NORWEGIAN SCHOOL OF SPORT SCIENCES

Elisabeth Teinung

Body Composition and Cardiorespiratory Fitness in women with Bulimia Nervosa and Binge Eating Disorder

Effect of Physical Exercise and Dietary Therapy compared to Cognitive Behavioral Therapy

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Abstract (ENG)

Objectives: The aim of this thesis on bulimia nervosa (BN) and binge eating disorder (BED) is 1) to examine if the effect of physical exercise and dietary therapy (PED-t) on body composition (BC) and cardiorespiratory fitness (CRF) differ between BN and BED, and 2) to examine if PED-t is superior to cognitive behavioral therapy (CBT) in terms of its effectiveness on these variables.

Method: Data in this study was collected from an ongoing treatment study on women with a diagnosis of BN or BED based on the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM -5), aged between 18 and 40 years with a BMI ranging from 17.5 to 35 kg/m². Participants were recruited from the general population, screened for inclusion, and randomized to either PED-t or CBT. The sample in this study includes 81 women, 57 with BN and 24 with BED, that have conducted pre and post test of Dual-energy x-ray absorptiometry (DXA) and/or a Cardiopulmonal exercise test (CPET) between 2013 and spring 2016. Effect on BC and CRF is determined using variables for weight, BMI, fat mass (% and kg), lean mass and VO_{2max} (1·min⁻¹ and $ml\cdot kg^{-1}\cdot min^{-1}$).

Results: PED-t increased weight (2kg, p=.002), BMI (0.7kg/m², p=.003) and lean mass (1.7kg, p=<.000) in BN from pre to post treatment, and decreased fat mass (-1.8kg, p=.006; -1.9%, p=.001), and increased lean mass (1.1kg, p=.005) in BED from pre to post treatment. Compared to CBT, PED-t have a superior effect on weight (+2.8kg, p=.004) and BMI (+1kg/m², p=.004) in women with BN, as well as lean mass (+1.2kg, p=.046) in women with BED.

Conclusion: PED-t induces a significant increase in weight, BMI and lean mass in BN. In BED a significant reduction in kg and percent fat mass, and an increase in lean mass is observed. PED-t does not change CRF in either BN or BED. Women with BN in PED-t have a significant higher increase in weight and BMI, and women with BED in PED-t have a significant higher increase in lean mass, compared to CBT. No effect of PED-t on CRF is observed when compared to CBT. The clinical significance of the alteration in BC is uncertain, consequently suggesting further research on the effect of combined physical exercise and dietary therapy on anthropometric measures and CRF in BN and BED, is needed.

Abstract (NO)

Bakgrunn: Hensikten med denne studien på Bulimia Nervosa (BN) og overspisingslidelse (BED) er 1) å se på om effekten av fysisk aktivitet og kostholdsterapi (FAKT) på kroppssammensetning og kardiorespiratorisk form (CRF) er forskjellig hos behandlingssøkende kvinner med BN og BED, og 2) å undersøke om effekten av FAKT er bedre enn kognitiv adferdsterapi (CBT) på disse variablene.
Metode: Data i denne studien er samlet inn i forbindelse med en pågående behandlingsstudie på kvinner diagnostiser med BN og BED basert på kriterier fra DSM-5, i alderen 18-40 år, med en kroppsmasseindeks (KMI) mellom 17,5 og 35 kg/m². Deltakerne ble rekruttert fra den generelle befolkningen, og ble randomisert til enten FAKT eller CBT etter inklusjon. Utvalget i denne studien består av 81 kvinner, 57 med BN og 24 med BED. Alle har gjennomført både pre og post test av Dual-energy x-ray absorptiometry (DXA) og/eller kardiopulmonal arbeidsbelastningsundersøkelse (CPET) i perioden 2013 til vår 2016. Effekt på kroppssammensetning og CRF er undersøkt ved hjelp av variabler for vekt, KMI, fettmasse (% og kg), muskelmasse og VO_{2maks} (l·min⁻¹ og ml·kg⁻¹·min⁻¹).

Resultater: FAKT økte vekt (2kg, p=,002), KMI (0,7, p=,003) og muskelmasse (1,7kg, p=<,000) hos kvinner med BN fra pre til post behandling, samt reduserte fettmasse (-1,8kg, p=,006; -1,9%, p=,001), og økte muskelmasse (1,1kg, p=,005) hos kvinner med BED fra pre til post behandling. Sammenlignet med CBT hadde FAKT en overlegen effekt på vekt (+2,8kg, p=,004) og KMI (+1kg/m², p=,004) hos kvinner med BN, samt på muskelmasse (+1,2kg, p=,046) hos kvinner med BED.

Konklusjon: FAKT førte til en signifikant økning i vekt, KMI og muskelmasse hos kvinner med BN. Hos kvinner med BED ble både kilo og prosent fettmasse signifikant redusert, og muskelmassen signifikant økt. FAKT ga ingen effekt på VO_{2max} hos verken BN eller BED deltakerne. Sammenlignet med CBT førte FAKT til en signifikat høyere økning i vekt og KMI hos kvinner med BN, og en signifikant høyere økning i muskelmasse hos kvinner med BED. Ingen forskjell i effekt på VO_{2max} ble observert mellom de to behandlingsgruppene. Den kliniske relevansen av endring i variabler tilknyttet kroppssammensetning er usikker, og mer forskning er nødvendig for å kunne si noe sikkert om effekten av FAKT på antropometriske variabler og VO_{2max}.

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1 Background

There is an increase in inactivity, low physical fitness and obesity worldwide (Hallal et al., 2012; WHO, 2000). Decreased cardiorespiratory fitness (CRF), high body mass index (BMI), obesity and inactivity are proven factors independently associated with mortality (Kodama et al., 2009; McGee, 2005; Padwal, Leslie, Lix, & Majumdar, 2016; Pedersen, 2007; WHO, 1995, 2000) and increased risk of diseases such as cardiovascular disease, diabetes type 2, certain types of cancer and metabolic syndrome (Grundy et al., 2005; Haslam & James, 2005; WHO, 1995). Furthermore, obesity has been found to be associated with psychological diseases (Pereira-Miranda, Costa, Queiroz, Pereira-Santos, & Santana, 2017; Scott et al., 2007), and abdominal fat distribution seem to mediate depression (Rivenes, Harvey, & Mykletun, 2009). However, within a given BMI, mortality risk seem to decrease with higher CRF and level of physical activity (PA) (LaMonte & Blair, 2006). High life-time prevalence of overweight and obesity are reported in groups of women with bulimia nervosa (BN) and binge eating disorder (BED) (Villarejo et al., 2012). Nevertheless, body composition (BC) and CRF is not thoroughly studied in the BN and BED population. Obese binge eaters have, however, been observed to have a higher degree of insulin resistance than obese non-BED, in addition to higher BMI, waist and hip circumference, waist to hip ratio, and fat mass (FM) (Succurro et al., 2015). BED and binge eating (BE) behavior may further increase the risk of hypertension and dyslipidemia in addition to diabetes type 2 (Olguin et al., 2017; Raevuori et al., 2015). In female adolescents factors predicting overweight (body dissatisfaction, weight concern, unhealthy weight control behavior, BE, dieting) (Quick, Wall, Larson, Haines, & Neumark-Sztainer, 2013), also predict eating disorders (American Psychiatric Association, 2013; Bratland-Sanda & Sundgot-Borgen, 2013).

PA is defined as "any bodily movement produced by skeletal muscles that result in energy expenditure", and physical exercise (PE) is defined as "PA that is planned, structured and repetitive, and has as objective to improve or maintain physical fitness" (Caspersen, Powell, & Christenson, 1985). PA has an effect on the aforementioned challenges, and studies have shown indisputable evidence for PAs effect on cardiovascular risk factors, diabetes type 2 (Myers et al., 2015; Pedersen & Saltin, 2006), certain types of cancer (Pedersen & Saltin, 2006), and various components of

mental health (Pedersen & Saltin, 2006; Rebar et al., 2015). In addition, PA is considered important in weight loss strategies (though high volume is needed for clinically significant weight loss), as well as being a contributing factor for adherence to weight loss, long-term retention (Swift, Johannsen, Lavie, Earnest, & Church, 2014) and important for altered CRF (Lakoski et al., 2011; McArdle, Katch, & Katch, 2015b). PE has been observed to reduce BE and drive for thinness in BN (Sundgot-Borgen, Rosenvinge, Bahr, & Schneider, 2002). Furthermore, walking has been observed to reduce BE and BMI in obese patients with BED (Levine, Marcus, & Moulton, 1996; Pendleton, Goodrick, Poston, Reeves, & Foreyt, 2002). Further, an increase in maximal oxygen uptake (VO_{2max}) and a decrease in %FM and kgFM in bulimic patients have been detected when treating BN with PE (Sundgot-Borgen et al., 2002), and combining aerobic exercise to CBT show facilitation of recovery in BN through psychological attributes (Vancampfort et al., 2014b).

With the severe health consequences of ED, and the positive effects of PA and PE also reported in persons with ED (Levine et al., 1996; Sundgot-Borgen et al., 2002), it is reasonable to suggest that PE should be included in the treatment of ED. Exercise as a component in treatment is, however, controversial, and considered as hazardous particularly among AN and BN (Giordano, 2010). A few studies have examined the effect of combining PA/PE and/or dietary therapy (DT) to other treatment conditions (Bratland-Sanda, Martinsen, & Sundgot-Borgen, 2012; Carnier et al., 2012; Fossati et al., 2004; Pendleton et al., 2002; Vancampfort et al., 2014a), PA/PE as treatment by itself (Levine et al., 1996; McIver, O'Halloran, & McGartland, 2009; Sundgot-Borgen et al., 2002) or exercise by itself on BC and/or CRF in BN or BED (Habibzadeh & Daneshmandi, 2010). An additive effect of DT to traditional CBT treatment is supported (Brauhardt, De Zwaan, & Hilbert, 2014), but no studies have yet examined the effect of combining PE and DT by itself on recovery and/or BC and CRF variables in BN and BED. Further, studies assessing physical fitness in ED are usually conducted on AN or BN patients using a cross-sectional or a longitudinal study design (El Ghoch, Soave, Calugi, & Dalle Grave, 2013). Additionally, these studies have limitations for generalization due to small sample sizes (Bratland-Sanda et al., 2012), examining children or adolescents (Nicholls, Wells, Singhal, & Stanhope, 2002), or the participants have a history of AN (El Ghoch et al., 2013; Vaz, Guisado, & Peñas-Iledó, 2003) or low BMI (Bratland-Sanda et al., 2012). Most studies examining PA/PE and/or DT in

treatment show heterogeneous and scarcity results (Vancampfort et al., 2013; Vancampfort et al., 2014b), or is combined with CBT (Fossati et al., 2004; Pendleton et al., 2002; Vancampfort et al., 2014a). Furthermore, a lack of evidence is to be found on how BN and BED differ/equals in response to treatment using PE and/or DT. Most studies and reviews compare AN and BN, both in relation to treatment (Vancampfort et al., 2014b) and BC (Morris et al., 2004; Zipfel et al., 2001), even though certain similarities between BN and BED exist (table 1) (American Psychiatric Association, 2013). Additionally, most studies examining BED focus on the overweight and obese patients (Fossati et al., 2004; Levine et al., 1996; Pendleton et al., 2002). One study has suggested that when depression levels and age are controlled for treatment-seeking women with BN and BED are generally similar (Barry, Grilo, & Masheb, 2003). The need for increased focus on PE and altered eating behavior in treatment of ED can further be emphasized by the disruption in normal dietary patterns observed in BN and BED, and the compensatory behaviors, such as excessive exercise, in BN (American Psychiatric Association, 2013).

Exercise, energy and nutrient intake seem to be important for the health status and treatment effects of patients with ED (Mountjoy et al., 2014), and none of the existing studies using PA/PE and/or DT in treatment have shown negative outcomes (Vancampfort et al., 2013; Vancampfort et al., 2014b). Only a single study was found that examined the effect of CBT against PE or DT, indicated positive effects of exercise by itself on both BC and CRF, and as a treatment for BN per se (Sundgot-Borgen et al., 2002). However, the power of the results in the abovementioned study was too low, and neither the combination of PE and DT, nor effect in BED patients was examined. Therefore, with the current knowledge, it is evident information on this subject is lacking. Information on the physical health of people with BN and BED has shown to have deficient evidence on the physical effects of PE and DT in treatment. Moreover, CBT treatment is not expected to change either BC or CRF, and show no effect on these variables compared to PE (Sundgot-Borgen et al., 2002). Therefore the main aim of this thesis is to examine the effect of PE and DT on BC and CRF separately in BN and BED, and to compare the outcome with traditional CBT treatment.

1.1 Purpose and objectives

The main purpose of this study was to examine the effect of a Physical Exercise and Dietary Therapy intervention (PED-t) on body composition and cardiorespiratory fitness variables in women with BN and BED. Furthermore, the results are compared to the effect of Cognitive Behavioral Therapy (CBT). Based on this the following research questions are drafted.

1.1.1 Main research question

What is the effect of PED-t compared to CBT on body composition and cardiorespiratory fitness (VO_{2max}) in women with BN and BED?

1.1.2 Hypotheses

- 1. The effect of PED-t on body composition and cardiorespiratory fitness, differ between BN and BED.
- 2. Compared to CBT, the PED-t intervention has a superior effect on body composition variables and cardiorespiratory fitness in both BN and BED.

2 Theory

2.1 Eating disorders

Eating disorders such as AN, BN, BED and other specified feeding or eating disorder (OSFED) are clinically defined and recognized by the American Psychiatric Association (APA) in the "Diagnostic and Statistical Manual of Mental Disorders, 5th edition" (DSM-5) (American Psychiatric Association, 2013) as mental disorders. Diagnosing the different feeding and eating disorders are mutually exclusive (American Psychiatric Association, 2013), though fluctuation between the disorders occur (Eddy et al., 2008; Schmidt, 2003). Among European women the prevalence of ED is reported to be <1-4% for AN, <1-2% for BN and 1-4% for BED (Keski-Rahkonen & Mustelin, 2016). Prevalence varies with area, age group and ethnic origin, and in Norwegian adolescents, the prevalence of AN is reported to be 0.7%, BN 1.2% and BED 1.5% when using the DSM-4 and DSM-3 (Kjelsås, Bjørnstrøm, & Götestam, 2004). In 1995, life time prevalence of EDs in females were in comparison reported to be 0.4% for AN, 1.6% for BN and 3.2% for BED (Gotestam & Agras, 1995). It is plausible that with the introduction of DSM-5 prevalence in the general population has increased in BN and BED (Hudson, Coit, Lalonde, & Pope, 2012; Rosenvinge & Pettersen, 2014). Comorbidity in eating disorders are common, and can often complicate treatment (Keski-Rahkonen & Mustelin, 2016). Anxiety disorders and mood disorders are common, and in both AN, BN and BED depression seem to be most prevalent (Keski-Rahkonen & Mustelin, 2016). For the purpose of this thesis, BN and BED will be emphasized, considering that the women included in this study meet the criteria for BN and BED.

2.1.1 Diagnostic criteria

The two most common diagnostic manuals are the WHOs' International Classification of Diseases (ICD-10) (classification of mental and behavioral disorders 10th edition), and DSM-5. In this thesis inclusion is based on DSM-5, and the criteria from this manual are presented in table 1.

Table 1. Diagnostic criteria for BN and BED. Adapted from DSM-5 (American Psychiatric Association, 2013).

	BN	BED		
A.	 Recurrent episodes of binge eating. An episode of binge eating is characterized by both of the following: 1. Eating, in a discrete period of time (e.g., within any 2-hour period), an amount of food that is definitely larger than what most individuals would eat in a similar period of time or under similar circumstances. 2. A sense of lack of control over eating during the episode (e.g., a feeling that one cannot stop eating). 	 A. Recurrent episodes of binge eating. An episode of binge eating is characterized by both of the following: Eating, in a discrete period of time (e.g., within any 2-hour period), an amount of food that is definitely larger than what most people would eat in a similar period of time or under similar circumstances. A sense of lack of control over eating during the episode (e.g., a feeling that one cannot stop eating or control what or how much one is eating). 		
B.	Recurrent inappropriate compensatory behaviors in order to prevent weight gain, such as:	B. The binge eating episodes are associated with three (or more) of the following:		
0 0	Self-induced vomiting Misuse of laxatives, diuretics, or other	 Eating much more rapidly than normal. Eating until feeling uncomfortably full. 		
	medications	• Eating large amounts of food when not		
0	Fasting Excessive exercise	 feeling physically hungry. Eating alone because of feeling embarrassed by how much one is eating. Feeling disgusted with oneself, depressed, or very guilty afterwards. 		
C.	The binge eating and inappropriate compensatory behaviors both occur, on average, at least once a week for three months.	C. Marked distress regarding binge eating is present.		
D.	Self evaluation is unduly influenced by body shape and weight	D. Binge eating occurs, on average, at least once a week for 3 months.		
E.	The disturbance does not occur exclusively during episodes of AN	E. The binge eating is not associated with the recurrent use of inappropriate compensatory behaviors as in BN and does not occur exclusively during the course of BN or AN.		
Severity		Severity		
0	Mild: An average of 1-3 episodes of inappropriate compensatory behaviors per week Moderate: An average of 4-7 episodes of	 Mild: 1-3 binge-eating episodes per week Moderate: 4-7 binge-eating episodes per week 		
0	inappropriate compensatory behaviors per week Severe: An average of 8-13 episodes of	 Severe: 8-13 binge-eating episodes per week Extreme: 14 or more binge-eating episodes 		
0	inappropriate compensatory behaviors per week Extreme: An average of 14 or more episodes of inappropriate compensatory behaviors per week	per week		

2.1.2 Bulimia nervosa (BN)

DSM-5 define BN as recurrent episodes of binge eating characterized by both eating large amounts of food within a limited period of time, in addition to inappropriate compensatory behavior (table 1). Individuals with BN may resemble those with AN in their fear of weight gain, in their desire to lose weight, and in the level of dissatisfaction with their bodies (American Psychiatric Association, 2013). Furthermore studies have shown that about a third of BN patients have had a history of AN, and another third

have had history with previous obesity (Eddy et al., 2008; Schmidt, 2003). In treatment seeking patients, crossover from BN to AN is however not common, though BN patients with a history of AN are likely to relapse back into AN (Eddy et al., 2008). Moreover, a crossover from AN to BED is uncommon, though about 20% of treatment seeking BN patients is observed to develop BED (Eddy et al., 2010). BN patients normally range between the normal and high-normal range of the BMI scale (Hudson, Hiripi, Pope, & Kessler, 2007), though BMI tend to be lower among BN patients with a history of AN (Bardone-Cone et al., 2008; Vaz et al., 2003). In addition, women with BN and history of AN show higher levels of purging and dietary restraint than women with BN and no history of AN (Bardone-Cone et al., 2008). Patients with BN often experience menstrual irregularity or amenorrhea, though it is unsure whether these disturbances are related to low energy availability, nutritional deficiencies, weight fluctuations, or emotional distress. Sometimes, the electrolyte disturbances resulting from the purging behavior can cause serious medical problems and complications (Giordano, 2010). The health consequences of ED are presented in section 2.2.

As mentioned previously, BN is associated with normal weight and BMI. However, Masheb and White (2012) reported the prevalence of overweight to be 64% among individuals with BN in a community sample. Noteworthy, the sample had a higher prevalence of non-Caucasian (ethnic minorities) individuals than clinical studies in the US (American Psychiatric Association, 2013), and in addition a higher percentage in the non-Caucasian group was overweight (Masheb & White, 2012). Further, Villarejo et al. (2012) observed a threefold increase in obesity among BN and BED patients over a 10year period. This is a much higher increase than what has been observed among women in the general population (Villarejo et al., 2012).

2.1.3 Binge eating disorder (BED)

BED was not included in DSM before the revised manual in 2013, and is still not recognized as a mental diagnose by WHOs' ICD-10 (WHO, 1999). By DSM-5, BED is categorized by the same two base criteria as BN (recurrent episodes of binge eating characterized by large amounts of food within a limited period of time, and lack of control), but BED is not associated with the recurrent use of inappropriate compensatory behavior as seen in BN (table 1) (American Psychiatric Association, 2013).

BED most commonly occurs in normal weight to overweight and obese individuals, and life-time prevalence of obesity in BED has been observed as high as 87% (Villarejo et al., 2012). Obesity, on the other hand, is not related to BED (American Psychiatric Association, 2013). Binge eating (BE) is further associated with increased body fat (BF), weight gain, and increases in psychological symptoms, and may (for some individuals) represent a precursor phase of eating disorders. The onset of BE typically begins in adolescence or young adulthood, but can sometimes begin later. Consequently BED patients seek treatment at older age than both BN and AN (American Psychiatric Association, 2013). In contrast to BN, development of BE will often lead to dieting and restrictive eating, while BN patients often diet before the onset of their disorder (American Psychiatric Association, 2013).

2.2 Health consequences of eating disorders

A number of somatic problems coexist with eating disorders (table 2). In AN, the body weight generally reflects their restricted behavior and focus on weight control. In BN body weight can however fluctuate between all categories (Gary, 2001). Weight fluctuation is associated with increased morbidity and mortality (WHO, 1995), though has not been seen to have detrimental effect on BC (Prentice et al., 1992). However, weight regain (after significant weight loss) is associated with rapid increase of adipose tissue, indicating the favoring of lipid storage in the weight gain phase (Strohacker, Carpenter, & McFarlin, 2009). In BN, starvation over time can lead to cardiovascular abnormalities, and the hearts ability to pump blood, and the vessels ability to transport blood and deliver oxygen may be altered (Gary, 2001; Giordano, 2010). The purging behavior associated with BN can lead to loss of body fluids and electrolytes that are essential for muscle contraction and conduction of nerve impulses in the cardiovascular system (Gary, 2001). Thus, cardiovascular collapse can occur despite normal weight (Giordano, 2010). In BED, risk of overweight and obesity is most common (Keski-Rahkonen & Mustelin, 2016; Masheb & White, 2012; Villarejo et al., 2012). Health complications observed in BED are essentially the same as observed in overweight and obesity, and include increased risk of metabolic syndrome, type 2 diabetes, and cardiovascular disease (Olguin et al., 2017). In fact, beyond obesity, prospective studies have found that BED alone increase the risk of developing risk factors associated with metabolic syndrome (Olguin et al., 2017). This is further emphasized by the lifetime prevalence of diabetes type 2 at 30.9% and the increased risk of diabetes type 2 (odds

ratio [OR]: 10.8, 95% CI: 6.1-19.1) observed in women with BED. An increased incidence of new cases of diabetes type 2 has also been observed in both men and women with BED (risk ratio: 6.48, 95% CI: 3.4-12.34) (Raevuori et al., 2015). Overweight and obesity has further been associated with disordered eating in adolescence (Herpertz-Dahlmann, Dempfle, Konrad, Klasen, & Ravens-Sieberer, 2015).

Table 2. Health complications that can occur in women with eating disorders. (Gary, 2001; Mehler & Andersen, 2010; Olguin et al., 2017; Torstveit & Sundgot-Borgen, 2015)

	AN	BN	BED
Cardiovascular	Bradycardia	Mitral valve prolapse	Coronary heart
	Hypotension	Cardiomyopathy	disease
	Arrhythmias	Cardiac arrhytmia	Heart failure
	Heart failure	Heart failure	Hypertension
	Palpitations	Heart palpitations	
	Akrosyanose		
Endocrine	Hypoglycemia	Menstrual dysfunction	Menstrual
	Reduced testosterone	Irregular menses	dysfunction
	(men)/estrogen (women)	Reduced bone mass	Polycystic ovary
	levels		syndrome
	Delayed onset of puberty		Metabolic syndrome
	Menstrual dysfunction		Type 2 diabetes
	Infertility		Hyperlipidemia
	Reduced bone mass		
Fluid and	Dehydration	Dehydration	
electrolyte	Electrolyte disturbances	Electrolyte disturbances	
·	Hypokalemia	Hypokalemia	
	Muscle cramps	Muscle cramps	
	Metabolic alkalosis	Metabolic alkalosis	
Gastrointestinal	Nonfocal abdominal pain	Nonfocal abdominal pain	Diarrhea
	Swollen parotid glands	Constipation	Bloating
	Constipation	Diarrhea	Functional
	Diarrhea	Abdominal bloating	gastrointestinal
	Bloating	Frequent sore throat	symptoms/disorders
Dermatological	Hair loss	Dorsal hand callus or	
8	Dry skin, brittle hair/nails	abrasions	
	Lanugo hair	Facial petechiae (red dots	
	Yellow skin	on the face)	
	Edema (ankle)	Edema (ankle)	
Other signs	Significant weight loss	Dental and gum problems	Overweight or
0	Hypotermi	Reflux oesophagitis	obesity
	Dry, flaky, yellow skin	Swollen glands/cheeks	Sleep
	Fatigue	Fatigue	problems/disorders
	Headache	Headache	Pain conditions
	Dizziness	Depression	Asthma
	Low muscle strength (loss	Weight fluctuations	
	of muscle mass)	Low weight despite a large	
	Low back pain	food intake	
	orwood DN-bulimia por		1. 1

AN=anorexia nervosa, BN=bulimia nervosa, BED=binge eating disorder

2.3 Body composition (BC)

BC refers to the components that make up the body (Kaminsky & Dwyer, 2006; Ratamess, 2012), and is included in The American college of Sports Medicine (ACSM) definition of physical fitness (Pescatello, Arena, Riebe, & Thompson, 2014). Physical fitness is defined by ACSM as "a set of attributes that relates to the ability to perform physical activity" and have five major components; muscular strength, muscular endurance, cardiovascular-respiratory capacity, flexibility and BC (Pescatello et al., 2014). BMI is used to assess body mass relative to height, and has in a number of studies been used to determine the risk of lifestyle related diseases such as diabetes type 2, hypertension, cardiovascular disease and certain types of cancer (Pescatello et al., 2014; Ratamess, 2012). Even though BMI does not measure FM or %BF, it is widely used to determine different levels of overweight, and the practical definition of obesity is based on BMI values (WHO, 1995). Further elaboration of BMI is found in section 2.3.2.

BC should be considered an indicator of health as high %BF over lean tissue indicate obesity (Pescatello et al., 2014). Usually, we are interested in the percentage of the body that is adipose (or fatty) tissue versus the percentage that is fat free. Percent BF increase with age, but how much of the variance that is associated with factors related to lifestyle versus aging is uncertain (Kaminsky & Dwyer, 2006). Obesity, or excess BF, is closely related to a number of health risks prevalent in western societies (cardiovascular disease, peripheral vascular disease, hypertension, and diabetes) (Haff & Dumke, 2012; Ratamess, 2012), and excessive intra-abdominal (visceral) fat is in particular association (Kaminsky & Dwyer, 2006). Further, the level of excess BF, in relation to body weight, explains how body weight and disease risk connect (McArdle, Katch, & Katch, 2015a). The lower limit of essential BF in men and women differ considerably. Men are thought to have a lower limit at 3% essential fat, while women should have a lower limit at 12% (McArdle et al., 2015a). Thus, low levels of BF can be damaging (Kaminsky & Dwyer, 2006). Loss of muscle mass due to aging is termed muscle athropy, or sarcopenia. Muscle athropy can be further magnified by inactivity (McArdle et al., 2015a) or low energy availability (Mountjoy et al., 2014). Consequently depletion of muscle mass is one of the consequences related to ED (Mountjoy et al., 2014; Wells et al., 2015).

2.3.1 Choice of body composition variables and reference values

All methods measuring BC have its limitations. One of the main issues is the interpretation of the estimated BF percentage, due to the measurement methods being indirect, and the lack of evidence for upper cut off points (Heymsfield, Lohman, Wang, & Going, 2005). Further, there is no universally accepted criterion measurement method, thus, many different estimation methods have been used in the search for normative values (Kaminsky & Dwyer, 2006). McArdle et al. (2015a) present three approaches more appropriate than BMI to measure BC and BF content: 1) percent of body mass composed of fat, 2) distribution of patterning of fat at different anatomic regions, and 3) size and number of individual fat cells. In this thesis percent of body fat composed of fat will be emphasized. BMI will also be accounted for as it is a widespread method for clinicians and in research (McArdle et al., 2015a).

2.3.1.1 Body mass index (BMI)

Cut off values for BMI are standardized and the same for men and women (Pescatello et al., 2014; Ratamess, 2012), is easy calculated using height and weight, and therefore widely used (McArdle et al., 2015a). BMI cut off points are <18.5 for underweight, 25-29.9 for overweight, and >30 for obesity. Risk of disease is suggested to increase with increased BMI (Pescatello et al., 2014; Ratamess, 2012). Due to the simplicity of the calculation, BMI is of greater practical relevance to studies of sedentary, clinical and large populations and can result in wrong or inaccurate classifications when used on muscular people or athletes (Ratamess, 2012). Thus, the use of BMI in classifying fatness in individuals can result in misclassification, as varying contribution of bone mass, FM, lean mass and fluids to body weight is not accounted for (Nuttall, 2015; WHO, 1995). The components of BC may vary without consequent alteration in BMI (Heymsfield et al., 2005), and a person can have a high BMI with a very low FM, or vice versa (Nuttall, 2015). This variability has also been observed in women with BN (Probst et al., 2004). Lastly, the relationship between BMI and fatness varies with age, gender, race and fat free mass (Heymsfield et al., 2005).

2.3.1.2 Lean mass

The terms lean body mass (lean mass) and fat-free body mass (FFM) are often used interchangeably. The small percentage of essential fat equivalent to approximately 3% of body mass is included in lean body mass. FFM, however, represents the body mass

free from all extractable fat. Notably, FFM measured with DXA include both lean mass and total body bone mineral (Heymsfield et al., 2005). Lean mass increase until we reach between the age of 20-30 years, and decrease with the age of 45 years (McArdle et al., 2015a), and is thought to be highly predictable in relation to body weight. This means that during weight fluctuations, lean mass should increase as a result of increased FM, and vise versa (Prentice et al., 1992). However, more recent studies have found that this is not always the case (Beavers et al., 2011; Byrne et al., 2003). Depletion of muscle mass is associated with fatigue, impaired strength, power and thermoregulation (Bosy-Westphal & Muller, 2015). However, resistance training can reverse this process, or at least delay it (Humphries, Dugan, & Doyle, 2006). This is not to be overlooked in treatment and rehabilitation of eating disorders, where loss of muscle strength is frequently observed (Mountjoy et al., 2014).

2.3.1.3 Fat mass (FM)

The term FM consists of all extractable lipids from adipose or other tissues. Both relative BF and %BF are acceptable terms (Heyward & Wagner, 2004). FM and BF will be used interchangeably in this thesis. The recommended levels of %BF differ between men and women, and between age groups. For females aged 18-35 the recommended values are 20-28%. BF levels exceeding 35% are considered within the obesity range (Heyward & Wagner, 2004). However, McArdle et al. (2015a) suggest that body fat should not exceed 30% regardless of age (which is the borderline for obesity in younger women) as people should not become fatter as they age. Normative data suggested by GE Lunar Healthcare (2014) do however show that values increase with age.

2.3.2 Methods for measuring body composition

Methods for measuring BC have different levels of complexity (Graves, Kanaley, Garzarella, & Pollock, 2006). The techniques use a two-, three-, or four-component model. The two-component model assume that BC consist of FM and FFM (Kaminsky & Dwyer, 2006), the three-component model include bone mineral in addition to FM and FFM, and the four-component model divide FFM into water, protein and mineral components (Heymsfield et al., 2005).

Underwater Weighing (UWW) is considered the criterion or gold standard method, and is based on the two-component model. It is very accurate (standard error of estimate

[SEE] $\pm 2.5\%$), though less used in science, as it is time consuming, expensive and requires additional equipment and measure of lung volume (Kaminsky & Dwyer, 2006). Bio-electrical impedance (BIA) (SEE $\pm 3.5-5\%$) is also based on the two-component model (Graves et al., 2006). Dual-energy x-ray absorptiometry (DXA) (SEE $\pm 1.8\%$) is based on the three-component model, is non-invasive, fast and quite accurate (Heyward & Wagner, 2004; Kaminsky & Dwyer, 2006). Two-component models, such as skinfold analysis are easy accessible. Skinfold analysis, however, assumes that the amount of subcutaneous fat is directly proportional to the total amount of BF, and requires a high level of technique training (Graves et al., 2006; Heyward & Wagner, 2004). As DXA is the preferred method in this study, it will now be further emphasized.

2.3.2.1 Dual-energy x-ray absorptiometry (DXA)

DXA provides estimates of bone, fat, and lean tissue densities (Haff & Dumke, 2012; Kaminsky & Dwyer, 2006), though provide no estimate of water (Graves et al., 2006). DXA uses low-level radiation, and is capable of measuring total BC, as well as segmental scanning of the body (Kaminsky & Dwyer, 2006). In other words DXA can estimate BC at certain places on the body (Kaminsky & Dwyer, 2006), hence estimating the distribution of lean soft tissue mass, FFM, FM and bone mineral content (Heymsfield et al., 2005; Kaminsky & Dwyer, 2006). DXA assume that lean body mass has a constant hydration state and electrolyte content, thus the method is affected by hydration status and potentially limited when used on populations with changes in water (Graves et al., 2006; Ratamess, 2012). DXA may further underestimate %BF in individuals with increased abdominal AT (Graves et al., 2006), and has shown to overestimate FM and FFM in underweight ED patients compared to the 4-component model (Wells et al., 2015).

2.4 Cardiorespiratory fitness (CRF)

The cardiovascular system consists of the heart, the blood vessels and the blood, and supplies the body with oxygen and nutrients. The function of the respiratory system includes pulmonary ventilation, external respiration, and internal respiration. Together they make up the cardiorespiratory system. Cardiorespiratory fitness (CRF) is an individual's ability, or capacity, to take in, transport and utilize oxygen in relation to the body's oxygen demand (Gary, 2001; Pescatello et al., 2014). High CRF benefits blood

pressure, reduces BF and heart rate, leads to higher lactate tolerance and increases the good cholesterol (HDL) (Pescatello et al., 2014).

CRF is often referred to as maximal oxygen uptake (VO_{2max}) (DeFina et al., 2015). VO_{2max} is a measure of the highest rate at which oxygen (O_2) can be taken up and utilized by the body during maximal exercise (Bassett & Howley, 2000; DeFina et al., 2015; Haff & Dumke, 2012), and is considered the most common method for measuring training effect of endurance training (Bassett & Howley, 2000). A graded exercise test (GxT) or a cardiopulmonal exercise test (CPET) on a treadmill or cycle ergometer using indirect calorimetry is usually performed for measuring VO_{2max} , and are generally considered the best non-invasive measures of CRF. The difference between GxT and CPET is mainly the test protocol used, a stepwise protocol or a ramp protocol respectively. In addition a GxT is generally performed on apparently healthy individuals, while a CPET is performed on individuals with symptoms and signs of disease. The main purposes of the tests are for GxT quantification of aerobic capacity, exercise prescription and/or response to training, and for CPET diagnosis, risk assessment, monitoring of progress and/or response to therapeutic interventions (Cooper & Storer, 2001; Wasserman, 2012). Measuring VO_{2max} by a GxT or a CPET is widely used in both clinical settings and in sports (Bassett & Howley, 2000). Studies have shown high correlation between VO_{2max} and maximal cardiac output (Q_{max}), and provide an excellent index of the hearts capacity to pump blood (Haff & Dumke, 2012). Further, obese individuals have been shown to have a high absolute VO_{2max} and a low VO_{2max} relative to body weight, and a lower performance compared to lean individuals (Wasserman, 2012). However, existing evidence argue that expressing VO_{2max} in relative values (ml·kg⁻¹·min) for the obese population is not optimal for the clinical evaluation of the cardiorespiratory function (Aadland, Jepsen, Andersen, & Anderssen, 2013), although relative values allow for meaningful comparison between individuals with different body weight (Pescatello et al., 2014).

Recently reported normative values for VO_{2max} in the Norwegian population has been collected using CPET and a modified Balke protocol (Edvardsen et al., 2013), thus CPET is the preferred method in this study. End criteria for VO_{2max} are accounted for in section 3.4.3.

2.4.1 Limiting factors for VO_{2max}

Maximal heart rate and arterial oxygen content are unrelated to aerobic exercise capacity (Saltin & Strange, 1992). However, cardiac output (Q) and VO_{2max} have a close relationship. During whole body workout Q is the most important factor concerning limitations in VO_{2max} (Bassett & Howley, 2000). Fick principle describes how VO_{2max} is the product of Q_{max} and arteriovenous oxygen difference ((C_a-C_v) O₂ difference) (Cooper & Storer, 2001). Pathology concerning one of the determinants in Fick equation, will lead to lower VO_{2max} (Davis, 2006), and can potentially be limited by four main physiological factors: 1) The pulmonary diffusion capacity, 2) maximal cardiac output, 3) oxygen carrying capacity of the blood, and 4) skeletal muscle characteristics. Basset and Howley (2000) characterize the first three as "central" factors and the fourth as a "peripheral" factor. Q_{max} is considered the most important limiting factor, and will therefore be accounted for first.

Q_{max} is a function of maximal heart rate (HR_{max}) and stroke volume (SV) (Davis, 2006), and 70-85% of the limitation in VO_{2max} is considered to be due to Q_{max} (Bassett & Howley, 2000). Variation in SV determines VO_{2max} values, hence an increase in blood flow is the main mechanism in the increase of VO_{2max} (Bassett & Howley, 2000). The pulmonary diffusion capacity can be limited when Q_{max} is higher than what is normal. Consequently decreased transit time in the pulmonary capillaries occur and as a consequence each hemoglobin molecule carry less O₂ (Bassett & Howley, 2000). As hemoglobin is crucial in the bloods delivery of O₂ the bloods hemoglobin content can also limit VO_{2max}. Further, an increase in muscle mitochondria may lead to a slightly greater extraction of O₂ from the blood to the working muscles, and thus lead to an increase in VO_{2max}. However, the main effect of increased mitochondrial density in the muscles may be improved performance, by fat oxidation at a higher rate and decreased lactate production during exercise (Bassett & Howley, 2000). In relation to the mentioned limiting factors, any disease process affecting the O₂ and CO₂ transport chain between the air and the muscle cell can cause a reduction in VO_{2max} (as Fick's principle show) (Cooper & Storer, 2001; Wasserman, 2012).

2.4.2 Evaluation of exercise response

CPET provides information of how the pulmonary and cardiovascular system functions, and enables accurate determination of functional capacity (Harber et al., 2017). To

interpret data extracted from a CPET, one approach is to study a nine-panel display. The graphs display 9 variables related to ventilatory response (e.g., minute ventilation $[V_E]$,), cardiovascular response (e.g., cardiovascular efficiency $[VO_2/HF]$) and gas exchange response/limitations in the pulmonary system (e.g., ventilatory threshold, equivalents of VO₂ and VCO₂ $[V_E/VO_2]$, $[V_E/VCO_2]$) (Cooper & Storer, 2001; Younes & Kivinen, 1984). Maximal voluntary ventilation is further an index of ventilatory *capacity*, and breathing reserve, which is the difference between maximal voluntary ventilation and VE_{max}, is observed to be reduced in obese individuals among others (Koenig, 2001). The variables included in the nine-panel display and maximal voluntary ventilation will not be further explained, as these variables are not included in this thesis.

2.4.3 Reference values

To my knowledge only two major studies on reference values for cardiorespiratory fitness in the Norwegian population has been conducted in the previous years. E. Edvardsen et al. (2013) studied cardiorespiratory response in 759 men and women aged between 20 to 85 years, and the HUNT 3 fitness study has reported reference data in 4631 healthy men and women aged 20-90 years (Loe, Steinshamn, & Wisloff, 2014). As the protocol used in this thesis is the same as the one used by Edvardsen et al. (2013), results in this thesis will be compared with reference values presented in their study for women aged 20-39 years (table 3).

	Age		
Response	20-29	30-39	20-39 (Mean)
$\overline{\mathrm{VO}}_{2\mathrm{max}}(\mathrm{L}\cdot\mathrm{min}^{-1})$	2.66 (0.47)	2.54 (0.41)	2.6 (0.44)
VO _{2max} (ml·kg ⁻¹ ·min)	40.3 (7.1)	37.6 (7.5)	39.0 (7.3)

Table 3. Physiological response at maximal exercise for women. Adapted from Edvardsen et al. (2013)

Data presented as mean (\pm SD); VO_{2max} = maximal oxygen uptake

2.5 Eating disorders and body composition

The most consistent findings on BC are found among anorectic patients, and include loss of lean body mass and fluids (El Ghoch et al., 2013), as well as loss in bone mineral density (Zipfel et al., 2001). ED patients have also been shown to have depleted FM and FFM compared to healthy controls (Wells et al., 2015). Nevertheless, in a study from 1998 no difference in either body weight, BMI or tissue fat was found between bulimic women and controls, even when exercise history was accounted for (Sundgot-Borgen, Bahr, Falch, & Schneider, 1998). BN patients have in fact been seen to have normal values in BMI, FM and lean mass (Monteleone et al., 2005; Naessen, Carlstrom, Glant, Jacobsson, & Hirschberg, 2006; Nicholls et al., 2002; Probst et al., 2004; Sunday & Halmi, 2003; Zipfel et al., 2001). Probst et al. (2004) did however find that underweight and overweight bulimics had a lower or higher %BF respectively, and that 15 to 44% of the variance in %BF could be predicted by BMI in this population. Further, BN patients show a significant increase in visceral adipose tissue volume compared to healthy controls independent of BMI and waist circumference (Ludescher et al., 2009). This study had however a low number of participants and power.

Evidence regarding the relationship between history of AN and BC in women with BN and BED is somewhat inconsistent. A few have shown no difference in BMI and FM in individuals with BN in relation to AN history (Morris et al., 2004), while others have found that women with BN and a history of AN have reduced BMI and FM (Vaz et al., 2003). However, compared to healthy controls, women with BN and previous AN have significantly lower mean weight, BMI and FM (Morris et al., 2004; Vaz et al., 2003). Carruth and Skinners (2002) emphasize this in their study where %BF was significantly higher among age-matched controls than among adolescents with a history of eating disorders (AN, BN and AN/BN) measured with BIA, though no significant differences were observed in BMI. Using DXA the differences did however disappear (Carruth & Skinner, 2000). Even so, BMI and FM due to AN history disappear in normal weight BN patients (Vaz et al., 2003).

Obese binge eaters have shown significantly higher FM and lean body mass compared to women with BN, non-obese binge eaters and healthy controls (Monteleone et al., 2005). ED patients with lifetime obesity also show larger fluctuations in BMI, higher age at onset and longer duration of ED than ED patients without lifetime obesity, across all diagnoses (Villarejo et al., 2012). In a cross-sectional study on treatment-seeking obese women with BED, engaging in sports and recreational activities was predictive of lower BMI (Hrabosky, White, Masheb, & Grilo, 2007). Though 87% percent of their sample was inactive or insufficiently active based on ACSM recommendations (30 min/day of moderate activity at least 5 days/week or 20 min/day of vigorous activity at

least 3 days/week). This sedentary behavior in BED patients with obesity (Hrabosky et al., 2007), can enhance medical comorbidity.

2.6 Eating disorders and cardiorespiratory fitness

Overweight and obesity can have detrimental effect on the respiratory system, and thus alter pulmonary function and reduce exercise capacity (Koenig, 2001). In BED the risk of respiratory and circulatory disease is increased, and the OR for comorbid disease in the circulation system is observed to be 1.9 (CI: 1.3-2.7). In addition, comorbid obesity represents an increased risk of lifetime history of respiratory disease (OR: 1.5, CI: 1.1-2.2) compared to non-obese individuals with BED (Thornton et al., 2017).

Forney, Buchman-Schmitt, Keel, and Frank (2016) found in their qualitative review that purging is associated with both cardiovascular complications and circulatory disease, and that the purging behavior related to BN has a detrimental effect on the cardiac system. Further self-induced vomiting may lead to hypokalemia, which is associated with markers of arrhythmias and heart damage (Forney et al., 2016; Thornton et al., 2017). Along with reduced VO_{2max} people with heart failure can also experience muscle atrophy, rapid exhaustion and diminished muscle strength (Pedersen & Saltin, 2006). Exercise is also seen as a purging method in ED (American Psychiatric Association, 2013; Hausenblas, Cook, & Chittester, 2008), and aerobic activity is the most frequently reported activity (Bratland-Sanda, Sundgot-Borgen, Rø, Rosenvinge, Hoffart & Martinsen, 2010a). Notably, ED patients have been observed to underreport their level of PA compared to objectively measured PA (Bratland-Sanda et al., 2010a). Further, higher physical fitness or PA may decrease the health risk obesity represents (LaMonte & Blair, 2006), impact important health benefits beyond weight loss (Swift et al., 2014), and decrease the influence of overweight in development of eating disorders (Veses et al., 2014).

The scarce literature on ED and CRF is inconsistent. Women with AN has been observed to have higher VO_{2max} (ml·kg⁻¹·min⁻¹) than both women with BN and control (Sundgot-Borgen et al., 1998). On the other hand, no difference in aerobic fitness measured as VO_{2max} on a treadmill in women with eating disorders (AN, BN and OSFED) compared to controls is observed (Bratland-Sanda, Sundgot-Borgen, Rosenvinge, Rø, Hoffart & Martinsen, 2010c). Further, one study examining the effect

of PE on underweight and normal weight ED patients found no alteration in aerobic capacity in response to exercise (Bratland-Sanda et al., 2012). In severely obese subjects, however, a dose-response relationship between change in PA level and VO_{2max} at one year follow up after a lifestyle intervention has been observed (Aadland et al., 2013).

Due to the fact that most studies addressing PE and ED use aerobic exercise as their preferred training method, one would expect to see more studies examining the effect of aerobic exercise on CRF. To my knowledge most studies rather report effect on BMI, weight or BC variables (Fossati et al., 2004; Habibzadeh & Daneshmandi, 2010; Pendleton et al., 2002; Vancampfort et al., 2014a). Thus, the knowledge about PE and effect on CRF in BN and BED is limited.

2.7 Effect of treatment

CBT eliminates BE and purging in approximately 30-50% of all BN cases treated (Wilson, Grilo, Vitousek, & Anderson, 2007), nevertheless approximately 50% maintain symptoms at the end of treatment (Thompson, 2004). CBT has further the strongest level of evidence in treatment of BED (McElroy, Guerdjikova, Mori, Munoz, & Keck, 2015; Palavras, Hay, Filho, & Claudino, 2017). The main aim of this thesis is to examine treatment effect on variables related to BC or CRF in BN and BED, thus this chapter is limited to studies targeting effect on these variables (mainly CBT, DT and PE in different combinations).

Exercise as a part of treatment of ED is not established, albeit not surprising considering the high prevalence of excessive exercise in patients with ED (Hausenblas et al., 2008; Levallius, Collin, & Birgegard, 2017). However, Bratland-Sanda et al. (2009) reported that treatment units regularly assess PA and integrate PA in their treatment programs, though PA is seen as more relevant in treating BED than AN and BN. Notably, PE show a superior effect than CBT in alteration of BC and VO_{2max} in BN patients after 16 weeks of treatment and at 18 months follow up (Sundgot-Borgen et al., 2002). Including 12 to 24 weeks of organized PA to inpatient treatment has further been observed to increased body weight and %BF in underweight and normal weight ED patients (Bratland-Sanda et al., 2012). In overweight and obese BED patients, combined exercise and CBT, and PA alone, are the only treatment options superior to CBT in

reduction of weight, BMI and BE (McElroy et al., 2015; Palavras et al., 2017; Vancampfort et al., 2013). Yoga has further shown to reduce BMI, hip and waist measurements, in addition to increasing overall PA level in BED patients (McIver et al., 2009). Levine et al. (1996) did in addition find walking to reduce BMI in obese women with BED. CBT alone has shown no effect on either short or long-term weight loss (McElroy et al., 2015).

Studies examining treatment of ED and exercise are almost exclusively based on aerobic activity (Bratland-Sanda et al., 2012; Levine et al., 1996; Pendleton et al., 2002; Sundgot-Borgen et al., 2002; Vancampfort et al., 2014a; Vancampfort et al., 2013), and/or examining the effect of PA or PE on BC variables (Bratland-Sanda et al., 2012; Habibzadeh & Daneshmandi, 2010). Further, the use of resistance training in treatment of ED has mainly been examined in studies on individuals with AN (Fernandez-del-Valle, Larumbe-Zabala, Morande-Lavin, & Perez Ruiz, 2016; Szabo & Green, 2002; Vancampfort et al., 2014b). However, one study has examined the effect of a combination of aerobic training (30 min) and resistance training (30 min) three times a week, in addition to nutritional therapy on BMI and BC (among other) in obese adolescents with eating disorder symptoms (Carnier et al., 2012).

As previous mentioned, high life-time prevalence of obesity is observed in women with BN and BED (Villarejo et al., 2012), hence weight loss, alteration of BC and increase of oxygen uptake is of relevance. PA and/or PE are considered key components of any weight management program. A combination of resistance training and aerobic exercise is considered optimal in weight loss strategies (Schwingshackl, Dias, Strasser, & Hoffmann, 2013; Swift et al., 2014) and is expedient to counteract loss of lean mass (McArdle et al., 2015a). A 10% loss in body weight does however cause a larger decrease in daily total energy expenditure than what could be expected, and a consequent decrease in resting metabolic rate (RMR) is observed in both obese and normal-weight individuals (McArdle et al., 2015a). RMR can, however be maintained, and even increased by PA through maintenance or increase in FFM (McArdle et al., 2015a). Even though activity in itself cannot be considered the main reason for longterm weight loss (Swift et al., 2014), it has important and well documented impact on health and its variables (Myers et al., 2015; Swift et al., 2014).

There is a major gap in literature on the effect of PE and DT on physiological variables in BN, and only a few studies have compared PE and/or DT with more common treatment strategies. The only study that to my knowledge has compared the effect of CBT with PE or DT in BN is the previously mentioned study by Sundgot-Borgen et al. (2002). It was the first to show that PE potentially can have a superior effect on both psychological and physiological variables compared to CBT. Thus, it is important to further examine the effect of this potential new treatment strategy, combining the evidence-based PE and the more uncertain DT in a treatment program. This study adds to the lack of knowledge on how the combination of PE and DT is important in treatment of BN.

3 Method

3.1 Procedures

This study is a part of a PhD project. It is a randomized controlled trial, the first to examine the combined effects of guided Physical exercise and Dietary therapy (PED-t) on eating disorder recovery, and the first to use a range of biopsychosocial and economic measures. The key hypothesis in the PhD project is to examine whether a new treatment combining guided PED-t performs equal or better than Cognitive Behavioral Therapy (CBT) in terms of treatment effect on ED symptoms (Mathisen et al., 2017). The main purpose of this master thesis is to examine the effect of this treatment on BC and fitness variables.

Study- and contact information was distributed through general practitioners in Oslo, magazines and websites of the ED patient organizations, newspaper ads, social media, posters at the University of Oslo and in colleges in Oslo and Akershus counties. Interviews were made to determine whether women who took contact met the DSM-5 criteria for BN or BED (American Psychiatric Association, 2013) and the other research based criteria for inclusion (Fairburn et al., 2009) (table 4). A final inclusion was based on informed consent (section 3.5).

Inclusion	Exclusion
Women aged 18-40 years	Suicidality, ongoing or planned pregnancy
Self-reported BMI 17,5-35	during the study period, being an athlete at a
Home address requiring $\leq 1,5$ hour	national or international competition level,
driving distance	having been received CBT for EDs during the
Symptoms ranging from subclinical	last two years, and subjects needing treatment
BN and BED with duration < 3	for a comorbid personality disorder and/or
months and BN or BED episodes <	substance abuse at the start of the study.
1/week (ie. OSFED type 1-2) to	During treatment a "stop-procedure" is activated
moderately severe BN or BED, ie,	for participants with BMI <19 who reduce their
up to 4-7 episodes/week and illness	weight >2 kg, or for other participants displaying
duration \geq 3 months	an acute exacerbation of ED-symptoms

Table 4. Inclusion and exclusion criteria in the Physical Exercise and Dietary Therapy study (PED-t)

Eligible participants were allocated to either CBT or PED-t groups running in a fixed time schedule of 20 sessions over 16 weeks. Participants who were recruited while a treatment group was running were put on a waiting list control condition of equal length

(16 weeks) where they completed all baseline measures (not included in this study). All outcome variables were measured at pre, post, 6, 12 and 24 months (Mathisen et al. 2017). For the purpose of my master thesis, the data set from the two treatment groups (PED-t and CBT groups), and outcome variables measured at pre and post intervention collected in the period from fall 2013 to, and including, spring 2016 are examined.

3.1.1 Physical Exercise and Dietary Therapy (PED-t)

The PED-t intervention aims to achieve and stabilize a normal body weight, a healthy body image, improved coping and affect regulation. The intervention follow the same methodological structure as CBT, though compressed to 20 sessions over 16 weeks due to practical considerations (Mathisen et al., 2017). The PE part was designed to increase maximal strength and maximal oxygen uptake (VO_{2max}). Participants were instructed to exercise three times a week, two sessions with progressive strength training (one under supervision of personal trainers), one with progressive intervals on a treadmill. During the first week, participants were guided through the interval program and instructed to progressively increase the speed of the treadmill throughout the intervention. Some personal preferences for exercise were allowed; otherwise, the PE-program adhered to the official minimal recommendations for a healthy level of PE (Mathisen et al., 2017). After each supervised session of resistance training, a consecutive session of DT was given. The DT focused on increasing nutritional knowledge, which is based on official recommendations for a healthy diet (Nordic Council of Ministers, 2014) and consensus statements for sports nutrition (IOC concencus report, 2010). Experts from our research group (the Phd student, Elisabeth Teinung and five other bachelor and master students) with advanced training (educated in exercise science at the Norwegian School of Sport Sciences) were responsible for running the PED-t intervention (Mathisen et al., 2017)

3.1.2 Cognitive behavioral therapy (CBT)

Cognitive behavioral therapy for eating disorders, or enhanced CBT for eating disorders (CBT-E), focus on the psychopathology of the ED rather than the diagnosis itself (Fairburn, 2008). It consists of 20 sessions divided into 4 stages focusing on different aspects of recovery (Fairburn, 2008; Glasofer & Devlin, 2013). The therapy emphasizes the factors maintaining the eating disorder, rather than the cause of onset (Glasofer & Devlin, 2013). The strategy is to construct a formulation of the factors contributing to the maintenance of the patients psychopathology, and use this formula to identify the

features that need to be focused on during treatment (Fairburn, 2008) For further reading, see Fairburn (2008).

3.2 Participants

Participants were 90 normal or overweight (BMI 17,5-35) treatment-seeking adult women (age 18-40) with either BN or BED. Participants who did not conduct both pre and post tests in either physical tests or DXA measures were excluded from the study. Among the 90 participants attending the pre test, 9 did not attend the post test (figure 1). This resulted in a final sample of 81 participants (PED-t group=43, CBT group=38), included in the statistical analyzes (figure 1).

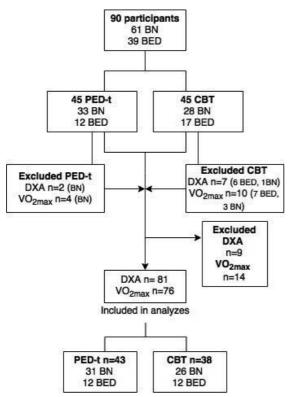


Figure 1. Flow chart of inclusion and exclusion of participants in the final analyzes. VO2max and DXA drop outs: 2 due to pregnancy, 3 because of illness, 1 because of knee arthroplasty, 3 were lost to follow up due to unknown reasons. VO2max: 1 due to hernia, 1 due to knee arthroplasty, 1 did not achieve VO2max pre, 3 were lost to follow up due to unknown reasons. BN=bulimia nervosa, BED=binge eating disorder, PED-t= Physical exercise and dietary therapy, CBT=cognitive behavioral therapy, DXA=dualenergy x-ray absorptiometry, VO2max=maximal oxygen consumption

3.3 Measures

3.3.1 Variables

The study used standardized instruments with known psychometric attributes and high clinical utility as well as biological variables acknowledged as the gold standard assessment of fitness (Maud & Foster, 2006; Pescatello et al., 2014), BC and bone health (Ackland et al., 2012). The figure displayed provides an overview of the measure points throughout the PhD study. Section 3.3.2 will elaborate the measure points relevant to my study. In this master thesis weight, BMI, FM (% and kg), lean mass, and VO_{2max} (absolute and in relation to weight) measured pre and post tests are included in the analysis.

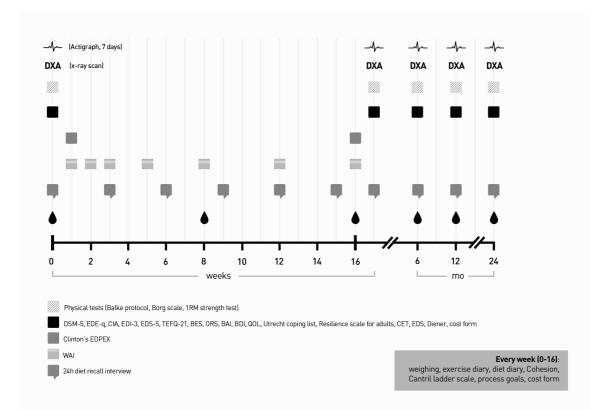


Figure 2. Measures/measure points for CBT, PED-t and wait list, conducted pre and post intervention, during intervention, and 6, 12 and 24 months after completed intervention. Physical tests (CPET and 1RM strength test), DXA, questionnaires, diagnostic interview, 24 hour diet recall interview, and a seven days objective activity measurement (actigraphGT3X) are conducted pre and post intervention, 6, 12 and 24 months after completed intervention (Mathisen et al., 2017).

3.3.2 Assessments

3.3.2.1 Body composition

Muscular strength was included as a part of the charting of the participants, and was tested through a 1RM (repetition maximum) test on three selected events (squats, bench press, seated row) (Mathisen et al., 2017). Criteria for approved conduction were set for each exercise. After each successful performance, weight increased until a failed attempt occurred. The results from this test are not included in my study, but the indirect effect of the resistance training on BC is discussed.

Dual-energy x-ray absorptiometry

BC was measured using DXA (Prodigy, GE Healthcare Lunar iDXA). DXA measure percent BF, regional and total-body measures of bone mineral density, fat content and lean tissue mass. Assessments from DXA reported in this thesis are weight (kg) and height (cm), body mass index (BMI, kg/m²), FM (% and kg), and lean mass (kg). Bone mineral density-values are not presented in this thesis.

The method is based on the principle that when two different energies (low: 40kV, high: 70 or 100 kV) are passed through a tissue, the ratio of the attenuation of the lower energy relative to the attenuation of the higher energy, can express the absorption. An X-ray tube with a filter is used to create high and low energy photons (Heyward & Wagner, 2004). Thus, to estimate bone mineral content and soft tissue composition the differential attenuation is used (Ratamess, 2012). All measurements in this thesis were standardized and performed by the same technician. The physical tests and DXA-measurements were all conducted in the laboratories at Norwegian School of Sport Sciences (NSSS) (Mathisen et al., 2017).

Body composition variables

BMI is easy calculated (BMI $(kg/m^2) = body mass (kg) / height squared <math>(m^2)$). See section 2.3.1.1 for further elaboration.

The user manual for iDXA presented by GE Lunar Healthcare provide normative data on %BF specific for the US and European citizens. The mean value for women aged 20-29 years was approximately 28.5% with a standard deviation on \pm 8%, and increased to 33.4% for women aged 45 years (GE Lunar Healtcare, 2014). However, these numbers do not specify what is considered high or low values, though corresponding to normative values suggested by both Heyward and Wagner (2004) and McArdle et al. (2015a).

FFM measured with DXA include both lean body mass and total body bone mineral (Heymsfield et al., 2005). Lean body mass consists of total body mass without FM and bone mineral mass (Bosy-Westphal & Muller, 2015; Heymsfield et al., 2005), thus lean body mass is the measure used in this thesis. To my knowledge few normative data for healthy levels of lean body mass exist. GE Lunar Healtcare (2014) does not present normative data, and several studies suggest lean body mass should be presented in relation to height (Bosy-Westphal & Muller, 2015; Hogler, Briody, Woodhead, Chan, & Cowell, 2003). However a few studies address the issue, and lean body mass in the healthy Mexican population women aged 20-49 years is observed to range from 32-35 kg (\pm 5.2) (Clark et al., 2016). In the Australian population, which is ethnically more similar to our population, mean values for women aged 20-39 is reported to be 40.9 kg (\pm 4.7) (Gould, Brennan, Kotowicz, Nicholson, & Pasco, 2014).

3.3.2.2 Cardiorespiratory fitness

Cardiopulmonary exercise testing

The cardiopulmonary exercise test (CPET) measuring VO_{2max} was conducted on a treadmill (Woodway, ELG 90/200 Sports, Weil am Rhein, Germany) with a modified Balke protocol (Edvardsen et al., 2013), performed at a constant walking speed and progressively increased inclination every minute. The "breath by breath" method was used, and the expiratory air in every breath was analyzed for volume and gas concentration in an OxyconPro analyzer (Jaeger, Würtzburg, Germany). After checking ambient temperature and humidity, gas and volume calibration of the Oxycon Pro system was conducted by using a certified calibration gas containing 15% O₂ and 6% CO₂, and a 3 liter syringe respectively.

A mask connected to the ergospirometry was adjusted and placed over the participants' nose and mouth. The participants started with three minutes habituation to the treadmill on 4% pitch angle and a speed of 4.5 km/h. After habituation, the speed was increased to 5 km/h and the inclination angle was increased to 6%. Further the inclination angle was increased by 3% every minute up to 15%. If the participant had not yet reached

exhaustion, the speed increased by 1 km/h per minute until exhaustion (or other reasons to stop the test occurred, e.g. injuries, anxiety etc.). The test should ideally have a duration of 8-12 minutes and end when the participant was totally exhausted. The participants were encouraged along the way not to give up before exhaustion.

A capillary sample for determination of blood lactate was taken one minute after completion of the test and analyzed immediately in a 1500 Sport lactate analyzer (YSI Incorporated, Yellow Springs Instruments Company, Ohio, USA) to set the degree of anaerobic contribution.

Oxygen uptake (VO₂) measured absolute ($1 \cdot min^{-1}$) and relative to body weight ($ml \cdot kg^{-1} \cdot min^{-1}$), heart rate (HR), minute ventilation (V_E), respiratory exchange ratio (RER) and breathing frequency was continuously measured throughout the test. Borg scale (Borg, 1998) was used as a subjective measure of fatigue.

End criteria for VO_{2max}

This thesis will be based on the reference values for women in the two age cohorts from the study of Edvardsen et al. (2013) that is consistent with our inclusion criteria for age (table 4). End criteria for VO_{2max} are therefore based on the recommendations in this study, in addition to the criteria of \geq 17 on Borg scale (Haff & Dumke, 2012). Hence, VO_{2max} was considered achieved when the participants reached a plateau, or one of the following secondary criteria were achieved: RER at \geq 1.10, BORG scale (\geq 17) (Haff & Dumke, 2012), or measured blood lactate (La⁻) of 7.0 mmol/L or higher (Edvardsen, Hem, Anderssen, & Reddy, 2014).

Measurement errors

Test-retest coefficients of variances in the range of 1-7% have been reported for VO_{2max} (Hopkins, Schabort, & Hawley, 2001). Carter and Jeukendrup (2002) examined the validity of three different breath-by-breath respiratory systems (breathing through a rubber mouth piece), including the Oxycon Pro system. These were compared to the gold standard of the Douglas bag method. The Oxycon Pro system provided valid and reliable measures of VO_2 , VCO_2 , and RER at workloads of 100 and 150 watt on a cycle ergometer. The coefficient of variation (CV) was 4.7-7.0% for VO_2 and VCO_2 . High correlations between the Oxycon Pro and the Douglas bag method has also been

obtained at low intensity as well as maximal intensity exercise (Rietjens, Kuipers, Kester, & Keizer, 2001). However, Foss and Hallen (2005) found in their study on the validity of Oxycon Pro using a mixing chamber (breathing through a rubber mouth piece), only a slight underestimation of the VO_2 (0.8%), as well as a lower CV (1.4%) than Carter and Jeukendrup (2002) did. This may indicate that using a mixing chamber is a better method than the breath-by-breath, though the latter is more used in both clinical and clinical research settings (Foss & Hallen, 2005).

3.4 Statistical analyses

The statistical analyzes were carried out in IBM SPSS statistics version 23. All data were checked for normal distribution. With guidance from a statistician at the Norwegian School of Sports Sciences variables that did not meet normal distribution using Kolmogorov-Smirnov, Shapiro-Wilk or log transformation, was examined using histograms and skewness index. All deviations were considered small enough to use parametric tests. Thus, categorical data are expressed as absolute numbers (*n*) and descriptive statistics are presented as mean values with the related standard deviations (SD). To compare mean group differences, an independent sample t-test was used. Mean change (Δ) between related samples was examined using a paired samples t-test. When checking for differences between PED-t and CBT pre and post intervention (diagnoses clustered together and separate) analyses of covariance (ANCOVA test) was used (simple linear regression). The level of significance was set to equal or less than 0.05 for all analyzes.

Because the data material in this study is collected from an ongoing intervention study, no sample size has been calculated. The study has therefor been done with a convenient sample, and the number of participants available when I started writing the thesis. Calculation of sample size for the original study can be found in Mathisen et al. (2017).

3.5 Ethical perspectives

All data collected in connection with the RCT from the parent PhD project are deidentified by using ID-numbers instead of names. The list connecting names to IDnumbers are destructed after the final 24-month follow up, thus completely anonymizing all data. The participants signed up for the intervention voluntarily, and signed an informed consent before inclusion. The PED-t study is approved of The Regional Ethics Committee for Medical Research Ethics (2014/420), meets the requirements of the Health Research Act and the Helsinki declaration, and is enrolled in the international database of controlled trials www.clinicaltrials.gov (NCT02079935) (Mathisen et al., 2017).

4 Results

A total of 90 women with ED participated in the intervention, 61 diagnosed with BN and 29 with BED. A final sample of 81 participants, BN=57, BED=24 (PED-t group=43, CBT group=38), is included in the study, all which have conducted DXA measures. Five out of these did not complete the physical tests either pre or post intervention and are therefore not included in the analyses on cardiorespiratory fitness (*n*=76) (figure 1, section 3.2). The participants had a mean (±SD) age of 27.9 years (± 5.2), mean height of 167.9 cm (±6.5), and mean weight of 70.6 kg (±14.6). The two groups (BN and BED) had approximately the same age (respectively 27.8±5.1 and 28.1±5.6, *p*=.772) and height (respectively 167.8±6.0cm and 168.1±7.5cm, *p*=.852), but differed in mean weight (respectively 66.2±11.4kg and 81.1±16.1kg, *p*≤.000), and BMI (respectively 23.4±3.5kg/m² and 28.7±5.3kg/m², *p*≤.000). Other baseline values for BN and BED split on intervention are found in table 5.

4.1 Pre and post values for BN and BED

*		Pre trea	tment PED-t	(<i>n</i> =43)	Post treatment PED-t (n=43)					
	BN (<i>n</i> =31)	BED (<i>n</i> =12)	Mean			BN (<i>n</i> =31)	BED (<i>n</i> =12)	Mean		
	Mean	Mean	difference			Mean	Mean	difference		
	(SD)	(SD)	\pm SD	t(df)	p-value	(SD)	(SD)	\pm SD	t(df)	p-value
BMI,	23.5	30.3	-6.8 ± 1.5	-4.0	.001**	24.2	29.9	-5.7 ± 1.8	-3.3	.005**
kg/m ²	(3.9)	(5.3)		(15.9)		(4.2)	(5.5)		(16.2)	
Fat mass	30.9	42.9	-12.1 ± 2.8	-4.3	<.000**	30.4	41.0	-10.6 ± 2.8	-3.7	.001**
(%)	(8.6)	(7.0)		(41)		(8.6)	(7.5)		(41)	
Fat mass	20.3	36.3	-16.0 ± 3.4	-4.7	<.000**	20.7	34.5	-13.8 ± 3.6	-3.8	<.000**
(kg)	(9.2)	(12.0)		(41)		(9.8)	(12.4)		(41)	
Lean	43.2	46.6	-3.4 ± 2.0	-1.7	.090	44.8	47.7	-2.9 ± 2.1	-1.4	.176
mass (kg)	(5.7)	(6.2)		(41)		(5.9)	(6.6)		(41)	
		Pre tre	atment CBT (Post treatment CBT (n=38)						
	BN	BED				BN	BED			
	(<i>n</i> =26)	(<i>n</i> =12)	Mean			(<i>n</i> =26)	(<i>n</i> =12)	Mean		
	Mean	Mean	difference			Mean	Mean	difference		
	(SD)	(SD)	\pm SD	t(df)	p-value	(SD)	(SD)	\pm SD	t(df)	p-value
BMI,	23.4	27.1	-3.7 ± 1.6	-2.4	.033*	23.1	27 (5.5)	-4.0 ± 1.7	-2.3	.035*
kg/m ²	(3.0)	(5.1)		(14.6)		(3.2)			(14.5)	
Fat mass	29.7	36.4	-6.7 ± 3.1	-2.2	.035*	28.9	36.1	-7.2 ± 3.0	-2.4	.021*
(%)	(8.0)	(10.2)		(36)		(8.1)	(9.5)		(36)	
Fat mass	19.6	27.6	-8.0 ± 3.8	-2.1	.050*	19.0 (8)	27.4	-8.4 ± 3.8	-2.2	.044*
(kg)	(7.6)	(11.9)		(15.3)			(12.1)		(15.6)	
Lean mass	43.8	43.5	-2.2 ± 2.5	-0.9	.381	44.8	45.7 (6)	-0.9 ± 1.7	-0.5	.594
(kg)	(7.2)	(7.2)		(36)		(4.4)	. /		(36)	

Table 5. Values for body composition variables pre and post intervention, split on type of treatment and diagnose.

BMI: body mass index; SD: standard deviation; PED-t: physical exercise and dietary therapy; CBT: cognitive behavioral therapy. $*p \le .05$; $**p \le .01$

There are no notable differences in BC variables between women with BN in PED-t and CBT at baseline. Women with BED in the PED-t group seem to have higher values in

BMI, %BF, kgFM, and lean mass pre and post intervention compared to the CBT group (table 5). Independent of intervention group women with BN had significantly lower BMI than those with BED both pre and post intervention, and lower FM measured in both percentage and kg pre and post intervention (table 5).

		Pre treat	tment PED-t (n=41)	Post treatment PED-t (<i>n</i> =41)					
	BN (<i>n</i> =29)	BED (<i>n</i> =12)	Mean			BN (<i>n</i> =29)	BED (<i>n</i> =12)	Mean		
	Mean (SD)	Mean (SD)	difference ± SD	t(df)	p-value ¹	Mean (SD)	Mean (SD)	difference ± SD	t(df)	p- value ¹
VO _{2max}	2.64	2.59	0.05 ± 0.17	0.3	.763	2.74	2.65	0.1 ± 0.17	0.6	.452
(l∙min ⁻¹)	(0.48)	(0.51)		(39)		(0.40)	(0.70)		(39)	
VO _{2max}	41.9	31.0 (8.0)	10.9 ± 2.7	4.1	<.000**	42.5	32.1	10.5 ± 2.8	3.7	.001**
(ml·kg ⁻¹ ·min ⁻¹)	(7.7)			(39)		(7.6)	(9.4)		(39)	
		Pre trea	ntment CBT (<i>n</i>	=35)		Post treatment CBT (n=35)				
	BN	BED				BN	BED			
	(<i>n</i> =24)	(<i>n</i> =11)	Mean			(<i>n</i> =24)	(<i>n</i> =11)	Mean		
	Mean (SD)	Mean (SD)	difference ± SD	t(df)	p-value ¹	Mean (SD)	Mean (SD)	difference ± SD	t(df)	p- value ¹
VO _{2max}	2.64	2.96	-0.3 ± 0.17	-1.9	.070	2.67	2.995	-0.33 ±	-1.9	.068
(l·min ⁻¹)	(0.47)	(0.48)				(0.50)	(0.42)	0.17	(33)	
	. /			(33)		. /	. /		. /	
VO _{2max}	40.0	40.2 (7.0)	-0.2 ± 2.4	-0.1	.921	41.2	41.1	0.05 ± 2.6	0.02	.986
(ml·kg ⁻¹ ·min ⁻¹)	(6.4)			(33)		(7.3)	(7.1)		(33)	

Table 6. Values for cardiorespiratory fitness variables pre and post intervention, split on type of treatment and diagnose.

VO_{2max}: maximal oxygen uptake; SD: standard deviation; PED-t: physical exercise and dietary therapy; CBT: cognitive behavioral therapy; ¹Independent t-test; $*p \le .05$; $**p \le .01$

Women with BN in PED-t and CBT seem to score equal in absolute VO_{2max} at baseline. Adjusted for weight, women with BN randomized to PED-t seem to score slightly higher in VO_{2max} than those randomized to CBT. Women with BED in the CBT group seem to score higher on both absolute and relative VO_{2max} values than women with BED in the PED-t group at baseline. A significant difference in VO_{2max} (ml·kg⁻¹·min⁻¹) between BN and BED participants was observed in the PED-t group, both pre and post intervention. This difference was not observed in absolute values, or between diagnoses in the CBT group (table 6).

4.2 H1: Change post intervention in BN and BED

*Table 7. Change post intervention for weight, BMI, body composition and VO*_{2max} split on diagnose.

	Δ PED-t Mean (95% CI)							Δ CBT Mean (95% CI)					
	BI	N (n=31)		BED (<i>n</i> =12)			BN (<i>n</i> =26)			BED (<i>n</i> =12)			
	Mean (95% CI)	<i>t</i> (df)	<i>p</i> -value	Mean (95% CI)	<i>t</i> (df)	<i>p</i> - value	Mean (95% CI)	<i>t</i> (df)	<i>p</i> - value	Mean (95% CI)	<i>t</i> (df)	<i>p</i> -value	
Weight (kg)	2.0 (0.8, 3.2)**	3.4 (30)	.002**	-0.9 (-2.47, 0.67)	-1.3 (11)	.234	-0.8 (-2.23, 0.72)	-1.1 (25)	.302	-0.1 (-1.96,1.69)	-0.2 (11)	.875	
BMI (kg/cm ²)	0.7 (0.26, 1.12)**	3.3 (30)	.003**	-0.4 (-0.96, 0.26)	-1.3 (11)	.232	-0.3 (-0.85, 0.23)	-1.2 (25)	.243	-0.1 (-0.72, 0.62)	-0.2 (11)	.870	
Fat mass (%)	-0.5 (-1.39, 0.44)	-1.1 (30)	.301	-1.9 (-2.89, -0.98)**	-4.5 (11)	.001**	-0.8 (-1.89, 0.29)	-1.5 (25)	.144	-0.3 (-1.82, 1.29)	-0.4 (11)	.713	
Fat mass (kg)	0.4 (-0.51, 1.34)	0.9 (30)	.366	-1.8 (-3.0, - 0.63)**	-3.4 (11)	.006**	-0.6 (-1.71, 0.44)	-1.2 (25)	.237	-0.2 (-1.60, 1.20)	-0.3 (11)	.759	
Lean mass (kg)	1.7 (1.14, 2.21)**	6.4 (30)	<.000**	1.1 (0.41, 1.79)**	3.5 (11)	.005**	1.2 (-1.25, 3.72)	1.0 (25)	.317	-0.02 (-1.01, 0.96)	-0.1 (11)	.957	
VO _{2max} (l·min ⁻¹)	0.104 (-0.7, 0.21)	1.9 (28)	.065	0.06 (-0.21, 0.32)	0.5 (11)	.648	0.03 (-0.04, 0.1)	0.9 (23)	.377	0.035 (-0.16, 0.22)	0.4 (10)	.690	
VO _{2max} (ml·kg ⁻¹ ·min ⁻ ¹)	0.6 (-1.1, 2.33)	0.7 (28)	.470	1.0 (-1.94, 4.02)	0.8 (11)	.458	1.2 (-0.59, 2.99)	1.4 (23)	.178	0.9 (-1.74, 3.57)	0.8 (10)	.459	

PED-t: Physical Exercise and dietary therapy; CBT: cognitive behavioral therapy; BMI: body mass index; VO_{2max} : maximal oxygen uptake; CI: confidence interval; * $p \le .05$; ** $p \le .01$

In the PED-t group participants with BN had a statistical significant increase in weight, BMI, and lean mass at post intervention. Participants with BED had a statistical significant reduction in FM (% and kg), and a statistical significant increase in lean mass, post intervention (table 7). No significant alterations were seen for any of the other variables examined, or in the CBT group.

4.3 H2: Between group difference in BN and BED

Table 8. Between group difference from pre to post intervention for weight, BMI, body composition and VO_{2max} split on diagnose.

	Between groups di	fference (CBT con	mpared to PED-t) mean (95%	CI)		
	BN (<i>n</i> =57)		BED (<i>n</i> =24)			
	Mean (95% CI)	<i>p</i> -value	Mean (95% CI)	<i>p</i> -value		
Weight (kg)	-2.8 (-4.64, -0.96)**	.004**	1.2 (-1.13, 3.57)	.293		
BMI (kg/cm ²)	-1.00 (-1.68, -0.33)**	.004**	0.44 (-0.45, 1.34)	.315		
Fat mass (%)	-0.4 (-1.76, 1.01)	.590	1.4 (-0.49, 3.22)	.142		
Fat mass (kg)	-1.04 (-2.43, 0.36)	.141	1.7 (-0.2, 3.59)	.078		
Lean mass (kg)	-0.3 (-2.2, 1.59)	.747	-1.2 (-2.31, -0.02)*	.046*		
VO _{2max} (l·min ⁻¹)	-0.074 (-0.2, 0.052)	.242	0.006 (-0.337, 0.348)	.972		
VO _{2max} (ml·kg ⁻¹ ·min ⁻¹)	0.3 (-2.1, 2.74)	.792	0.3 (-4.34, 4.87)	.905		

PED-t: Physical Exercise and dietary therapy; CBT: cognitive behavioral therapy; BMI: body mass index; VO_{2max} : maximal oxygen uptake; CI: confidence interval; * $p \le .05$; ** $p \le .01$

When studying the results from the two intervention groups, BN participants in the PED-t group had significantly increased their weight with 2.8 kg and their BMI with 1.0

kg/cm² compared to BN participants in the CBT group (table 8). Due to the PED-t intervention they also significantly increased their lean mass with 1.7 kg (table 7). BED participants in the PED-t group had increased their lean mass (1.2 kg) significantly more than BED participants in the CBT group. No other differences between the groups were observed when effect of diagnose was examined (table 8).

5 Discussion

The main findings in this study were 1) the effect of PED-t on BC differs between BN and BED, and 2) compared to CBT, PED-t show a statistically superior effect on certain BC variables in BN and BED. The hypotheses are partially confirmed. As expected the effect of PED-t on BC differ between the diagnoses, still surprisingly no difference in CRF is observed. Between the treatment groups, the PED-t intervention demonstrated a statistically superior effect on body weight and BMI in BN, and on lean mass in BED compared to CBT.

No other studies examining the effect of a PE and DT intervention on BC and CRF in both BN and BED was found in the process of completing this thesis. Studies as highlighted in this thesis have examined the effect of PA/PE by itself on BC and/or weight loss in BN (Habibzadeh & Daneshmandi, 2010; Sundgot-Borgen et al., 2002) and BED (Levine et al., 1996). Moreover, further examined studies have addressed effect on aerobic capacity (Bratland-Sanda et al., 2012; Sundgot-Borgen et al., 2002). Other studies have examined the effect of combining DT and/or PA/PE, with CBT in BED on BC (Fossati et al., 2004), BMI (Pendleton et al., 2002) or physical fitness (Vancampfort et al., 2014a).

5.1 Effect of PED-t and CBT in BN and BED

5.1.1 Body composition

As hypothesized, the effect of PED-t on BC is evidently different between BN and BED. Further, no effect on BC is seen in any of the diagnostic groups receiving CBT. The results of this thesis also show that women with BN have a significant different alteration in weight and BMI in the PED-t group compared to those receiving CBT, and that women with BED in the PED-t group have a significant increase in lean mass compared to women receiving CBT.

5.1.1.1 Change in body composition in BN and BED post intervention

BN participants in the PED-t group had a significant increase in weight, BMI and lean mass. In the group receiving CBT no change in any of the BC variables was found. BED participants receiving PED-t reduced the percent and kgFM, and increased lean mass. No change in BC variables in women with BED was observed for the group receiving CBT.

The findings for the participants with BN are somewhat expected. In the healthy normal weight population an adaptation to resistance training and consequently an increase in weight, BMI and lean mass has been observed (Mosti et al., 2014; Prestes, De Lima, Frollini, Donatto, & Conte, 2009; Singh, Schmitz, & Petit, 2009). Thus, as the mean BMI in our BN participants is within the normal weigh category similar adaptation to resistance training is not striking. In previous studies women with BN fall within the same BMI category as our participants (Morris et al., 2004; Naessen et al., 2006; Sunday & Halmi, 2003; Sundgot-Borgen et al., 2002; Vaz et al., 2003; Zipfel et al., 2001) indicating that this adaptation potentially can be generalized to the BN population. However, in a previous study focusing on normalizing eating habits in BN during inpatient treatment (patients received three meals a day in addition to two snacks), a different effect of treatment on BC was found. Underweight bulimics increased %BF, while a decrease was observed in normal weight and overweight bulimics (Probst et al., 2004). Furthermore, Sundgot-Borgen et al. (2002) examined the effect of aerobic exercise on BC and reported a reduction in %FM after 16 weeks of moderate aerobic exercise. In a different study, Bratland-Sanda et al. (2012) examined the effect of moderate PA (ball games, walking, Nordic walking, horseback riding, strength training) in women with eating disorders (AN, BN and OSFED) in relation to their starting BMI, and found that %FM and lean mass (kg) significantly increased among normal weight patients who had normal BF percentage at admission. The women with normal weight included BN and EDNOS diagnoses, and mean BMI and %BF in this group was equal to the baseline values in our participants. The presented discrepancy in the existing literature indicates that there is a lack of knowledge on how women with BN respond physiologically to PA/PE. As a result, the PE component in our study focused more on resistance training than the other studies mentioned, where moderate aerobic PA is the primary focus. Moreover, previous PA/PE interventions on ED patients do not follow principles for PE to increase muscle growth/lean mass and strength as suggested by ACSM (Ratamess et al., 2009). Further the aerobic exercise implemented is almost exclusively conducted on low or moderate intensity (Bratland-Sanda et al., 2012; Fossati et al., 2004; Habibzadeh & Daneshmandi, 2010; Levine et al., 1996; Sundgot-Borgen et al., 2002), while the aerobic exercise component in PED-t

focused on high intensity exercise (Mathisen et al., 2017). The increase in lean mass observed in our women with BN, contributing to an increased weight and BMI, may be due to the fact that the PE intervention program included both aerobic exercise and resistance training. Aerobic exercise is the most prevalent form of exercise observed in physically active women with BN, and is also considered as a form of compensatory behavior (American Psychiatric Association, 2013). Thus, including resistance training and consequently potentially decreasing aerobic exercise volume in our BN participants can have lead to the increase in lean mass and the absent effect on FM observed. In fact, the volume of aerobic exercise included may not have been adequate for a change in FM (McArdle et al., 2015a). Also, for this thesis energy and nutrient intake during the intervention-period is not reported. But referring to the protocol (Mathisen et al., 2017) the PED-t intervention has a focus on normalizing energy and eating behavior, and emphasize to the participants the importance of adequate energy intake to be able to exercise. This might have had an effect on change in BC variables. These differences in study design and intervention content might partially explain the discrepancy in observed effect on BC, but more research is needed to draw further conclusions.

A discrepancy in reported BMI, FM and lean mass in BN exist, and may reflect their chaotic behavior with fluctuation between dieting, binging, vomiting and other weight control measures (Gary, 2001). The relationship between frequency of compensatory behaviors in BN and %BF measured with UWW is however observed to be low (r=0.20), but significant (Probst et al., 2004). Notably, BN participants in both treatment groups have a mean %BF of 30.9%±8.6 (PED-t) and 29.7%±8.0 (CBT), which is close to what McArdle et al., (2015a) suggested as the borderline for obesity in women. In comparison, a mean BF of 33% seem to be expected for women with a BMI of \geq 25 (Gallagher et al., 2000), indicating that our BN participants might not have BF percentages far from normative values. Lower mean %BF (26.6%±4.2) in BN patients with normal BMI has however been reported (Probst et al., 2004). Considerable variation of BF at a given BMI (Probst et al., 2004) is further reported, and the association between BMI and %BF is found to be week, particularly in the normal weight BMI category (Meeuwsen, Horgan, & Elia, 2010). A constant BMI over time can thus be misinterpreted as a stable BC or weight, though loss of muscle mass, bone loss or increased adipose tissue may have occurred (Heymsfield et al., 2005). The week association between BF and BMI mentioned might explain why it is hard to detect

alteration of FM in a population that based on BMI seem to be healthy. Thus the observed increase in BMI and weight in BN, and the stable BMI in BED post intervention, give little information about the actual alterations in BC variables, and indicate the importance of reporting alterations in BC in health research.

Previous research on treatment of BED examining the effect of PA or PE on BC has to a great extent been concentrated on overweight or obese individuals (Fossati et al., 2004; Levine et al., 1996; McIver et al., 2009; Pendleton et al., 2002; Vancampfort et al., 2014a). As previously mentioned BED participants show significantly higher mean BC values than participants with BN, and fall within the obesity category with regards to %BF (McArdle et al., 2015a). With respect to these differences it is not surprising that the BED participants in the PED-t group, but not the BN participants, show a significant decrease in both percent and kgFM. Yet, it is somewhat surprising that BED participants in PED-t did not achieve weight loss or alter their BMI. However, the primary aim of the PED-t intervention was not weight loss, but weight stability during the treatment process (Mathisen et al., 2017). Nevertheless, potential reduction of BE frequency may reduce body weight in the long term, as BE alone is suggested to be a risk factor of overweight and obesity (Dingemans, Bruna, & Van Furth, 2002). Increased PA has previously been associated with a reduction in BE (Levine, 1996), and a combination with CBT has been seen to reduce both BMI and BE (Pendleton et al., 2002). Thus, it is plausible for our BED participants to show the same reduction in BE as previous studies have found, and a potential long-term weight loss can be discovered due to this reduction. However, effect on BE is not examined in this thesis.

Weight loss strategies for the overweight and obese emphasizing PA seem to favor aerobic exercise, and loss of lean mass is therefore common (Beavers et al., 2014; Mæhlum, Danielsen, Heggebø, & Schiøll, 2012; Stoner et al., 2016; Washburn et al., 2014). Inclusion of resistance training can potentially protect from depletion of lean mass (Said, Lamya, Olfa, & Hamda, 2017), and may be important in long-term weight loss as lean mass contribute to an increase in energy expenditure (Donnelly et al., 2009). Thus, the absent effect on weight loss and BMI in women with BED receiving PED-t may be a consequence of a simultaneous increase in lean mass and loss of FM, and in the long term this mechanism might alter body weight. Further, the alteration in BC represent a positive alteration, as an increase in lean mass with a simultaneous decrease in FM is expedient for the metabolic profile in the overweight and obese population (McArdle et al., 2015a). However, even though PED-t combined aerobic exercise and resistance training, which is observed to have a better effect on body weight and kgFM than either of the two alone (Schwingshackl et al., 2013), there is still uncertainty on why our BED participants did not lose weight. One plausible explanation for the absent weight loss might however be adherence to the exercise program, though this is not examined in this thesis. However, according to my personal experience as a physical trainer in the PED-t group, neither BN nor BED participants completed all of the scheduled training sessions, thus indicating that full compliance was not met in the PED-t group.

It is plausible to expect our BN and BED participants to have a history of weight fluctuations since that is an observed feature of BN (Fairburn & Cooper, 1984) and BED (Ferguson & Spitzer, 1995; Giusti, Heraief, Gaillard, & Burckhardt, 2004). Populations that are exposed to fluctuating food supplies or inadequate food intake (which may be the case for our participants) are hypothesized to have a high level of efficiency in caloric utilization or fat storage (WHO, 1995). However weight fluctuation is not observed to cause excessive loss of lean tissue (Prentice et al., 1992; Tothill & Hannan, 2004). Nevertheless, studies show that the body seems to be favoring fat accretion, rather than lean mass accretion in weight regain at one year follow up after weigh loss in women (Beavers et al., 2011; Byrne et al., 2003; Strohacker et al., 2009). This happens despite inclusion of exercise during weight loss (Beavers et al., 2011). As a consequence of the low lean mass accretion, RMR and daily total energy expenditure decrease compared to initial level (McArdle et al., 2015a). In relation to number of weight fluctuation episodes one could expect a similar effect on BC variables among our participants as Byrne et al. (2003) and Beavers et al. (2011) detected. Thus, the mentioned increase in lean mass observed in BED participants randomized to PED-t may have contributed to protection from the energy efficiency both obese and normalweight individuals experience due to weight loss strategies (McArdle et al., 2015a).

5.1.1.2 Between group difference in BN and BED

Our results show that the PED-t intervention significantly increase weight and BMI more than CBT among women with BN. BED participants in the PED-t group significantly increase their lean mass by 1.1 kg (CI: 0.41 - 1.79, p <.005) more than

BED participants in CBT. However, comparing the two interventions, no difference in change of FM is found.

As mentioned there is a major gap in literature on the effect of PE and DT on physiological variables in BN, and again to date only one study has compared and reported on the effect of PE or DT with CBT (Sundgot-Borgen et al., 2002). Our findings are however different to the results from their study, indicating that more research is needed to address whether PED-t has a superior effect on BC compared to CBT. BN participants in PED-t do however show a small, though significant, increase in weight and BMI compared to CBT. This finding is different from previous research where PE shows a superior effect in reduction of both BF and BE compared to CBT (Sundgot-Borgen et al., 2002). It can be argued that the PE part of the intervention potentially can have decreased number of binges in our BN participants, consequently weight loss, change in BMI and reduction of BF in the long term may occur. However, frequency of BE has a low but significant correlation to BMI (r=0.26) (Probst et al., 2004). Because the increase in weight and BMI in BN is quite small, and because the participants remain within the normal weight category, the increase might not be of clinical significance. One can therefore argue that these alterations do not have a negative impact on overall health, as FM seems to be stable. However these results call for further research on long-term effect of PED-t on BC in women with BN.

Initial PA/PE level in our participants is not included or controlled for, thus if the PED-t intervention contributed to increased activity level in either BN or BED participants included in this study is uncertain. Further, CBT also emphasize regular meals, moderation of binging and PA in therapy, which may have lead to changes in these behaviors in participants receiving CBT as well. If so, this might explain the quite small difference in change of BC variables between PED-t and CBT. As PE and DT were combined in this study, the method differed from the study by Sundgot-Borgen et al. (2002) where PE and DT where examined separately. In relation to the findings on how PE alone reduced %BF and BE, one can speculate in that combining the two may have lead to a temporary increase in weight, due to improved energy and nutrient intake, and consequently increased lean mass in BN. Information on diet and nutrition may also have lead to reduced BE in BN and BED and purging frequency in BN.

Further, the absent effect of PED-t on body weight and BMI observed in BED is different from what previous studies have found (Fossati et al., 2004; McIver et al., 2009; Pendleton et al., 2002). For example, Fossati et al. (2004) found that combining CBT with PE and DT lead to a significant weight loss compared to CBT and DT and CBT alone in women with BED. This discrepancy may partially be due to the fact that studies examining BED often include individuals with both BED and obesity, and partially by the fact that BMI inclusion criteria in our study range from 17.5 to 35 in BMI, leading our BED participants to have lower weight, BMI and %BF at start of intervention compared to BED participants in other studies (Fossati et al., 2004; Levine et al., 1996; Pendleton et al., 2002; Succurro et al., 2015). However, the clinical significance of the reduction in BMI and weight loss in previous studies can be questioned, as only a small loss (1-3 kg) in body weight has been observed (Fossati et al., 2004; McIver et al., 2009; Pendleton et al., 2002). Different effect on alteration of BC compared to BED participants with higher weight and BMI may therefore have a physiological explanation. However, previous studies examining CBT, PE and DT have as mentioned combined the three or examined the effect of them separately. Thus, comparing with CBT may not be the most appropriate since both groups are receiving therapy to normalize their eating habits. A waiting list control group will be examined in the PhD dissertation, but due to lack of recourses this is not examined in the present thesis.

Other treatment strategies for BED examining BC have shown inconsistent results. CBT and interpersonal therapy have shown to decrease BE both short and long term among BED patients, though no effect on weight loss or change in BC variables have been observed (McElroy et al., 2015). This is consistent with our findings of no significant alterations in any BC variables in the group receiving CBT treatment. Behavioral weight loss treatment has however shown short-term effect on BE and weight loss, but no long-term effect is observed (McElroy et al., 2015). Our results show no weight loss in the women with BED participating in the PED-t intervention. Though a positive alteration of fat and lean mass is observed, changes are too small to be of clinical significance (approximately 2% and 2kg reduction in fat mass) and do not reduce BF to healthy levels (McArdle et al., 2015a). However, a recent review indicate that %FM has a significant effect on health regardless of BMI (Padwal et al., 2016), and should therefore be seen as a strong marker of health. Thus, as BED participants in PED-t

increase lean mass compared to CBT participants, BC may be changing towards a better fat to lean mass ratio in the long term. However, in this thesis, long-term effect is not examined.

5.1.2 Cardiorespiratory fitness

Due to the absent effect on CRF in BN and BED in both treatment groups, the two hypotheses will be discussed together.

In our participants mean values at baseline for absolute VO_{2max} range within reference values proposed by Edvardsen et al. (2013). No difference is observed between BN and BED participants for absolute values, though relative to body weight BN show significantly higher mean value than BED (only in the PED-t group). Further, no significant effect of the PED-t intervention is observed for either of the groups, and consequently no difference in effect between PED-t and CBT with regards to CRF is observed. These findings are consistent with a study from 2012, where no effect on physical fitness in underweight and normal weight adult females with eating disorders was observed after on average, $14.2 (\pm 4.9)$ weeks of treatment (nutritional counseling) and 2x60 min weekly moderate PA in addition to psychotherapy) (Bratland-Sanda et al., 2012). PE is however observed to significantly increase VO_{2max} in BN post treatment, and further increase at 6 and 18 month follow up compared to CBT and DT (Sundgot-Borgen et al., 2002). These findings should however be interpreted carefully due to the observations only being reported relative to weigh $(ml \cdot kg^{-1} \cdot min^{-1})$. In fact, the observed significant decrease in %BF in the exercise group may have an impact on the observed increase in VO_{2max} at post treatment, as a decrease in body weight alone induce a higher result on VO_{2max} expressed relative to body weight (Harris, Adams, & Keith, 2006). However, VO_{2max} does not seem to be influenced by FM or body weight in obese and normal-weight adolescents (Ekelund, Franks, Wareham, & Aman, 2004), and VO_{2max} in relation to body weight is a good indicator of movement economy (Ekelund et al., 2004). One can therefore assert that the increase in VO_{2max} in relation to body weight may have practical implications to everyday health and physical capacity. It has however been suggest that VO_{2max} should be examined in relation to lean mass (Buskirk & Taylor, 1957). It is possible that a difference in VO_{2max} had been observed if this had been examined. Nevertheless, expressing VO_{2max} in relation to body weight and in absolute values may be a satisfactory indication of the general level and alteration in

CRF, in addition to being the most common way of expressing effect on VO_{2max} (Pescatello et al., 2014).

As women with BED often are overweight or obese, one may assume that more O_2 is needed to perform external work in this population. Thus, compared to normal weight individuals, less O_2 transport is available for effective external work (Wasserman, 2012). Increased RMR, and a higher resting Q have also been observed in obese individuals. This can further lead to a lower reserve in Q, and consequently reduced possibility for the body to support increased O_2 requirements from the active muscle mass during exercise (Wasserman, 2012). As the BED participants did not reduce their weight or BMI, it is possible that the absent alteration of VO_{2max} might partially be due to the mentioned mechanisms.

There are four factors considered to affect response to aerobic exercise: 1) initial level of aerobic fitness, 2) training intensity, 3) training frequency, and 4) training duration (McArdle et al., 2015b). A low correlation between VO_{2max} and the reported hours of exercise per week among bulimic patients has been reported (Sundgot-Borgen et al., 1998). This can partly explain why BN participants in the PED-t group did not show any effect on VO_{2max}. Having low energy availability may further affect the cardiovascular system and induce muscle depletion (Mountjoy et al., 2014). A combination of low energy availability and potential excessive exercise (high training frequency/intensity/duration) can explain why our participants did not increase VO_{2max}. High amounts of exercise, low energy availability, and psychological distress (e.g. high stress level, low amount of sleep and rest) may induce a longer recovery period, and potentially have a negative effect BC and VO_{2max}. However, my experience as a physical trainer for these participants indicates that widespread excessive exercise might not have been the case for our BN participants (PED-t group). Thus, another possible explanation for the absent effect on CRF may be a potential varying adherence to the exercise program among the participants. According to my experience, much indicated that the participants tended to not attend the interval training sessions more often than the resistance training sessions during the 16 weeks of therapy. For the purpose of this thesis adherence is not controlled for, but this information will be included in the PhD thesis.

In a meta analysis from 2014, the effect of low amounts of high intensity training was examined (Weston, Taylor, Batterham, & Hopkins, 2014). This study shows that high intensity training may have an adaptive effect that favors the less fit population. However the actual intensity our participants conducted their intervals on is not examined in this thesis. We did however tell our participants to keep high intensity, and to use Borg scale as an indicator of perceived exertion. Borg scale is considered a good indication of objective intensity (Borg, 1998; McArdle et al., 2015b). Further, as training frequency has an effect on adaptation to exercise and thus effect on VO_{2max}, aerobic intervals once a week, cannot be expected to change aerobic capacity or BC (McArdle et al., 2015b). Genetics, nutritional status, menstrual and hormonal irregularities, training history, and the interventions low amount of aerobic training can therefore explain the absent effect (McArdle et al., 2015a). Other studies examining CRF in eating disorders should therefore control for exercise status, energy availability, history of eating disorders, and exercise beyond what is intended by the researcher. In the introduction to this thesis, it is proposed that CBT probably have no effect on BC or CRF. In relation to CRF, CBT does not impose participants to conduct structured PE with the aim of increasing CRF. Thus, one cannot expect the participants to increase VO_{2max} as no change in their exercise routine is imposed.

5.2 Limitations

5.2.1 Sample and inclusion

In this study there are a number of limitations connected to the sample that needs to be addressed. Method for inclusion of participants, inclusion criteria, and the PED-t treatment may have affected the characteristics of the women signing up to participate in the study.

It is plausible to say that the study may have appealed to younger women. This is also evidenced by the inclusion criteria setting an upper limit for age on 40 years and a lower limit at 18 years. This may have resulted in including younger women with shorter duration of illness, preferably with BN, as BED patients are less likely to seek treatment, and often have a long duration of illness when they do (Hudson et al., 2007; Striegel-Moore et al., 2001). The upper limit of BMI being 35 kg/m² may further have attracted more BN patients than BED patients as BED patients are observed to have a higher BMI compared to BN (American Psychiatric Association, 2013; Striegel-Moore

et al., 2001). Since the main aim of the study was to examine the effect of a PE and DT program, the treatment-seeking women in this study may further have wanted this type of treatment, and the sample may therefore differ from a community sample of women with BN and BED. In addition the study did only include women with BN and BED resident in the eastern part of Norway, and 10-15.6% of the initial participants were excluded in the analyzes for different reasons (figure 1). In the screening process the women applying for inclusion self-reported their BMI. A few of the participants included underreported their BMI in the inclusion interview, which happened by phone. Two of these are included in this study due to lack of BED participants and ethical considerations. The BMI of these women with BED was higher than our inclusion criteria at 35 kg/m² (BMI at 36.7 and 38.9). The inclusion of these may potentially affect the mean BMI, weight, kg and %BF reported in this study, and this is important to be aware of. There is uncertainty on whether the excluded participants differ from the included. However, the BED participants excluded were all randomized to CBT leading to the number of BED participants in each group to level out, suggesting that the attrition did not lead to systematic bias.

Further, all participants were treatment-seeking women from the eastern part of Norway. Due to being treatment-seeking, it is plausible to believe that these women differ from women with BN or BED not seeking treatment (treatment-seeking in BED is uncommon (Striegel-Moore et al., 2001)). Thus, in relation to the latter and all the other mentioned limitations one should be careful to generalizing the results from this thesis to all women with BN and BED.

In this thesis a calculation of sample size has not been conducted. However, as mentioned, in the protocol for the ongoing PhD a sample size is suggested (Mathisen et al., 2017). Thus in relation to their calculations, the sample size in this thesis is too small to be representative of the population, and to draw conclusions regarding the actual treatment effect of the two interventions. Further, because the participants are split into intervention groups, and further into groups based on diagnose, each intervention group ended up with an even lower number of participants with BN and BED. However, regarding variables related to BC and VO_{2max} one might say that fewer participants in the sample are necessary to be able to generalize effect on these variables.

Even though this thesis is based on a convenience sample, and all of the participants included have done both the pre and post tests, no data on whether or not the participants adhered to their treatment program is included in this thesis. However, the participants were encouraged to adhere to the three weekly sessions of resistance and endurance training. Thus, if the participants failed to show up and receive the treatment they were supposed to, or if they did more than what was expected, it is not controlled for. Further, the participants in the CBT group may have participated in PA or PE on their free time. Both of these factors can be possible issues, as exercise in BN is observed as a form of purging behavior (American Psychiatric Association, 2013), and likely to affect the measured effect of both PED-t and CBT on BC and CRF. Further, this thesis does not control for actual food intake. Thus, participants may not have implemented the advices they have been given, and this may further have affected their adaptation to exercise.

History of AN in BN is not accounted for in this thesis. Studies on BC in which it has BN patients with and without history of AN has been compared, and have inconsistent findings in regards to weight, BMI and percent FM (Morris et al., 2004; Sullivan, Bulik, Carter, Gendall, & Joyce, 1996; Vaz et al., 2003). The significance of subdividing BN patients in relation to AN has further been discussed, as the similarities seem to outweigh the differences (Sullivan et al., 1996). However, women with BN and a history of AN seem to differ in levels of eating pathology, with higher levels of purging and dietary restraint than women with BN and no history of AN (Bardone-Cone et al., 2008). Thus, eating disorder history in our participants could have been interesting to examine.

5.2.2 Intervention

The PED-t intervention had a focus on resistance training rather than aerobic exercise for the purpose of motivation and facilitation of mastery, as well as introducing a different form of exercise than aerobic training. Thus, no alteration in VO_{2max} , due to low volume in aerobic exercise, could be expected even though it was purposed in the project proposal (Mathisen et al., 2017). Further, the PE included in the PED-t intervention is thought to adhere to the official minimum recommendations for healthy levels of PA (Mathisen et al., 2017). This recommendation is however though to maintain physical fitness, rather than increasing the level (Donnelly et al., 2009), thus

indicating that additional PE had to be implemented to expect changes in the fitness level of our participants.

Data on adherence to the intervention, or activity level in general, is not included in this thesis, and may be a limitation to the study as mentioned. Though, on the other hand, the results may reflect the effect of PED-t and CBT in an actual therapy setting, as full adherence cannot be expected in a real life situation. Further, it is plausible to expect the majority of women with BN to adhere to at least some sort of exercise independent of treatment, as previous research has found BN patients to exercise (both compulsively and excessively) (American Psychiatric Association, 2013; Levallius et al., 2017). Thus, it would have additional value for this study to examine training logs and/or objective measures of PA for participants in both PED-t and CBT.

5.2.3 DXA

DXA is considered a valid and reliable method to measure BC (Heymsfield et al., 2005; Heyward & Wagner, 2004; Ratamess, 2012), and has a standard error of estimate on $\pm 1.8\%$, which is lower than what has been reported for both BIA and UWW (Graves et al., 2006). However, overestimation of %BF and lean mass may occur when used on underweight ED patients (Tothill & Hannan, 2004; Wells et al., 2015), and underestimation may occur when examining severely obese populations (Graves et al., 2006). This may have lead to underreporting of %BF in the heaviest subjects in this study.

5.2.4 CPET

The Oxycon Pro system is considered valid and reliable in measuring VO₂, VCO₂, and RER. However, the "breath by breath" method used in this study has a slightly greater CV than the use of a "mixing chamber" (Carter & Jeukendrup, 2002; Foss & Hallen, 2005). And test-retest CV is observed to be as high as 7% (Hopkins et al., 2001) indicating that post-test results can be greatly affected by measurement errors. Not all participants had the motivation to achieve actual VO_{2max}, and in addition the high increase of inclination angle in the protocol could have lead to a premature termination. Further, the population studied is diverse, where anxiety, stress and large difference in body size can have an effect on the VO_{2max} (Howley, Bassett, & Welch, 1995). Further, "the effect of learning" may lead to a greater VO_{2max} at post and follow-up tests despite

no actual change in VO_{2max} . Underestimation of VO_{2max} may also occur due to the participants not being familiar with walking/running on a treadmill. This is however controlled for through measures of RER, blood lactate and BORG scale. Though, to my knowledge Borg scale has not been validated for women with ED.

5.2.5 Statistical analyses

Statistical processing of available data may affect the results in several directions. First, the small sample size in each group may affect the effect size and significance. Second, parametric tests were conducted on all variables despite skewed normal distribution. Even though this was decided under supervision of a statistician, it may have affected the interpretation of my results. Third, the exclusion of participants who did not conduct both pre and post test may have lead to different values on BC variables and CRF. However, as they were lost to follow up for different reasons their participation to therapy may not have been satisfactory to expect effect after all.

5.3 Practical implications

Our study substantiates the results from the previously mentioned study from Sundgot-Borgen et al. (2002) in the superior effect of PE in altering BC compared to CBT. Exercise and DT have been reported to alter BC and CRF in healthy women with and without excess BF (Baker, Sirois-Leclerc, & Tulloch, 2016; Garber et al., 2011; Mosti et al., 2014; Stoner et al., 2016). This study indicates that similar effects appear in women with BN and BED with regards to BC, but not CRF. Sundgot-Borgen et al. (2002) suggest in their study that a certain training intensity is required to accomplish increased fitness and reduced BF. The present study may indicate similar findings as BC but not CRF is altered due to the PED-t intervention. The low amount of aerobic exercise may be the reason for the absent effect on CRF, as exercise volume is an important predictor for increased VO_{2max} (Garber et al., 2011; McArdle et al., 2015b).

The small alteration in BC variables and the absent alteration in CRF indicate the complexity of an eating disorder diagnose. One can speculate whether normalization of eating habits and exercise volume has a more profound effect on the psychological parameters coexisting with eating disorders, than the physiological aspects related to the conditions. This suggestion may be supported by existing literature. In fact, combining CBT with either DT or PE, or both, provides additional effect to several components

related to the particular eating disorders (e.g. number of binges, depression, anxiety, loss of control eating, body dissatisfaction, and drive for thinness) (Fossati et al., 2004; Levine et al., 1996; Pendleton et al., 2002; Sundgot-Borgen et al., 2002; Vancampfort et al., 2014a). However, studies have also shown supporting evidence for the effect of exercise on physiological variables as well (e.g. altered BC and increased VO_{2max}) (Bratland-Sanda et al., 2012; Sundgot-Borgen et al., 2002). As the primary goal of the PhD study was recovery from ED, one can argue that the effect on BC and VO_{2max} may only represent an additional effect to treatment.

Research on the effect of PE and DT on physiological variables in BN and BED may help us to further investigate how to reverse comorbidity and the severe health consequences of the destructive behavior related to these disorders. This thesis contributes to the lack of evidence on alteration of BC and CRF in BN and BED. Further, as the presence of comorbidity in BED is not simply due to the effects of obesity (e.g. components of metabolic syndrome) (Thornton et al., 2017), the importance of engaging individuals with BED in PA and healthy eating behavior, independent of BMI, should be further investigated. For further research it would also be interesting to look at the relationship between BC and VO_{2max} in this population, and potentially subdivide BN and BED in relation to either BMI or %BF. Moreover, pending the results from the ongoing PhD dissertation, one can further speculate in if a more flexible choice of type of activity/exercise would increase adherence, and potentially effect size.

6 Conclusion

In women with BN PED-t produced a significant increase in weight, BMI and lean mass, but had no effect on percent and kg fat mass. In women with BED PED-t produced a significant reduction in kg and percent fat mass, in addition to a significant increase in lean mass. PED-t did not change VO_{2max} in either BN or BED.

Compared to CBT, the PED-t intervention produced a significant higher increase in weight and BMI in women with BN, and a significant higher increase in lean mass in women with BED. No effect on VO_{2max} was observed.

The clinical significance of the alteration in body composition is uncertain, and it is therefore a need for further research on the effect of physical exercise and dietary therapy on anthropometric measures and cardiorespiratory fitness in BN and BED. Further, results can only be generalized to treatment-seeking women, equal to our included participants.

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Abbreviations

ACSM	American College of Sports Medicine
AN	Anorexia Nervosa
ANCOVA	Analyses of covariance
APA	American psychiatric association
AT	Adipose tissue
BC	Body composition
BE	Binge eating
BED	Binge eating disorder
BF	Body fat
BIA	Bio-electrical impedance
BMI	Body mass index
BN	Bulimia Nervosa
СВТ	Cognitive behavioral therapy
CI	Confidence interval
CO ₂	Carbon dioxide
CPET	Cardiopulmonal exercise test
CRF	Cardiorespiratory fitness
CV	Coefficient of variation
DSM-5	Diagnostic and Statistical Manual of Mental Disorders, 5 th edition
DXA	Dual-energy x-ray absorptiometry
ED	Eating disorder
OSFED	Other Specified Feeding and Eating disorder
FM	Fat mass
FFM	Fat free mass
GxT	Graded exercise test

HR	Heart rate
ICD-10	International Classification of mental and behavioral disorders, 10^{th} edition
OR	Odds ratio
O ₂	Oxygen
PA	Physical activity
PE	Physical exercise
PED-t	Physical Exercise and Dietary Therapy
Q	Cardiac output
Q _{max}	Maximal cardiac output
RCT	Randomized controlled trial
RER	Respiratory exchange ratio
RM	Repetition maximum
RMR	Resting metabolic rate
RT	Resistance training
SD	Standard deviation
SEE	Standard error of estimate
SV	Stroke volume
UWW	Underwater weighing
VCO ₂	Carbon dioxide output
\mathbf{V}_{E}	Minute ventilation
V E _{max}	Maximal minute ventilation
VO ₂	Oxygen uptake
VO _{2max}	Maximal oxygen uptake
Δ	Mean change

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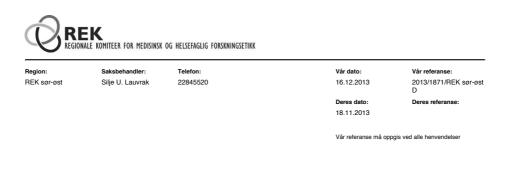
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Appendix

- 1. Approval from The Regional Ethics Committee for Medical Research Ethics
- 2. CPET protocol

Appendix 1. Approval from The Regional Ethics Committee for Medical Research Ethics



Til Jorunn Sundgot-Borgen

2013/1871 Behandling av spiseforstyrrelser: - en randomisert, kontrollert prospektiv studie

Vi viser til tilbakemelding fra prosjektleder, mottatt 18.11.2013, i forbindelse med ovennevnte søknad. Tilbakemeldingen ble behandlet av komiteens leder på delegert fullmakt.

Forskningsansvarlig: Norges Idrettshøgskole Prosjektleder: Jorunn Sundgot-Borgen

Prosjektomtale

Konrollerte behandlingsstudier, samt oversiktsartikler, viser at kognitiv terapi har et godt kunnskapsgrunnlag og er et førstevalg i behandling av bulimi, uspesifikke spiseforstyrrelser og overspisingslidelse. Søkers forskningsgruppe har i tidligere studier vist at terapeutisk ledet fysisk aktivitet reduserte bulimisymptomer like godt som kognitiv terapi, men at også kostrådgivning hadde effekt. Dette kan bety at kostrådsgivning pluss fysisk aktivitet kan ha en additiv effekt som kan være like god eller bedre enn den man ser ved kognitiv terapi. Formålet med den omsøkte studien er å teste ut effekten av tre ulike behandlingsformer: 1) kognitiv terapi, 2) fysisk aktivitet og kostveiledning og 3) kontrollgruppe med behandling som vanlig hos fastlege. Det skal inkluderes 105 kvinner i alderen 18-35 år, og det skal gjøres en rekke tester som måler fysisk aktivitet, samt DXA-målinger av beinmineraltethet, fettprosent og fettfri kroppsvekt. Studien skal måle effektendringer over 36 måneder og ta utgangspunkt i symptomendringer, brukertilfredshet og helsekostnader.

Saksgang

Søknaden ble første gang behandlet i møtet 23.10.13, hvor komiteen utsatte vedtak i saken.

Slik komiteen oppfattet søknaden, er kognitiv terapi antatt å være mest effektiv for pasienter med spiseforstyrrelser. Komiteen var derfor bekymret for om pasienter som ikke ble inkludert i denne armen, ble fratatt best mulig behandling, og ba prosjektleder redegjøre for om det var etisk forsvarlig å la en gruppe deltakere gå i tre år uten å få kognitiv terapi.

Prosjektleders tilbakemelding ble mottatt 18.11.2013.

Komiteens vurdering

Når det gjelder spiseforstyrrelser, er det god dokumentasjon på at kognitiv terapi er effektiv. I en randomisert studie skal kontrollgruppen vanligvis få beste behandling, dersom en slik finnes. I dette tilfellet vil imidlertid den realistiske kontrollgruppen være deltakere som får behandling via fastlege, siden de fleste ikke har tilgang til kognitiv terapi. Prosjektleder argumenterer godt for at alle de tre behandlingsalternativene (kognitiv terapi, fysisk aktivitet og kostveiledning, og behandling som vanlig hos fastlege) er vist å ha effekt. På bakgrunn av prosjektleders tilbakemelding mener komiteen at prosjektets design er etisk forsvarlig.

Besøksadresse: Gullhaugveien 1-3, 0484 Oslo Telefon: 22845511 E-post: post@helseforskning.etikkom.no Web: http://helseforskning.etikkom.no/ All post og e-post som inngår i saksbehandlingen, bes adressert til REK sør-øst og ikke til enkelte personer

Kindly address all mail and e-mails to the Regional Ethics Committee, REK sør-øst, not to individual staff Komiteen anser beredskapen i prosjektet som tilfredsstillende ivaretatt. Dersom det fremkommer at en deltaker har en aktiv suicidalproblematikk, kontaktes psykiatrisk legevakt. Det vil også være en stopp-prosedyre for deltakere som ved studiestart har BMI <19 og som taper seg mer enn 2 kg. Tiltakene som gjøres dersom noen deltakere opplever ubehag ved å bli filmet under gruppeterapien er også tilfredsstillende.

Etter en helhetlig vurdering har komiteen kommet til at den godkjenner at prosjektet kan gjennomføres som beskrevet i søknad og protokoll.

Vedtak

Med hjemmel i helseforskningsloven § 9 jf. 33 godkjenner komiteen at prosjektet gjennomføres.

Godkjenningen er gitt under forutsetning av at prosjektet gjennomføres slik det er beskrevet i søknad, protokoll, tilbakemelding fra prosjektleder og de bestemmelser som følger av helseforskningsloven med forskrifter.

Tillatelsen gjelder til 31.12.2017. Av dokumentasjonshensyn skal opplysningene likevel bevares inntil 31.12.2022. Opplysningene skal lagres avidentifisert, dvs. atskilt i en nøkkel- og en opplysningsfil. Opplysningene skal deretter slettes eller anonymiseres, senest innen et halvt år fra denne dato.

Forskningsprosjektets data skal oppbevares forsvarlig, se personopplysningsforskriften kapittel 2, og Helsedirektoratets veileder for «Personvern og informasjonssikkerhet i forskningsprosjekter innenfor helse og omsorgssektoren».

Dersom det skal gjøres vesentlige endringer i prosjektet i forhold til de opplysninger som er gitt i søknaden, må prosjektleder sende endringsmelding til REK.

Prosjektet skal sende sluttmelding på eget skjema, senest et halvt år etter prosjektslutt.

Du kan klage på komiteens vedtak, jf. forvaltningslovens § 28 flg. Klagen sendes til REK sør-øst D. Klagefristen er tre uker fra du mottar dette brevet. Dersom vedtaket opprettholdes av REK sør-øst D, sendes klagen videre til Den nasjonale forskningsetiske komité for medisin og helsefag for endelig vurdering.

Vi ber om at alle henvendelser sendes inn på korrekt skjema via vår saksportal: http://helseforskning.etikkom.no. Dersom det ikke finnes passende skjema kan henvendelsen rettes på e-post til: post@helseforskning.etikkom.no.

Vennligst oppgi vårt referansenummer i korrespondansen.

Med vennlig hilsen

Finn Wisløff Professor em. dr. med. Leder

> Silje U. Lauvrak Rådgiver

Kopi til: turid.sjøstedt@nih.no; postmottak@nih.no

Appendix 2. CPET protocol

ID nummer

Størrelse på maske			
RMR	V02	VE	RER
Puls i hvile			
Blodtrykk			
Flow volume			
MVV			

Balke gåprotokoll

Min	Stigning (%)	Hastighet (km/t)		HF	Borgs skala
0	4	4,5			
1	4	4,5 4,5			
2	4				
3	6	5,0	5,5		
4	9	5,0	5,5		
5	12	5,0	5,5		
6	15	5,0	5,5		
7	15	6,0	6,5		
8	15	7,0	7,5		
9	15	8,0	8,5		
10	15	9,0	9,5		
11	15	10,0	10,5		
12	15	11,0	11,5		