of size 12 x 15 centimeters.

**Table 16** Kilocalories in each weighed dinner portion during the four week rollover menu (“Grunnmeny”).  
Beverages and dessert not included.

	Week 1	Week 2	Week 3	Week 4	Average	Minimum - maximum
Monday	662	631	417	431	535	417-662
Tuesday	547	570	488	494	525	488-570
Wednesday	386	595	421	575	494	386-595
Thursday	433	477	431	234	394	234-477
Friday	442	514	584	604	536	442-604
Saturday	410	339	410	339	375	339-410
Sunday	567	458	576	456	514	456-576
Total average	492	512	475	448	482	234-662

**Table 17** Kilocalories in each dinner portion in the “Halv grunnmeny” during the four-week rollover menu.  
Beverages and dessert not included.

	Week 1	Week 2	Week 3	Week 4	Average	Minimum - maximum
Monday	331	315	208	215	267	208-331
Tuesday	273	285	244	247	262	244-285
Wednesday	193	298	211	288	248	193-298
Thursday	217	239	216	117	197	117-239
Friday	221	257	292	302	268	221-302
Saturday	205	170	205	170	188	170-205
Sunday	284	229	288	228	257	228-288
Total average	246	256	238	224	241	117-331

From the weighing of dinner portions from “Grunnmeny”, the dinner portions of “Halv grunnmeny” was calculated concerning energy and nutrient content. These portions were not weighed, but only calculated from “Kostholdsplanleggeren”. The amount of kilocalories calculated in these dinner portions varied from 117-331 kcal, with a mean energy content of 241 kcal (SD 50).

In the following, “Grunnmeny” and “Halv grunnmeny” is separated into two different chapters. First, the results from the analysis of “Grunnmeny” are presented. Thereafter, the results from the analysis of “Halv grunnmeny” are presented.

### 4.3.1 Basic reference menu – “Grunnmeny”

“Grunnmeny” is the comprehensive food system that is the main framework for the nutritional treatment and rehabilitation of the patients with AN and EDs at RASP. This system has been worked out to secure the patients enough energy and nutrients but also to expose the patients to different normal foods and tastes that is a challenge to these patients. The “Grunnmeny” system makes predictability for the patients of what to eat and that are considered important due to the high anxiety these patients have related to food. All results and tables below include not only the dinner portions, but analysis of all food prescribed in four meals during one day.

**Table 18** The average daily energy prescribed, including all meals, snacks and beverages

	Week 1	Week 2	Week 3	Week 4	4 weeks average
Average energy prescribed/day, kcals	2618	2718	2566	2612	2629
Minimum - maximum	2463-2818	2481-2929	2471-2700	2237-2841	2237-2929

Week 4 includes the dinner that was very low in calories (table 15), and thus the energy content of the whole day is affected, resulting in a prescribed energy content of 2237 kcal, which is more than 250 kcal below the recommendations.

**Table 19** Energy distribution (E %) in “Grunnmeny” at RASP

	Week 1	Week 2	Week 3	Week 4	Average	Recommended
Carbohydrates, E %	53	50	55	52	53	45-60
- Sugar, E %	6	5	5	4	5	< 10
Dietary fiber, g	44	46	46	45	45	25-35
Fat, E %	28	32	26	29	29	25-40
Protein, E % (g)	19 (125)	18 (125)	19 (119)	18 (119)	19 (122)	10-20

**Table 20** Contents of vitamins and electrolytes in “Grunnmeny”

	Week 1	Week 2	Week 3	Week 4	Average	Min-max	Recommended
Thiamine, mg	2.73	2.51	2.73	2.73	2.68	2.51-2.73	1.1
Folate, µg	456	436	434	420	436.5	420-456	300 (400 <sup>17</sup> )
Calcium, mg	1933	1823	1887	1908	1887.8	1823-1933	800
Iron, mg	14.5	14.7	14.7	13.1	14.25	13.1-14.7	15
Sodium, mg	3210	2837	3149	2902	3024.5	2837-3210	< 2300
Potassium, mg	5215	5282	5278	5289	5266	5215-5289	3100
Magnesium, mg	539	550	558	542	542	539-558	280
Phosphorus, mg	2936	2912	2849	2881	2894.5	2849-2936	600
Vitamin D, µg	24.2	30.2	24.3	28.8	26.8	24.2-30.2	10

Omega 3 capsules or “tran” are implemented in the basic reference menu at RASP, and included in the analysis. Without this supplementation, levels of vitamin D would have decreased with almost 4 fifths, highlights the importance of this supplementation. As an example, the vitamin D content of one day in week 1 would be as low as 4.7 µg, with an average of 7.5 µg during the whole week. The recommendations of omega 3 will not be met without this supplements either, and contribute to less than the recommended 1 E % if not supplemented.

<sup>17</sup> Women of reproductive age

Multivitamin and calcium supplements are not included in the results. These supplements should be added to the “Grunnmeny” and “Halv grunnmeny”. It varies if patients receive these supplements or not, depending on previously food intake, which supplements they already receive and the patients’ willingness to take these supplements.

### 4.3.2 Reduced basic reference menu – “Halv grunnmeny”

Results from the analysis of “Halv grunnmeny” are presented in the following chapter. All results and tables below include not only the dinner portions, but also analysis of all food and beverages prescribed during a day or week.

**Table 21** The average daily energy prescribed, including all meals, snacks and beverages

	Week 1	Week 2	Week 3	Week 4	4 weeks average
Average energy prescribed/day, kcals	1352	1538	1343	1413	1411
Minimum - maximum	1236 - 1421	1455 - 1674	1247 - 1458	1212 – 1567	1212 - 1674

The estimated amount of kilocalories given each day in “Halv Grunnmeny” varied from 1212-1674 kcal, which was a difference of 462 kcal. This variation would again be higher or lower due to the patients’ specific choices and possibilities in the “Grunnmeny”.

**Table 22** Energy distribution in “Halv grunnmeny” at RASP

	Week 1	Week 2	Week 3	Week 4	Average	Recommended
Carbohydrates, E %	48	44	49	49	48	45-60
- Sugar, E %	6	4	5	7	6	< 10
Dietary fiber (g)	18	19	18	18	18	25-35
Fat, E %	32	37	31	32	33	25-40
Protein, E % (g)	21 (70)	19 (72)	20 (67)	19 (67)	20 (69)	10-20

The energy distribution of macronutrients and sugar in “Halv grunnmeny” is similar to that in “Grunnmeny” (table 19). The contents of fiber (in grams) are lower due to less food and energy. As for the “Grunnmeny”, the micronutrients in “Halv grunnmeny” are calculated and presented in the table below.

**Table 23** Contents of vitamins and electrolytes in “Halv grunnmeny”

	Week 1	Week 2	Week 3	Week 4	Average	Min-max	Recommended
Thiamine, mg	1.39	1.54	1.26	1.38	1.39	1.26-1.54	1.1
Folate, µg	203	225	189	190	201.75	189-225	300 (400 <sup>18</sup> )
Calcium, mg	1387	1200	1420	1340	1336.75	1200-1420	800
Iron, mg	6.4	7.8	6.1	6.3	6.65	6.1-7.8	15
Sodium, mg	1586	1978	1618	1862	1761	1586-1978	< 2300
Potassium, mg	2858	2855	2835	2716	2816	2716-2858	3100
Magnesium, mg	296	316	292	296	300	292-316	280
Phosphorus, mg	1813	1788	1777	1780	1789.5	1777-1813	600
Vitamin D, µg	16.9	20.5	15.6	15.3	17.1	15.3-20.5	10

The recommendations for most micronutrients are covered, with the exception of folate, iron and potassium in ”Halv grunnmeny” at RASP. Supplements of omega 3 are included in the analysis, but not calcium and multivitamin supplements.

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<sup>18</sup> Women of reproductive age

## 5 Discussion

The discussion is presented in the same order as the results; discussion and differentiation between the procedures, discussion of the results from the questionnaire and discussion of the basic reference menus, “Grunnmeny” and “Halv grunnmeny”, at RASP. Strengths and weaknesses of the methods used, and strengths and weaknesses of the results, are discussed after each result.

### 5.1 Procedures

Results from the procedure collection found that there is a difference between if the regional departments of EDs have developed their own procedures to prevent RFS, if they do not have such procedures or if they use international guidelines. There is variety in treatment options within a certain guideline, implying that individual customization for each patient has to be made. That these discrepancies are found between the regional departments of EDs in Norway is not surprising, considering the inequalities of other (international) guidelines, both regarding RFS and treatment of patients with AN (O'Connor & Nicholls, 2013) (table 8 and 9).

Considering the patient group that is hospitalised at the regional departments of EDs in Norway, there is a bit of a concern that not all of them have procedures to detect and treat patients at risk of RFS or that they follow common guidelines. In the literature, AN patients are referred to as a group of patients that may be in high risk of RFS (Kraft et al., 2005; H. Mehanna et al., 2009). Patients with other EDs may also be at risk, like BN (due to purging/vomiting), or patients with extreme weight fluctuations or extreme exercise (Mehler & Rylander, 2015), all possible patients at a regional department of EDs. Without procedures, the system is vulnerable if experienced health personnel quit their job. A procedure may be favourable for the safety of patients, because a procedure may secure that all patients are assessed and monitored. If a common procedure does not exist, some patients that may be at high risk are not detected.

The criteria for which patients that should be identified as at risk of RFS differ between RESSP (Bodø) and RKSF (Levanger). The difference between BMI cut-offs of patients considered at risk vary between BMI 16-18.5 in RESSP (Bodø) and BMI < 7-11 in RKSF (Levanger) procedure.

Why there is such huge discrepancy between the recommendations should be a topic of further investigation. A possible explanation is that the health personnel working at RKSF (Levanger) have extensive experience and feel confident that RFS is not relevant in patients that are moderate malnourished. One other contributing factor could be that NICE-guidelines, which are used by RESSP (Bodø), are made to identify all patients at risk of RFS, and may consider patients with other comorbidities as in higher risk than AN patients. Guidelines that are made to identify patients at risk of RFS and guidelines how to refeed patients at risk is debatable in terms of the transferability to AN patients. The NICE-guidelines may also be too restrictive, or the procedure made by RKSF may be too radical.

The regional departments of EDs treat different age groups, and this may contribute to the difference in awareness of RFS among the clinicians. The risk of RFS in AN patients may differ between adults and adolescents. Adults may be at higher risk because of longstanding malnutrition, while adolescents may have higher risk due to higher metabolic rates (Whitelaw, Gilbertson, Lam, & Sawyer, 2010). Compared to the results from procedure collection, a difference in how to identify patients at risk of RFS may be seen between RKSF (Levanger) and RESSP (Bodø) due to age of patients (table 11).

Refeeding of patients with AN considering calculation of initial calorie recommendations is varying in the procedures collected. The procedures to avoid RFS in the regional departments have an initial feeding of 10-30 kcal/kg, dependent on severity and underweight of the patients. Most units operate with half food lists or food lists of about 1000-1500 kcal. Initial refeeding range is further discussed in chapter 5.2.

Studies have found that there is no association between initial energy prescription and cases of hypophosphatemia (the hallmark of RFS), but rather an association between % of IBW and cases of hypophosphatemia (Le Grange, 2013). This correlation between % of IBW and cases of hypophosphatemia is also shown by Ornstein et al. (2003). In adolescents, studies have found that percent of IBW (< 70 %) is a better predictor of patients at risk than energy intake (O'Connor & Nicholls, 2013).

Other studies have found that there is a direct link between the risk of RFS and degree of weight loss before admission (Mehler et al., 2010). The risk of developing RFS would also depend on the patient's previous intake of micronutrients, purging and exercise (Stanga et al., 2008). How aggressively the refeeding is thought to be should also be assessed against how much the individual patient has eaten e.g. the last week(s), and give the gastrointestinal tract a possibility to cope with the food given and to reduce eventual abdominal pain (Mehler et al., 2010)

Close monitoring and evaluation of each patient at risk of RFS are important (Ornstein et al., 2003), and instead of giving supplements to all patients, it may be just as effective to treat hypophosphatemia if it occurs. RSS (Tromsø) pointed out that only one patient has had to be supplemented with phosphate during the last six years. RASP (Oslo) provides phosphate prophylactically in high-risk patients, while RKSF (Levanger) and RESSP (Bodø) evaluate the requirements for each patient according to their procedures. "Seksjon for spiseforstyringer (Bergen)" supplements with phosphate mixture if necessary.

It seem like during this investigation that RFS is something all regional departments of EDs have in mind, but something they do not experience to be a common part of their practice. This may be due to the procedures in the regional departments of EDs in Norway being satisfactory, the physicians and RDs may be trained to detect these patients or it may also be due to that the most severe cases of AN being hospitalized in medical wards, not in ED units. As it is today, each department has their own procedures regarding medical examination, refeeding and monitoring. Such inconsistency produces several limitations to consider whether the treatments in the different departments are comparable.

There are few publications considering the importance of RDs in ED units, but a RD is important in the nutrition care of a patient with an ED (Mehler et al., 2010). A food history of recent and normal food intake is often more accurate to predict micronutrient deficiencies than laboratory test (Ozier & Henry, 2011). A RD calculate energy needs, monitor and make meal plans to achieve weight restoration (Mehler et al., 2010). In addition, "Elektrolyttveilederen" (2014) recommends that all patients in high risk of RFS should consult a RD. The RD closely follows blood tests during the refeeding state, and this would most likely detect any nutritional shortcomings. If the patient refuse to eat or need EN or PN of other reasons, an RD is important in the planning and monitoring of these patients (Mehler et al., 2010). One of the main nutritional



treatment goals as considered from the RDs is to help the patients relearn or experience by themselves what normal food should consist of and how much energy that is actually needed both to reduce underweight but also how much food actually is needed to keep a healthy weight. This nutritional rehabilitation is considered important to start early at inpatient units due to the importance of good habits to develop and to reduce the risk of relapse (Sachs et al., 2015). After discharge the patients usually have quite some experience in healthy recommended food habits and food choices that could be one of several pieces to avoid relapse due to bad food habits or lack of knowledge how to take care of the body (Sachs et al., 2015).

Table 11 shows that the number of RDs working at an ED unit per 01.01.2016 is as low as 5. A further concern is that three of them are working at RASP (in addition to 1 at RESSP (Bodø) and 1 at Modum Bad), which means that the other units do not have an RD at all. Even if not investigated in this thesis, the impression made by the master student is that RASP (Oslo) and RESSP (Bodø) also have an attention to the individual dietary lists and the contents of this, to a greater extent than the other departments. How this affect the total treatment offers, risk of relapse or patient experience needs to be investigated.

### **5.1.1 Strengths and weaknesses of the procedure collection**

One of the greater weaknesses within this study is the difficulty of receiving proper or true information from the different regional departments of EDs, and to know whether this information is actually true for all clinicians. This may be due to lack of knowledge from the person that was contacted, or that they did not prioritize to answer the questions given. Some did just answer in a short mail, while others sent detailed information of their written procedures. Even with several remainder emails, it was difficult to get an affirmative or negating answer on the question if the information received was written procedures and followed by their clinical staff within their department or not, or if the information given just was routines (not written), or common practise. The information gathered from the departments that claimed that they do not have a procedure regarding RFS, may still have the information written down in other procedures. Overall, the information gathered was deficient, and it is tempting to believe that relevant and important information are missing.

Physicians pointed out that RFS is a rare problem in their department, and the difficulties with getting information from the head physicians may have been due to that they do not see the importance of investigating the procedures. Even if international guidelines recommends that patients with AN should be monitored regarding RFS (National Institute for Health and Clinical Excellence, 2006), this view may not be shared among clinicians working at the regional departments of EDs in Norway. However, that a department does not have procedure do not directly imply that they do not detect these patients and have routines to treat patients at risk of RFS. There is difficult to conclude if recommendations are followed based on the collected data in this thesis.

A better method to collect the procedures could have been to visit each regional department and ask for the procedures in person through a personal interview with the head physician. In that way, confusion and misunderstanding regarding what was asked for could have been eliminated, and instead of having email correspondences lasting for months, the procedures would have been collected during a few hours. Otherwise, this option was not used due to economic reasons, because there was no budget for travelling, and it would maybe have been difficult to arrange an appointment in an otherwise hectic workday with the head physicians.

## 5.2 Questionnaire

What physicians and RDs define as full-blown RFS is comparable to the diagnostic criteria found in the literature (Hofer et al., 2014). That all RDs and only one of the physicians responding to the questionnaire remember to have learned about RFS during education was an interesting result. Considering only 3 out of 8 units of EDs included in the questionnaire have a RD, this could contribute to the differences of awareness of this syndrome between the different ED units.

The high number of physicians and RDs (93 %) reporting to have been in contact with patients at risk of RFS is not surprising since this survey was done among physicians and RDs working at specialized ED units. The diagnostic criterion of AN is among others to have a BMI < 17.5 and NICE-guidelines define everyone with a BMI < 18.5 as at risk of RFS (table 4).

The rarity of RFS was confirmed in this survey. Only one of the responders claims to have seen the syndrome, even though 38 % of the responders have worked in this field for 10 years or more. The incidence of a full-blown RFS is not investigated in this thesis and due to the rarity of the syndrome (expressed by answers in the questionnaire), and the number of incidences would have been extremely low or zero considering the time limits of a master thesis of a year.

Decline in electrolyte levels and symptoms indicating that a patient is developing RFS are observed by nine of the responders to the questionnaire. That hypophosphatemia is the most common symptom reported, may be due to that the awareness of hypophosphatemia in patients at risk of RFS are highlighted in several articles (H. M. Mehanna, Moledina, & Travis, 2008; M. A. Crook, 2014 ). Symptoms as hypophosphatemia seems to be common accepted as a symptom of RFS, while others are debatable (H. M. Mehanna, Moledina, & Travis, 2008). It may be confusing for clinicians that several signs and symptoms have to be present to identify a patient experiencing RFS. A drop in phosphate or other electrolytes will be corrected by supplements, and other measures may contribute to the low incidence of severe symptoms. A diet with focus on phosphate rich foods, or supplementation of thiamine and multivitamins prophylactically may eliminate the incidence of full-blown RFS (Royal College of Psychiatrists, 2014).

According to “Elektrolyttveilederen” (2014), the most important blood test and medical examination to detect RFS are phosphorus, potassium, magnesium and glucose, as well as ECG and weight. This is almost what was found in the answers from the questionnaire, with the exception of that most responders also mentioned sodium as important to assess. Weight and ECG was not an option in the questionnaire.

Results from the questionnaire show that several of the physicians and RDs experience that patients lose weight initially when starting refeeding, even if they eat what they are prescribed. This indicates that the dietary lists and calculated energy needs may be underestimated, and may result in a worsening of the disease for the patient, and increase the risk of cardiac problems, increased length of hospitalization and increased mortality (Kohn et al., 2011). Other factors favourable a lower energy intake initially, due to the fear of food and weight gain in AN patients (Zipfel et al., 2015). A slowly increase in energy may contribute to more cooperative patients and that the patients feel safe and comfortable with the treatment they get (Sachs et al., 2015).

High calorie diets given continuously with EN, together with food, may reduce length of stay with 17 days compared to bolus fed patients (Agostino et al., 2013). This is important both to the patient (and patient families) social life, economy of the hospital and statistical relevance. Continuous feeding with EN may reduce the insulin surges that normally are induced with bolus feeding (Agostino et al., 2013), and EN may be used to refeed patients at high risk of RFS. Even though this might be true, the practicality of continuous EN has to be questioned due to a common problem that the patient quite often would refuse this option.

One of the questions in the questionnaire was about initial feeding range of a case presented. The answers varied from 1000-1400 kcal, and this equals to 35-50 kcal/kg in this patient of 28 kg. This is higher than the international guidelines propose (table 8 and 9), and higher than all the procedures at the regional departments of EDs in Norway, that varies from 10-30 kcal/kg in high-risk groups. It should be noted that the patient in the case was already prescribed 1000 kcal, and presumably, this was taken into consideration when recommending initial feeding range. On the other hand, 1000-1400 kcal corresponds to the procedures and routines that recommend starting feeding with half food lists. International guidelines do also recommend feeding ranges in terms of kcal/day instead of kcal/kg, and these recommendations ranges from 600-1600 kcal/day (table 9).

In a study from northern America by Schwartz, Mansbach, Marion, Katzman, & Forman (2008), a wide variety in refeeding range of initial energy content in patients diagnosed with AN between physicians was found. The prescribed energy varied from 100-1500 kcal/day and solid foods, liquids, EN and PN were used. Only 37 % of the physicians followed protocols that were standardized. Fifteen percent prescribed supplements at admission for all patients, while others had an individual customization. The differences are not this big in our material, but we found that both procedures and recommendations from the physicians and RDs differ both in initial feeding and in supplements.

Initial nutrition range is a topic of discussion in several studies. Some studies point out that recommended prescribed initial energy from guidelines may be too restrictive for many patients, and may contribute to initial weight loss (Golden et al., 2013; Whitelaw et al., 2010), which again leads to increased length of hospitalization, longer bed rest, decreased lean body mass and poorer

outcome of the disease (Kohn, Madden, & Clarke, 2011; Sachs et al., 2015). Garber, Michihata, Hetnal, Shafer, and Moscicki (2012) found that 83 % of hospitalized AN patients starting at a diet of 1200 calories initially lost weight. A summary of studies done by Le Grange (2013), conclude that moderately malnourished (75-85 % of IBW) adolescents with AN could have a more aggressively nutrition program than proposed in the guidelines. They found that an initial feeding of 1764 kcal/day vs 1093 kcal/day resulted in faster weight gain and reduced hospitalization of 6 days. Sachs et al. (2015) point out the importance of evaluating current guidelines and recommendations, and distinguish between moderate and severely malnourished patients. This association is also found in other studies, showing that patients with expected body weight of > 68 % could benefit from a more aggressively initial feeding than current guidelines suggest (Whitelaw et al., 2010).

From the questionnaire, two responders pointed out that caution with carbohydrates could be necessary in the refeeding state of a patient at risk of RFS. Other than that, responders answered that the patients should be feed with 45-60 % of energy coming from carbohydrates, 10-20 % from protein and 25-40 % from fat, as recommended by the Nordic Nutrition Recommendations (2012). Several studies have pointed out the role of carbohydrates in the contribution of RFS (Royal College of Psychiatrists, 2014). A study from O'Connor and Goldin (2011) emphasizes a reduced carbohydrate load in combination with a higher percentage of fat in the diet of a patient at risk of RFS. A reduced carbohydrate load will reduce the glucose load and therefore the release of insulin (O'Connor & Goldin, 2011). Kohn et al. (2011) recommends starting feeding with no more than 40 % of energy from carbohydrates. Only the procedure from RESSP (Bodø) recommends starting refeeding of (fast) carbohydrates with caution.

### **5.2.1 Strengths and weaknesses of the questionnaire**

The questionnaire was sent out to 25 participants, naturally delimited by the number of physicians and RDs working at an ED unit. Two additional units with hospitalized patients (not regional departments) were included in this part of the thesis in order to get a higher number of responders, but still the response rate was low. The low response rate of 52 % is a weakness and a constraint for the validity of the study, and no conclusion can be made with this amount of data.

However, a trend in the answers received can be seen, and some of it can be compared to exciting literature within this field.

The questionnaire itself has several weaknesses. In some of the questions the informants answered more than requested (ticked several options), and therefore it was necessary to remove their answer on these specific questions from the analysis. Some of the responders also misunderstood some questions. Physicians and RDs in the same unit had different answers on questions regarding procedures. This may be due to both that the physicians and RDs asked not are aware that their department has a procedure to identify and/or treat patients at risk of RFS or misunderstanding of the question.

The questionnaire also had some questions that have given little or no information, and these questions could therefore have been left out when making the questionnaire. Other and more precise questions could have been asked to obtain more informative answers. However, a longer questionnaire may have resulted in an even lower response rate. Even though a preliminary test of the questionnaire was carried out on a few RDs, the outcome of the questionnaire was difficult to predict.

### **5.3 “Grunnmeny” and “Halv grunnmeny”**

The results from the analysis of the “Grunnmeny” and “Halv grunnmeny” at RASP are results of a four-week menu. The challenge is still what is actually eaten by the individual patients, but this is not evaluated here.

The amount of calories given the patients during refeeding does not always correlate with the rate of weight gain, and the amount of energy needed for weight gain vary between 1800-4500 kcal/day in AN patients (Mehler et al., 2010). Before refeeding, the AN patient is in a hypo metabolic state, which means that weight gain could be met even though the energy intake is below the expected energy requirements. On the other hand, there may also be an extra increase in the resting metabolic rate in AN patients during weight gain, increasing the requirements of calories up to 70-80 kcal/kg/day during this hyper metabolic phase. This specially occurs when the patient is close to their IBW (Mehler et al., 2010).

In the “Grunnmeny” at RASP the amount of calories are higher than The Norwegian Directorate of Health recommend for healthy women aged 18-30. However, the experiences from RASP have been that this amount of energy has been too low for many patients (especially for adolescents), and “Grunnmeny” has therefore been increased to meet the energy needs for these patients. For weight maintenance, Marzola, Nasser, Hashim, Shih, and Kaye (2013) found that weight-restored patients with AN often require more calories than sex-, age-, weight-, and height-matched control subjects (50-60 kcal/kg/day vs 20-40 kcal/kg/day) to maintain weight for a certain period or all life through, due to slow normalisation of neuroendocrine processes. Most patients normalize metabolism after 3 to 6 months of weight maintenance (Zipfel et al., 2015). During refeeding of these patients, this should be taken into consideration.

The analysis of the basic reference menu at RASP showed that kilocalories in the weighted dinner portions varied from 234-662 kcal, which is a difference of 428 kcal. The mean energy content was 480 kcal (SD 100). However, the dinner that was low in calories was a mistake from the kitchen that special day due to misunderstanding of the recipe. The dinner that was second lowest in calories was at 339 kcal, and may be a more accurate estimate of the differences in calories between the dinner portions. Even if one dinner was very low in calories, the average energy content through the four-week dinner menu was within the recommendations, implying that, if such mistakes do not happen often, it may not be of crucial relevance for the patients` weight gain.

If the patients choose porridge and cereals for breakfast and evening meal, the calorie content is lower than if they choose bread as an option. The calories in the bread meals vary depending on which spread and topping they use, but when possible, the RDs experience is that the patients would choose the options that are low in calories. As an example; a meal with two slices of bread, one portion of both turkey and cream cheese will give a total of 52 kcal, compared to if the patient would choose brown goat cheese and white cheese the calorie content would have a total of 135 kcal, only with this topping (not included the bread and butter/margarine). Therefore, in one meal with bread, the patient`s choice of topping could vary with at least 83 kcal. To prevent that the patients could choose low calorie options for each meal, different types of spread and toppings are served to each meal, forcing the patients to choose more energy dense options.

The distribution of macronutrients (table 19) is within the recommendations (Helsedirektoratet, 2015), with protein in the upper levels and carbohydrates in the lower recommendation range. As discussed with the procedures and questionnaire, the recommendations presented in the literature with reduced carbohydrate intake are not a part of the procedure at RASP. However, the basic reference menu focuses on enough energy, enough protein and enough micronutrients, and to achieve this within the recommended energy contents, E % of carbohydrates may automatically decrease. In addition, even if not clarified in procedures, the “Halv grunnmeny” excludes sugary drinks for the benefit of milk products high in minerals (especially phosphorus) and protein.

Recommended dietary fiber intake is 25-35 g/day (Helsedirektoratet, 2015). In “Halv grunnmeny” the recommendations of fiber is not covered, while in “Grunnmeny” the recommendations are exceeded with an average of an additional 10 g/day. This is a lot, considering that these patients often have digestive problems, feeling full and discomfort after a meal (Zipfel et al., 2006). Fiber may increase this discomfort and increase the satiety after a meal, which could make it even more difficult to stick to the diet plan and obtain a favourable weight gain. When analysing the “Grunnmeny” in “Kostholdsplanleggeren”, bread with 50-75 % wholegrain was used. The bread they use at RASP may vary, and will differ between days and meals, but the RDs recommend using bread with about 50 % wholegrain. The high fiber content found in this analysis may be falsely high due to that wholegrain bread was used more often as an option in the “Kostholdsplanleggeren” than bread with lower fiber content. However, the RDs suspect that high fiber and wholegrain bread are used more today than initially recommended, due to the general opinion that more fiber is healthy.

“Grunnmeny” and “Halv grunnmeny” cover most of the recommendations of micronutrients and minerals recommended by the Norwegian Directorate of Health, except from iron in “Grunnmeny” and phosphate, iron and potassium in “Halv grunnmeny” (Helsedirektoratet, 2015). In “Halv grunnmeny”, milk is the only beverage of option (besides water) for every meal. This is to secure the patients’ requirements for proteins, calcium and phosphorus despite that their diets are lower than recommended in calories. A diet higher in protein to cover the nutritional requirements of nitrogen may be favourable when eating a low calorie diet, as the “Halv grunnmeny” is (Fuentebella & Kerner, 2009). Calcium prescribed is well above the recommendation of 800 mg, even in the “Halv grunnmeny”. A further supplementation in



addition to this will not have any beneficial effects, even if it is recommended by the general procedure for the hospitalized patients. Multivitamin and mineral is recommended as a supplement for all individuals consuming a diet lower than 1500 kcal (Helsedirektoratet, 2015), as the “Halv grunnmeny”.

The Norwegian Directorate of Health recommend to keep the sodium intake below 2.3 g/day, equals to 6 g salt/day (Helsedirektoratet, 2015), but a lower intake might be even more favourable. The average prescribed salt intake at in “Grunnmeny” exceeds the recommended levels, with an average excess of about 700 mg sodium/day, or nearly an excess of 2 g salt/day. Optional salt at the table is not included in the analyses, so the levels may be even higher. As described in chapter 2.1.2, a low sodium diet is recommended for patients at risk of RFS. However, the average salt prescribed in “Grunnmeny” at RASP are lower than the average intake in Norway, which is 10 g salt/day (Helsedirektoratet, 2015). The high salt content found in this analysis may be due to that bread available in “Kostholdsplanleggeren” contains more salt than the bread served at RASP. Even if not investigated, the homemade bread at RASP served to lunch is likely to contain less salt than bread available in “Kostholdsplanleggeren”.

During the procedure collection, some of the dietary lists at the other regional departments were collected as well. The general observation was that the other dietary lists were lower in energy than “Grunnmeny”, with about 500 kcal. This again means that half of the dietary lists that they have at the other departments (which they report to be the dietary lists for patients at risk of RFS) will be lower in energy than “Halv grunnmeny”. If this difference affects the patients in a great extent is not investigated, but a difference of 500 kcal/day could result in a difference of 0.5 kg weight gain/week (The National Institute for Health and Care Excellence 2004). At RASP they recommend a weight gain each week 1-1.5 kg, for inpatients and it is not discussed or evaluated here how much the reduction of underweight are prescribed in other departments. As discussed, weight gain is crucial in the treatment of AN patients, and normalization of food intake, reduced hospitalization and higher weight at discharge may influence recovery and lower risk of relapse in the patients. In addition, the focus on phosphorus rich foods and protein in the half dietary lists at the other departments are not investigated, and the awareness may not be the same as it is at RASP. If the dietary lists at other departments than RASP are developed by RDs are unclear and have not been specifically investigated.

### **5.3.1 Strengths and weaknesses of the basic reference menu**

Only the ingredients of the dinner portions were actually weighed. The four-week dinner rollover menu was also only weighed once, and several weighing's could have been more preferable to find the average. However, it is assumed that the average of four weeks of weighing would give a reasonable good estimate of the average nutrient content, and making this a fairly good estimate of the reality during a hospitalization period at RASP. At least if the patient eat the dinner menu, but some patients use nutritional drinks that would complicate these calculations of micronutrient content even more. This assumption is also made according to the analysis of the whole four-week menu, because every patient is different and choose different foods, so even if the whole menu had been weighed, this menu would have been representative for only one patient. When the basic reference food menu at RASP were analysed, it was taken into consideration that some of the meal options are more likely to be chosen by the patients than others. Most patients would rather choose low fat or low calorie options when possible, whole fruits rather than juice and yoghurt more often than the department's dessert.

Considering the weighing of the dinner portions, there were some limitations to consider. First, some of the meals consisted of different food types, where the sauce was poured over the whole plate. In such dishes, it was difficult to separate the food on the plate and to do exact weighing of each component. Other limitations were that some of the dinner plates were weighed the day after the meal was prepared, which could have affected the true weight of the food. The fact that some of the dinner portions also were weighed with a different scale could have affected the results.

A limitation is also linked to the use of "Kostholdsplanleggeren" as an analyse program. In "Kostholdsplanleggeren" it is possible to look up 1543 ingredients and dishes, which includes the contents of 38 different nutrients (Matportalen, 2016). This was a limitation when calculating the nutrient content of the four-week rollover menu. Not all preferred food choices were available, and sometimes only the best available similar option could be chosen. The food choices in "Kostholdsplanleggeren" are updated once a year with new foods from "Matvaretabellen" (Matportalen, 2016), which may contribute to that not all preferred food choices is available. Other analyse programs may have been more favourable to use, but "Kostholdsplanleggeren" was the only program available when analyses was done. One strength may be that the results here

correspond quite good with the calculations of nutrient content and energy performed formerly by the RDs at RASP.

## **5.4 Future research**

A proposed suggestion for further research is to look at true incidences of RFS in EDs through medical records, and to differentiate between hypophosphatemia to a certain limit and to a full-blown RFS. This implies that a clear definition of RFS is determined. This would also be time consuming and difficult when a clear diagnosis of RFS exists, but this could probably be a better approach to be able to recommend something specific for this particular patient group. To achieve enough material and validity or reproducibility, this group would need to be investigated for several years. International studies have looked at cases of hypophosphatemia, and this could have been done (Brown, Sabel, Gaudiani, & Mehler, 2015; Ornstein et al., 2003), however, hypophosphatemia is not alone a predictor for whether patients develop RFS or not. The goal in this thesis was to study the procedures themselves and the subjective opinions from the physicians and RDs. Further research could be to investigate these procedures and if they are followed.

Another research option for the future is to investigate how much of the food in the dietary list the patients actually eat. In this thesis the amount of food prescribed has been evaluated, and whether these lists are within the recommendations and could be favourable for patients at risk of RFS. What the patients actually eat is not investigated. A study where the portions were weighed before it was served to the patients, and then weighing what is left afterwards could give a good estimate of what a patient actually eat during a day. Still, there would be challenges to what the patient actually would digest and absorb due to for example spitting of food and vomiting that is quite common.

## 5.5 Conclusion

Of the six regional departments of EDs in Norway, three of them (RASP (Oslo), RKSF (Levanger) and RESSP (Bodø)) have specific procedures to detect and treat patients at risk of RFS. Considering that these departments hospitalize patients that in the literature are defined as at risk of RFS, a procedure ought to have been present in every department treating patients with AN. The collaboration of a common procedure between the different regional departments of EDs in Norway could usefully be enhanced. The existing procedures vary, and should be evaluated compared to new literature, but more research is needed to give satisfying knowledge about the risk of RFS in AN patients, and about identification, treatment and monitoring of these patients.

Due to the low response rate of 52 % to our questionnaire, the results of the survey are uncertain. However, the questionnaire detected that there are some uncertainties between the physicians and RDs of the definition of RFS. Hypophosphatemia (<0.5 mmol/L), cardiac arrhythmias, peripheral oedemas, pulmonary oedemas and heart failure are the most accepted symptoms.

“Grunnmeny” is the basic reference menu at RASP. The energy content and the distribution of energy yielding macronutrients in the dinner portions are as calculated by the RDs, but a clarification within the recipes ought to be made to eliminate the chances for the milieu therapists and kitchen personnel to make mistakes regarding portion sizes.

The energy prescribed in “Halv grunnmeny” is higher than most of the international guidelines for initial refeeding of patients at risk of RFS, equivalent to 35 kcal/kg body weight in a patient of 40 kg, which is likely to be the weight of a patient at an ED unit. However, individual customization is made, and the “Halv grunnmeny” makes an important frame for and is a good guidance for the milieu therapists that serve the patients during the nutritional rehabilitation at RASP.

The analysis shows that iron supplementation should be assessed in both of the basic reference menus. The importance of supplementation of omega 3 and vitamin D was confirmed during this analysis. A supplementation of multivitamins in addition to the “Grunnmeny” is not necessary based on the results from this analysis, but might be more relevant when energy intake are below

1500 kcal, as the content prescribed in “Halv grunnmeny”. Calcium supplementation may also be superfluous. A further restriction of sodium and fiber in “Grunnmeny” may also be favourable.

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## **7 Appendix**

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## 7.1 Appendix 1

Spørreundersøkelse til leger og kliniske ernæringsfysiologer ved spesialavdelinger for spiseforstyrrelser om reernæringssyndrom

Kjønn: Mann Kvinne      Alder:      Arbeidssted:      Yrkestittel:

Hvor lenge har du jobbet med spiseforstyrrelser?      år

**Opplever du at du har tilstrekkelig kunnskap om risiko for reernæringssyndrom og hva reernæringssyndrom er?**

- Ja, jeg kunne satt i gang behandling og føler meg trygg på hva som må gjøres
- Ja, men ville rådført meg med annet helsepersonell før behandling
- Nei
- Vet ikke

**Fikk du undervisning om reernæringssyndrom på studiet?**

- Ja
- Nei
- Vet ikke

**4. Det er ikke entydig i litteraturen hva som defineres som reernæringssyndrom; Hva mener du skal til for å kalle noe et reernæringssyndrom? Kryss av de symptomene og verdiene du mener bør være til stede/er de viktigste.**

- |  |  |
|--|--|
| <input type="checkbox"/> fosfat<0,85mmol/L   | <input type="checkbox"/> perifere ødemer   |
| <input type="checkbox"/> fosfat<0,50mmol/L   | <input type="checkbox"/> wernicke-korsakoffs syndrom                             |
| <input type="checkbox"/> fosfat<0,32mmol/L   | <input type="checkbox"/> hypervolemi   |
| <input type="checkbox"/> kalium<3,5mmol/L    | <input type="checkbox"/> lungeødem   |
| <input type="checkbox"/> kalium<2,5mmol/L    | <input type="checkbox"/> metabolsk acidose                                       |
| <input type="checkbox"/> magnesium<0,7mmol/L | <input type="checkbox"/> koma  |
| <input type="checkbox"/> magnesium<0,5mmol/L | <input type="checkbox"/> ataksi  |
| <input type="checkbox"/> kramper             | <input type="checkbox"/> hjertesvikt/infarkt                                     |
| <input type="checkbox"/> hjerterytmier       | <input type="checkbox"/> anemi   |
| <input type="checkbox"/> rabdomyolyse        | <input type="checkbox"/> respirasjonssvikt                                       |
| <input type="checkbox"/> enkefalopati        | <input type="checkbox"/> Hypoglykemi   |
| <input type="checkbox"/> Andre:              | <input type="checkbox"/> Vet ikke, må slå opp for å få eksakte verdier/symptomer |

Eventuelle kommentarer:

**5. Har dere på din arbeidsplass skriftlige prosedyrer som er spesifikt utviklet for å identifisere og behandle pasienter i risiko for reernæringssyndrom?**

- Ja
- Nei
- Vet ikke

- a. Hvis ja; hvilke prosedyrer? Beskriv:

Eventuelle kommentarer:

6. **Har dere på din arbeidsplass skriftlige prosedyrer som vil identifisere og beskrive behandling av pasienter som er i risiko for reernæringsyndrom selv om prosedyren ikke spesifikt er laget for dette** (dette inkluderer prosedyrer for somatisk undersøkelse, blodprøver, tilskudd av vitaminer og mineraler, monitorering, energi og væskemengde ved oppstart av ernæring, som brukes generelt for alle pasientene)?

- Ja  
Nei  
Vet ikke

- a. Hvis ja; hvilke prosedyrer? Beskriv:  
b. Hvis nei, hva gjøres? Beskriv:

Eventuelle kommentarer:

7. **Har du vært i kontakt med pasienter i risiko for reernæringsyndrom på din arbeidsplass?**

- Ja  
Nei

Eventuelle kommentarer:

8. **Har du sett pasienter med symptomer eller labverdier utenfor referanseverdiene (begynnende reernæringsyndrom) som følge av oppstart av reernæring?**

- Ja  
Nei

- a. Hvis ja; Hvor mange pasienter har du sett med slike symptomer (anslå)?

i. Totalt:                   stk  
ii. Det siste året:       stk

- b. Hvis ja; Hva er de vanligste symptomene eller labverdiene du har sett (nevnt de tre hyppigste)?

Svar:

- c. Hvis ja; Ble denne/disse pasientene ernært via... (fyll inn antall pasienter som ble ernært via de ulike rutene):

Vanlig mat:	stk
Sondeernæring:	stk
Intravenøs ernæring	stk
En kombinasjon av disse:	stk
Husker ikke/vet ikke:	stk

Eventuelle kommentarer:

9. **Har du på din arbeidsplass sett pasienter som har fullt utviklet reernæringsyndrom?**

Ja

Nei

a. Hvis ja; Hvor mange pasienter har du sett med reernæringsyndrom?

i. totalt: stk

ii. det siste året: stk

b. Hvis ja; Ble denne/disse pasientene ernært via...(fyll inn antall pasienter som ble ernært via de ulike rutene):

Vanlig mat: stk

Sondeernæring: stk

Intravenøs ernæring: stk

En kombinasjon av disse: stk

Husker ikke/vet ikke: stk

Eventuelle kommentarer:

10. **Opplever du at kunnskapen om reernæringsyndrom og risikoen for dette er tilstrekkelig på din arbeidsplass hos...**

a. Leger:

Ja

Nei

I varierende grad

Vet ikke

b. KEFer:

Ja

Nei

I varierende grad

Vet ikke

c. Annet helsepersonell:

Ja

Nei

I varierende grad

Vet ikke

11. **Opplever du at reernæringsyndrom eller lignende komplikasjoner er et hyppig problem i den kliniske hverdagen på din arbeidsplass?**

Ja

Nei

Vet ikke

12. **Opplever dere at pasienter går ned i vekt etter innleggelse selv om de følger oppsatt reernæringsplan?**

Ja, ofte

Ja, noen ganger

Sjelden

Nei, aldri



**13. Hva er gjennomsnittlig innleggelsestid for pasienter på din arbeidsplass?**

Svar:

**Videre følger en case, og spørsmål knyttet opp mot denne;**

*Kvinne 19 år, spiseforstyrrelser siden 14- års alder. Restriktiv anoreksi med oppkast, aktivitetstrang og misbruk av laksativer. Løs avføring/diare. Veier 28kg og har en BMI på 12,6kg/m<sup>2</sup> ved innkomst. Får i seg ca 1000kcal/dag via sonde og mat.*

*Du skal gjøre en vurdering av denne pasienten ved innleggelse.*

**14. Hvilke blodprøver ville du anbefalt å ta/rekvirert på denne pasienten (velg ut de Sviktigste)?**

- |                                     |                                     |  |                                       |
|-------------------------------------|-------------------------------------|--|---------------------------------------|
| <input type="checkbox"/> Hemoglobin | <input type="checkbox"/> Glukose    | <input type="checkbox"/> Leukocytter   | <input type="checkbox"/> Trombocytter |
| <input type="checkbox"/> Natrium    | <input type="checkbox"/> Kalium     | <input type="checkbox"/> Cystatin c    | <input type="checkbox"/> CRP          |
| <input type="checkbox"/> Kreatinin  | <input type="checkbox"/> Kalsium    | <input type="checkbox"/> Albumin       | <input type="checkbox"/> TSH          |
| <input type="checkbox"/> Fosfat     | <input type="checkbox"/> Alat       | <input type="checkbox"/> Klorid        | <input type="checkbox"/> Vit d        |
| <input type="checkbox"/> Amylase    | <input type="checkbox"/> Lipase     | <input type="checkbox"/> Homocystein   | <input type="checkbox"/> Magnesium    |
| <input type="checkbox"/> Asat       | <input type="checkbox"/> Bilirubin  | <input type="checkbox"/> Ferritin      | <input type="checkbox"/> Kobalamin    |
| <input type="checkbox"/> Hba1c      | <input type="checkbox"/> Kolesterol | <input type="checkbox"/> Triglyserider | <input type="checkbox"/> Karbamid     |

**15. Hvor mye energi/kilokalorier ville du gitt første dag?**

Svar:

**16. Hvordan ville du tilført energien de første dagene?**

- vanlig mat
- sondeernæring
- intravenøst
- en kombinasjon av disse

Eventuelle kommentarer:

**17. Hvordan ville du prostennis fordelt makronæringsstoffer (karbohydrater, fett og proteiner) de første dagene?**

Svar:

- Vet ikke, må undersøke for å finne svar på dette

**18. Hvilke tilskudd du ville gitt, og på hvilken måte(tidspunkt og tilførselsvei) de første 3 dagene?:**

	Tidspunkt		Tilførselsvei		
	Profylaktisk	Ved behov/verdier utenfor referanseområde	Per os	Intramuskulært	Intravenøst
Tiamin	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Fosfat	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Kalium	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Magnesium	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Omega 3	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Multivitamin	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Vit D	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Kalsium	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Kopper	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Selen	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Sink	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Jern	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
B-vitaminer	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Vit C	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Andre:	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Andre:	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Eventuelle kommentarer:

**19. Hvor ofte ville du anbefalt å monitorere pasienten (blodprøver og somatisk undersøkelse) de første to ukene?**

- Flere ganger daglig
- Daglig
- Annenhver dag
- 2 ganger/uke
- sjeldnere

Eventuelle kommentarer:

**20. Hvor lenge ville du anbefalt å monitorere (blodprøver og somatisk undersøkelse) pasienten utover dette?**

- Er ikke nødvendig å monitorere pasienten videre etter dette
- Til prøvene er stabile
- 1 uke
- 2 uker
- Lengre enn 2 uker

Eventuelle kommentarer:

Har du eventuelle andre kommentarer knyttet til spørreskjema eller reernæringssyndrom kan det skrives her:

Tusen takk for at du tok deg tid til å svare 😊

## 7.2 Appendix 2

### Blood tests and supplements

The blood tests presented in table 24 are not exclusively for patients at risk of RFS, but blood tests that are analysed in all patients hospitalized at a regional department of eating disorders. The answers from the blood samples could contribute to the evaluation whether a patient is at risk of developing RFS, and is an important tool in this identification.

**Table 24** Blood tests at admission for all patients hospitalized at the regional departments of eating disorders in Norway

		RASP (Oslo)	Seksjon for spiseforstyrrelser (Bergen)	RKSF (Stjørdal)	RKSF (Levanger)	RESSP (Bodø)	RSS (Tromsø)
<b>Hematology</b>	Hemoglobin	X	X	X	X	X	No procedures, at indication
	SR					X	
	Hematocrit	X					
	Leukocytes	X	X	X	X	X	
	Thrombocytes	X	X	X	X	X	
	Erythrocytes	X					
	Neutrophils		X		X		
	Eosinophils	X					
	Lymphocytes				X		
	Monocytes		X				
	MCV	X	X		X		
	MCH	X					
	Differential cell counting			X		X	
	Ferritin	X	X		X	X	
	Vitamin B12	X	X		X	X	
	Methylmalonate					X	
	Folate	X	X		X	X	
	Homocysteine					X	
	PT-INR	X	X				
	Zink		X		X		

<b>Electrolytes</b>	Sodium	X	X	X	X	X
	Potassium	X	X	X	X	X
	Calcium total	X				X
	Calcium ionized	X			X	
	Magnesium	X	X	X	X	X
	Phosphate	X	X	X	X	X
	Chloride	X	X	X	X	X
	Osmolality	X				
<b>Metabolites</b>	Bilirubin	X			X	
	Urea/carbamide	X				X
	Creatinine	X	X	X	X	X
<b>Carbohydrates</b>	Glucose	X	X		X	X
	HbA1c					X
<b>Enzymes</b>	ALAT	X			X	X
	GT	X				X
	LD	X				
	Creatine kinase	X				
	ALP	X			X	X
	Amylase	X				X
	Lipase					X
	ASAT				X	X
	Cystatin C					X
	<b>Blod gas</b>	Acid/base	X	X		X
<b>Lipids</b>	Cholesterol total	X				X
	HDL	X				X
	LDL					X
	Triglycerides	X				X
<b>Proteins</b>	Albumin	X	X		X	X
	CRP	X				X
<b>Hormones</b>	TSH	X	X	X	X	X
	FT4	X	X	X	X	X
	FT3	X				X
	PTH	X				
	Prolactin			X		X
	FSH			X		
	Estradiol			X		
	LH			X		
<b>Vitamins</b>	25OHvitD	X	X			X
	1.25OH2vitD	X				

SR: sedimentation rate, MCV: middle cell volume, MCH: mean cell hemoglobin, PR-INR: prothrombine-international normalized ratio, ALAT: alanine aminotransferase, ASAT: aspartate aminotransferase, GT: gamma-glutamyltransferase, LD: lactate dehydrogenase, ALP: alkaline phosphatase, HDL: high density lipoprotein, LDL: low density lipoprotein, CRP: C-reactive protein, TSH: thyroid stimulating hormone, FT4/FT3: free thyroxin, PTH: parathyroid hormone, FSH: follicle stimulating hormone, LH: luteinizing hormone

Table 25 gives an overview of which supplements all patients receives during hospitalization at the different regional departments. The supplements are given independently of blood test and blood levels, and are supplements to the dietary lists.

**Table 25** Supplementation of all patients at each regional department

	<b>Oslo</b>	<b>Bergen</b>	<b>Stjørdal</b>	<b>Levanger</b>	<b>Bodø</b>	<b>Tromsø</b>
<b>Calcium</b>	500mg with vitamin D*	**				**
<b>Omega 3</b>	2 capsules/day or tran	**	1 capsule/day	1 capsule/day	Yes	**
<b>Vitamin D</b>		**				**
<b>Multivitamins</b>	Nycoplus 1x1*	**	1/day	1/day	Yes	**

\*vitamin D max 20ug from supplements/day

\*\* missing data

## 7.3 Appendix 3

### 7.3.1 Procedures from RASP (Oslo)

#### 4. Medikamentell behandling:

a) Alle pasienter skal settes på følgende medisiner:

- i. Nycoplus Multivitaminer tabl. 1 x 1\*
- ii. Kalsium 500mg m. vit D\*  
Ved påvist osteoporose: 1500mg kalsium og 20µg vit D
- iii. Omega-3-kapsler 2 kapsler per dag\*  
\* Vit. D fra kosttilskudd maks 20µg/dag

b) Vurdere følgende medisiner:

- i. Fosfat tilskudd ved fare for reernæringssyndrom:  
MonoKaliumfosfat 15 mmol x 2 el. Fosfat-Sandoz 500mg x 2 forebyggende,  
tilsvarende x 3 ved hypofosfatemi.
- ii. Tiamin inj. 50 mg. daglig i 5 dager ved alvorlig under-/feilernæring  
forut for innleggelse.
- iii. Behandling av komorbide tilstander (depresjon, angst, smerter etc.).

#### 5. Vurdere [observasjonsstatus](#) og [Egenmestringstrening og permisjoner for pasient](#).

#### 6. Daglige undersøkelser:

a) Puls, blodtrykk, temperatur. Dette skal føres i kurven på medisinarke til pasienten daglig, med ansvar hos sykepleier. Hensikt er at det blir lettere å monitorere av lege.

Resultatene skal også føres på [vektbehandlingsskjema](#) som registreres i KPO.

b) Blodprøver/elektrolytter (**Mal 3**) **daglig** ved **stor** fare for reernæringssyndrom, (og 2x/uke ved moderat fare for reernæringssyndrom).

**Mal 3:** Na, K, Cl, Fosfat, Calcium total, Calcium ionisert, Mg.

## 7.3.2 Procedures from RKSF (Levanger)

Prosedyrer på å forebygge reernæringsyndrom ved RKSF:

Det er spesielt en risiko for reernæringsyndrom hos pasienter med Anoreksia nervosa med BMI>11. Heldigvis er det sjelden at vi har så dårlige pasienter innlagt. Derfor er det få av oss legene som har erfaring med dette.

Ved underernæring over tid venner kroppen seg til dette, og i det øyeblikket ernæring tilføres oppstår ubalanse. Komplikasjoner ved reernæring er vanlig og noe vi følger nøye med på. Vi forsøker å få det til mest mulig peroralt.

I oppstart av kontakten til RKSF blir pasienten undersøkt av lege gjennom en generell somatisk undersøkelse der vi ser spesielt etter tegn på underernæring- senfølger etter langvarig anoreksi.

Biokjemisk utredning:

Elektrolytter:

Natrium: oftest lav

Kalium: ofte lav spesielt ved oppkast og ved innadkvat inntak

Klorid

Ionisert kalsium

Fosfat: denne prøven er sentral i å oppdage reernæringsyndrom og et fall i denne verdien kan indikere utvikling av tilstanden

Magnesium

Albumin

Sink

Elektrolytter tas rutinemessig, men ved høyere vekt og mindre risiko for reernæringsyndrom avgrenses oftest antall prøver til Na og K. Kreatinin tas på alle, så også Hb, maskindiff, ALAT, ASAT, ionisert kalsium, glucose, jernstatus, B12, folat, stoffskifteprøver og albumin.

Ck- kan benyttes for bevegelsesbegrensning og er et uttrykk for muskelskade

EKG: tas på alle og ved funn sendes disse over til vurdering av kardiolog

Etter den første legeundersøkelsen identifiseres risikopasienter for reernæringsyndrom. Eventuell hypokalemi, hypomagnesemi, hypofosfatemi eller annen elektrolyttforstyrrelse bør korrigeres langsomt før reernæringen starter.

Klinisk viktigst: Fall i fosfat, kalium, magnesium og forbruk av tiamin.

Se- elektrolytter og fosfat kontrolleres daglig den første uka ved reernæring til høyriskopasienter, siden ukjentlig til situasjonen er stabilisert.

For de med liten- moderat risiko for reernæringsyndrom BMI 9,5-11) gis halv evt enda mer redusert spiseliste ( se vedlagt spiseliste)

Syre-base

Hemoglobin: ofte lav, men kan være falsk høy pga dehydrering. Ofte gis jernsubstitusjon parallelt med reernæring

Ferritin: Ofte lave jernlager

MCV( middel celle volum) : ofte økt MCV da beinmarg får forsinket dannelse av røde blodlegemer og de blir store og umodne

LPK: obs immunforsvaret kan bli svekket da produksjonen av hvite blodlegemer kan være svekket. Dersom verdiene på granulocytter blir svært lave kontaktes medisiner ved somatisk enhet.

Granulocytter

Lymfocytter

TPK: kan bli lav som følge av beinmargsdepresjon ( beinmargen greier ikke å produsere de cellene den skal)

B12 : kan være lav og de dårligste må få tiamin intramuskulært

Folat

TSH/FT4: ofte endringer i stoffskifte som vi som regel ser at normaliseres ved reernæring

s- glucose

ALAT, ALAT, ALP, bilirubin: Ofte forhøyet ALAT og ASAT ut fra lette hepatittforandringer under reernæringen som oftest normaliseres under behandlingsforløpet

Kreatinin: kan ofte være forhøyet ut fra prerenal nyresvikt pga at det lave inntaket også har omfattet væske

Væskebehandling:

Vurderer hydreringsgrad og risiko for hjertesvikt

Vanlig start er :

20-30 ml/kg/døgn

Etter 4 døgn 25-30 ml/kg/døgn

Farris i starten, men vanlig vann når saltbehovet er avklart

Gradvis opptrapping av ernæring og væske.

Ved alvorlig underernæring prøver vi å unngå sondeernæring. Det beste er vanlig peroral ernæring

Reernæring ved høyere risiko:

Høy risiko: BMI 9,5-11 og næringsinntak 10-15 kcal/kg/døgn siste ti døgn

Ekstremt høy risiko: BMI 7,0-9,5 og næringsinntak under 10 kcal/kg/døgn

For de med høy og ekstremt høy risiko introduseres reernæringen med næringsdrikke eller sondeernæring: 10-20 kcal/ml etter tabell

Hvis betydelig elektrolyttforstyrrelse: 10kcal/kg/døgn

Reernæring i samarbeid med medisinsk avdeling

Hyppige små måltider( 8-12 måltider/ døgn inkludert kl. 0200)

Samtidig må elektrolyttforstyrrelser kontinuerlig følges opp og korrigeres

## 7.3.3 Procedures from RESSP (Bodø)



### Reemæring til pasienter med fare for reemæringssyndrom ved Regional døgnetthet for spiseforstyrrelser hos voksne - PRK

Dokumentansvarlig: Thomas Annaniassen  
Godkjent av: Silje Fredheim  
Gyldig for: PRK-Døgnetthet spiseforstyrrelser REDE

Dokumentnummer: PR28322  
Versjon: 1

#### 1. Hensikt

Formålet med prosedyren er å ha klare retningslinjer for identifisering, forebygging og behandling av reemæringssyndrom.

#### 2. Omfang

Prosedyren er enhetsomfattende/senteromfattende, og gjelder for alt helsepersonell som vurderer pasientens væske og ernæringsstatus.

#### 3. Grunnlagsinformasjon

Reemæringssyndrom er en alvorlig komplikasjon som kan oppstå som følge av for rask reemæring av underernærte pasienter. Reemæringssyndrom gir seg utslag i elektrolytt og væskeforstyrrelser samt alvorlige somatiske symptomer. Blodprøver og somatisk status kan være normale i underernært tilstand og derfor er tett oppfølging svært viktig for å avdekke tidlige tegn på reemæringssyndrom.

Viktige markører på reemæringssyndrom er hypofosfatemi, hypokalemi og hypomagnesemi. Hjertesvikt, lungeødem og arytmer er alvorlige konsekvenser av mangeltilstander og kan være livstruende. Det å forebygge at reemæringssyndrom utvikles, er derfor svært viktig.

For å vurdere om det foreligger høy risiko for utvikling av reemæringssyndrom kan følgende kriterier brukes:

Pasienter som oppfyller en eller flere av følgende faktorer:	ELLER pasienter som oppfyller to eller flere av følgende faktorer:
BMI < 16	BMI < 18,5 kg/m <sup>2</sup>
Vekttap (uavhengig av BMI): >15 % de siste 3-6 mnd	Lite matinntak > 5 dager
Lite eller manglende matinntak i > 10 dager	Vekttap > 10 % siste 3-6 mnd
Lave serumnivåer av kalium, fosfat og magnesium før ernæring igangsettes	Bakgrunn med: misbruk av alkohol, narkotika eller medikamenter, f.eks insulin, diuretika, antacida.

#### 4. Arbeidsbeskrivelse

Lege har overordnet ansvar for risikovurdering, reemæringsplan og rehydreringsplan. Prosedyren er senteromfattende og gjelder alt helsepersonell som vurderer pasientens væske og ernæringsstatus. Den enkelte sykepleier/miljøterapeut har ansvar for gjennomføring av planene, grundige daglige observasjoner av pasientens status, og for umiddelbart å gi tilbakemelding til lege ved endringer.



## 4.1 Handling

Kostanamnese gjennomføres av lege og miljøterapeut. Somatisk undersøkelse med blodprøver og EKG før reemæring starter. Det skal dokumenteres i journal om det foreligger risiko for reemæringsyndrom og tiltak i forhold til dette.

### Ernæring

- Lege vurderer i samarbeid med klinisk ernæringsfysiolog oppstart av mat og væske og dokumenterer dette i journal
- Alvorlige elektrolyttforstyrrelser og syre-base forstyrrelse skal være korrigert før reemæring starter.
- Gi tiamin 100 mg x 1 i 3 dager eller 50 mg x 1 i 5 dager. Gis IM.
- Begynn forsiktig med 20-30 kcal/ kg/ dogn. Trappes gradvis opp over 4-7 (10) dager. Ved svært lav BMI eller lite næringsinntak skal lavere energimengde vurderes.
- Avvent øking av næring til det foreligger svar på reemæringsprøver, konsulter lege ved behov.
- Ved behov for IV ernæring skal pasienten behandles på med. avd. NLSH
- Ikke bruk brun ost, syltetøy eller dessert før pasienten er stabil og spiser A meny  
Væske: mellom 1-1,5 liter i døgnet ut fra hydreringsstilstand. Pasienten kan drikke Biola med smak og lettmeik. Ikke sukkerholdige drikker som juice, brus eller sukker/horning i te/kaffe før pasienten er stabil, og pasienten spiser A meny.

### Tilskudd

- Alltid første dose Tiamin @ I.M. før reemæring starter.
- Tilskudd av kalium, fosfat og kalsium vurderes.
- Alle skal ha tilskudd av omgea 3 og multivitamin daglig.

### Somatisk oppfølging.

- Daglige reemæringsprøver (Na, K, Mg, fosfat) til pasienten er på A meny. Senere mandag, onsdag og fredag i 21 dager eller til stabil vekt, etter det en gang per uke.
- Daglige observasjoner av ekg, puls, blodtrykk, dyspnø og ødemtvøking. Vær obs på relativ takykardi som tegn på hjertesvikt.
- Ved særdeles alvorlig tilstand vurderes daglig vekt
- Obs postprandial hypoglykemi på grunn av lave glykogenlagre

Noen pasienter trapper gradvis opp ernæring av andre grunner enn fare for reemæringsyndrom (andre somatiske hensyn, ekstrem angst for mat eller andre årsaker) Disse pasientene kan gis sukker, honning, dessert, brunost og brus, eller andre matvarer med sukker i

## 5. Feilkilder

## 6. Eksterne referanser

NICE 2006 2.BMJ, 2010; Gunarathne, McKay, Pillans, Mckinlay, Crockett  
Birmingham and Treasure: [Medical Management of Eating Disorders, 2. Edition, Cambridge University Press 2010](#)  
Mehanna HM et al 2008

## 7.4 Appendix 4

### Grunnmeny

#### Frokost

3 brødskeer med margarin + pålegg  
eller Grøt (mand-fred)  
eller Frokostblanding med melk

Til 3 skiver: 1,5 pk margarin

1 glass melk + 1 glass juice

*kl 10.30: Mellommåltid: individuelt*

#### Lunsj

Salat og rundstykke (dressing eller margarin) (hverdager)  
eller 3 brødskeer + 1 knekkebrød med margarin + pålegg

1 glass melk + 1 glass juice

*kl 14.30: Mellommåltid: Individuelt*

Til 3 skiver og 1 kn.brød:  
2 pk margarin  
Til salat: 1 pk margarin eller 1  
dressing

#### Middag

Avdelingens middag

1 glass juice/saft/melk

1 porsjon dessert eller 1 stk yoghurt (150 ml)

*kl 19.00: Mellommåltid: Individuelt*

#### Kvelds

3 brødskeer med margarin + pålegg  
eller Frokostblanding med melk

1 glass melk + 1 glass juice

Til 3 skiver: 1,5 pk margarin

**Kosttillegg:** Tran /trankapsler

## 7.5 Appendix 5

### Grunnmeny - halv

#### Frokost

1½ brødskeer med margarin + pålegg  
eller ½ porsjon grøt (mand-fred)  
eller ½ porsjon frokostblanding med melk

Til 1,5 skive: 1 pakke  
margarin

1 glass melk

*kl 10.30: Mellommåltid: individuelt*

#### Lunsj

½ porsjon salat og ½ rundstykke m/marg el dressing (hverdager)  
eller 2 brødskeer med margarin + pålegg

1 glass melk

Til 2 skiver: 1 pk margarin  
Til salat: 1 pk dressing eller 1 pk  
margarin

*kl 14.30: Mellommåltid: Individuelt*

#### Middag

½ porsjon avdelingens middag

1 glass juice/saft/melk

*kl 19.00: Mellommåltid: Individuelt*

#### Kvelds

1½ brødskeer med margarin + pålegg  
eller ½ porsjon frokostblanding med melk

Til 1,5 skive: 1 pakke  
margarin

1 glass melk

**Kosttillegg:** Tran /trankapsler