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Original Research

Maximal Resistance Training in the Treatment of Anorexia Nervosa – A Case Report Series

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ABSTRACT

International Journal of Exercise Science 17(3): 308-326, 2024. Objective: Anorexia Nervosa (AN) has one of the highest mortality rates of all mental health disorders, low recovery rate and is associated with widespread endocrine dysfunction. Resistance training (RT) has been consistently shown to provide beneficial effects on health outcomes that are often negatively affected by AN, however participation in exercise is controversial for individuals with AN. The objective of this study was to assess the effects of maximal RT as an add-on to standard of care in patients with AN. Methods: Originally, a controlled clinical trial was planned but due to COVID-19 pandemic, the study was prematurely ended and reported as a case series design. Three female inpatients with AN (Age 18-29 years, body mass index (BMI) 14.5-16.3 kg/m^2, illness duration 1-7 years) underwent a supervised 6-week RT intervention as an add-on to standard of care. Primary outcome was muscular strength, as measured by a 1-repetition maximum. Secondary outcomes included BMI, eating disorder psychopathology and maladaptive exercise tendencies. Results: No adverse events were reported. All three participants improved lower body muscle strength, ranging from 32% to 134% in the leg press. Changes of 4% to 134% in the bench press and -3% to 38% in the pulldown were also observed. Conclusions: RT improved muscular strength in the participants. RT as part of standard of care may also provide additional benefits for individuals with AN, although further research is required to determine which subtype of patients would benefit from the addition of RT to their treatment protocol.

KEY WORDS: Eating disorder, maladaptive exercise, body dissatisfaction, drive for thinness

INTRODUCTION

Anorexia Nervosa (AN) is characterised as an inability to maintain a minimally normal body weight, an intense fear of gaining weight and a disturbance in body image (63). Individuals with AN may present different patterns of weight-related behaviours: individuals who restrict food

intake, possibly in addition to increased energy expenditure (AN-R), and individuals who undergo binge-eating or purging episodes (AN-BP) (63). AN can be further classified as "typical" or "atypical", where a key feature of AN is absent, such as significant weight loss (63). AN has one of the highest mortality rate of all psychiatric disorders (2). According to a 2021 population-based cohort study, the standardised mortality rate of AN is 5.06 (35), while it has been reported that one in five deaths of individuals with AN is due to suicide (2, 56). A population-based sample of twins in Sweden showed an overall prevalence of AN to be 1.2% in females and 0.29% in males during a 4-year study period (9), while lifetime prevalence might be as high as 4% in females (20). Disconcertingly, follow-up studies have observed that only 34% of patients with AN were recovered 5-10 years following treatment (22), with 62.8% to be fully recovered after 22 years (19).

Along with body image disturbance and a lower-than-expected body weight, there is often undernutrition present in AN, which can manifest in widespread endocrine dysfunction (64). Individuals with AN often present with various disturbed physiological processes that are associated with low energy availability (47), which include disturbed bone turnover (27, 46), lowered metabolic rate beyond predicted (38) and dysregulation of menstrual cycle (43). AN is associated with an increased risk of comorbidities such as osteoporosis, a disease process which frequently remains even after recovery from AN, with recovered patients with AN remaining a high-risk group (3, 35). This is supported by long-term studies showing a continued lack of bone mineral density normalisation (12, 33, 49), coupled with increased fracture risk 40 years after diagnosis of AN (40). Other physiological complications can be present in AN, such as reduced muscle mass (22, 39), while some individuals recovered from AN or in partial remission still have lower than normal levels of skeletal muscle mass (51). In other populations, exercise, such as resistance training, is advocated for its improvements in physical and mental well-being and can promote muscular strength and bone mass (27). A positive effect is also seen with exercise and body image, with exercisers observed to have improved body image scores following completion of an exercise intervention (33). Although there is a growing body of evidence suggesting that closely monitored, supervised exercise together with nutritional support is safe, and may provide multiple benefits in the treatment of eating disorders (50), it is still overlooked as a potential contributor in overall standard of care.

The use of exercise in the treatment of eating disorders is controversial. Concerns around the use of exercise in the treatment of eating disorders are understandable, with maladaptive exercise behaviour seen in 31-80% of the patients (17, 54). Some patients with eating disorders may be motivated to partake in maladaptive exercise to avoid a dreaded consequence, which can manifest as a desire use exercise to control their weight and shape and/or avoid negative feelings that may arise as a result of not exercising (18). There may also be physiological complications of engaging in exercise. It has been observed that individuals with AN have higher bone fracture rates (25, 38) and increased prevalence of soft tissue injuries and surgeries (54). Other complications include cardiovascular events, and these complications can persist long term (56). Bradycardia is one of the conditions most commonly seen in Anorexia Nervosa (28), which can also be induced by exercise training (4, 7). While concerns are understandable,

there is a growing body of evidence that supports the safety of resistance training in the treatment of AN. It has been demonstrated that in individuals with Anorexia Nervosa, resistance training is well-tolerated (26, 62) and does not negatively impact weight status (26, 60). In individuals with Bulimia Nervosa, moderate exercise was also observed to improve drive for thinness and body dissatisfaction greater than cognitive behavioural therapy (57). A study on the use of exercise to reduce exercise abuse in patients with eating disorders also observed an improvement in attitudes (emotional commitment and involvement) towards exercise from women in the exercise group (10). While it has been observed that a light resistance program can increase strength in individuals with Anorexia Nervosa (13), this evidence is conflicting (61). Interestingly, while del Valle *et al.*, did not observe consistent increases in strength in the a low-intensity resistance training intervention, they did observe improvements across all strength measures following a high-intensity resistance training intervention (25). Implementing supervised exercise in the treatment of eating disorders has also been reported to facilitate weight gain in patients with AN (10), increase strength and bone mineral density (8), and improve quality of life (1, 16). Despite this, evidence on the use of resistance training in AN is limited, and the success of exercise interventions in the treatment of AN requires further research, especially at higher intensities (60).

Given the long-term impact of AN and the difficulty in achieving recovery, there is a need to identify additional treatment options to help improve an individual's prognosis. Exercise, specifically resistance training, could be one approach to help improve bone and muscle health and body image. Conducting supervised exercise sessions as part of standard of care with individuals with AN can provide a controlled environment for patients to practice normal exercise behaviours. Thus, the objective of this study was to investigate the effect of adding resistance training as an add-on to standard of care for patients with AN, while exploring if individuals with AN could sustain a program of maximal resistance training. We hypothesise that patients with AN who participate in a maximal resistance training program as part of their standard of care will increase muscular strength following 6 weeks of training.

METHODS

Participants

This study is an add-on to the Prospective Longitudinal All-comer inclusion study on Eating Disorders (PROLED; ID: H-15012537; addendum 77106). PROLED is a clinical naturalistic 10-year follow-up study, with annual visits, that started in January 2016 and end in 2021. The study had an expected inclusion rate of at least 100 patients with AN per year. Between November 2019 and March 2020, patients for the study were recruited from the day-care unit and inpatient wards for treatment of eating disorders at Psychiatric Centre Ballerup. Participation in the training intervention in the treatment of eating disorders is possible without participation in the PROLED study. Psychiatric Centre Ballerup is the only unit for treatment of eating disorders in the capitol region of Denmark, having a catchment area of 2 million inhabitants and an expected prevalence of eating disorders of around 25,000.

Inclusion criteria were women, diagnosis of AN according to International Statistical Classification of Diseases and Related Health Problems (ICD)-10 (64), 18-60 years, with a body mass index (BMI) greater than 14.5 kg/m^2 and signed informed consent. Exclusion criteria were forced care, unstable medical or psychiatric health, presence of osteoporosis and issues with compliance to treatment or study protocol. Eligibility criteria related to the health and treatment of potential participants was determined by competent on-site staff (physicians/psychiatrists). Upon successful inclusion to the study, blood samples were collected. Relevant information from the patients' medical records related to medical history and initial clinical assessment were also obtained. Three female inpatients with AN (Age 18-29 years, BMI 14.5-16.3kg/m^2, illness duration 1-7 years) were recruited to participate in the study.

The current study was approved by the Regional Ethics committee of the capitol region of Denmark (ID: H-19037864; addendum 71552) and registered at ClinicalTrial.gov (NCT04185727). This research was carried out fully in accordance to the ethical standards of the International Journal of Exercise Science (49).

Protocol

Standard of Care: As this study was an add-on to standard of care, participants were required to be compliant with their current treatment plan as per the eligibility criteria. As part of their treatment, weekly measures of weight are conducted, and all patients undergo medical and psychiatric examinations, with any psychiatric or medical complications addressed. Patients aim to increase weight by approximately 0.5kg (daycare) to 1kg (inpatient) per week up to an ideal body weight. Individual meetings with psychologists, dieticians and nurses are offered to patients, while a dietician also hosts workshops aimed to develop patient cooking skills. Body awareness therapy is also provided by a trained physiotherapist (12). A set of stopping criteria in addition to inclusion/exclusion criteria was set to ensure that participation in the study did not interfere with the patients' standard of care. A lack of weight gain over three consecutive weeks (21 days) would lead to stop of treatment, and therefore also exclusion from intervention. Furthermore, an attendance of < 70% of sessions and/or more than 4 sessions missed in a row would lead to exclusion from the study.

Weight gain is achieved through the provision of supervised daily meals, which are planned by a dietician. This included three meals (two main meals, one snack) for participants from the daycare unit and five meals (three main meals, two snacks) for participants present at the inpatient unit. This weight gain is typically achieved through a combination of monitored meals, post-meal rest and restrictions in physical activity. However, as this was an intervention based on the incorporation of exercise, individuals may have been required to consume a slight increase in calories to ensure they complied with the required weekly weight gain. This was accomplished following discussion between the patient and their dietician to determine an acceptable source of extra calories, such as consumption of a small portion of juice. The study timeline for the study intervention is presented in Figure 1.

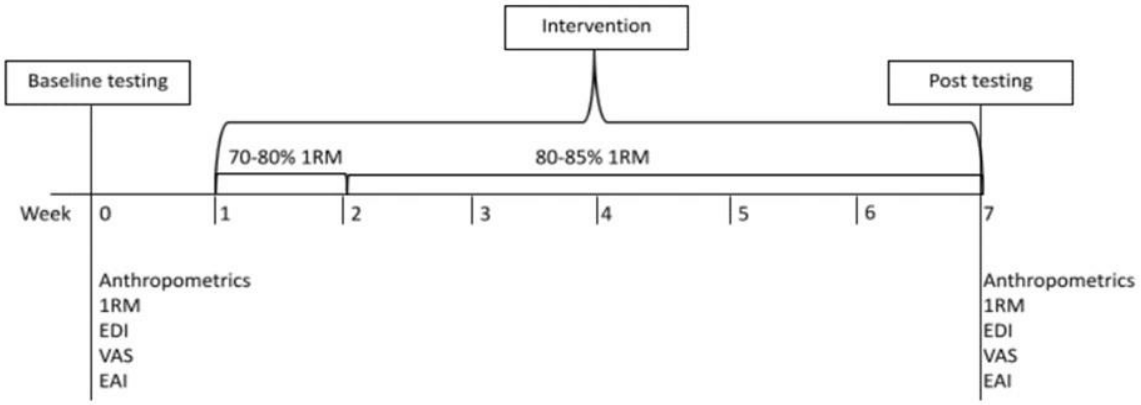

Figure 1. Study Intervention Timeline.
Anthropometric measurements = weight, height, and body mass index.
1RM: 1 repetition maximum, EDI: Eating Disorder Inventory, VAS: Visual Analogue Scale, EAI: Exercise Addiction Inventory.

Training: Participants completed a 6-week supervised resistance training intervention consisting of four exercises. The program consisted of 3 sets of 5 repetitions completed at 5 repetition maximum (RM) per exercise, with three minutes of rest between each set. Participants completed three weekly workouts. Exercises included three resistance exercises: leg press (Matrix Fitness, Johnson Health Tech Denmark, Denmark), bench press and pulldown (HUR Health and Fitness Equipment, HUR, Finland), and one plyometric exercise (dropdowns). In the first week after baseline testing, participants progressed loading from 70% (Session 1) to 80% (Session 3) 1RM, before continuing at a prescribed 85% 1RM throughout the intervention. Every time a participant completed all repetitions successfully for an exercise in a training session, an incremental increase in difficulty was added for the following session (through exercise/weight progression). Instructions and feedback were given to participants throughout the entire intervention to ensure consistency and correct technique.

1RM Test: At least two days prior to baseline strength testing, a familiarisation session was conducted at Psychiatric Center Ballerup to demonstrate and practice correct exercise technique. Lower body and upper body strength were assessed through 1RM tests on incline leg press (Technogym, Gambettola, Italy), bench press and cable pull-down (Technogym, Gambettola, Italy) at baseline and week six. This test started using 10 repetitions at a weight load assumed to be approximately 50% of the participants' 1RM. After three minutes of rest, participants completed five repetitions at approximately 60% 1RM. After another three minutes rest, participants completed three repetitions at approximately 70% 1RM, then a further three minutes of rest before completing one repetition at approximately 80% 1RM. From there on, participants completed one repetition at a weight load increased by 2.5–5 kg from the subsequent lift, followed by five minutes of resting, until they were no longer able to complete a repetition. Upon failure to complete the 1RM repetition, the previous successful attempt was recorded as their 1RM.

EAI: The Exercise Addiction Inventory (EAI) questionnaire consists of six questions based on the six general components of addiction (salience, mood modification, tolerance, withdrawal symptoms, social conflict, and relapse). The responses are rated on a 5-point Likert scale ranging from 1 (strongly disagree) to 5 (strongly agree) and a sum score is calculated (range 6-30 points), where a score ≥ 24 indicates probable exercise addiction (30, 31).

EDI: The Eating Disorder Inventory (EDI)-3 is a 91-item self-report questionnaire that assesses the presence of eating disorder psychopathology and related features, comprising 12 primary scales. A total EDI score, as well as two subscales (drive for thinness and body dissatisfaction) were assessed. The EQI-3 is validated in measuring eating disorder-related symptoms in Danish adults, with internal consistency for the two subscales measured at .86 and .90 (14).

VAS: The Visual Analogue Scale (VAS) questionnaire consists of 7 questions regarding feelings and anxiety around meals (39). A score of 0-10 is given for each question giving a total score of 0-70, with higher scores showing higher meal-based anxiety.

Anthropometrics: Anthropometric measurements were obtained from medical records at Psychiatric Center Ballerup. Height was obtained once, and body weight was obtained weekly. BMI was calculated as body weight in kg/height in m^2.

Activity Level: Activity levels were objectively measured with ActiGraph GT3X+ (Actigraph LLC, Pensacola, FL, USA). This is an accelerometer that measures acceleration in three axes, one for each axis of motion. While the ActiGraph collects raw data, the ActiLife software was used for data processing and analysis. Acceleration was expressed through counts per minute, and the epoch length was set to 60s. Participants were asked to always wear the ActiGraphs on the non-dominant wrist, except for when showering, at baseline and post-intervention for one week.

Statistical Analysis

Statistical power for the maximal resistance training intervention was calculated based on a session-to-session improvement of 0.7-1% improvement in muscle strength. The control group can expect a 5% improvement in muscle strength from pre- to post-intervention testing due to a learning effect. A 12-week intervention with three sessions per week and 80% adherence suggests an increase of 20% in muscle strength from the intervention. Given a power of 0.80, a significance level of 0.05 and a 20% dropout, it was determined that a total of nine participants would be required for the maximal resistance training regime. Unfortunately, the study was interrupted due to the COVID-19 pandemic which resulted in changes to the study. Firstly, the rolling recruitment was halted, and only three participants had been recruited. All participants were in the intervention group, so no control group was established. Finally, the intervention was shortened from 12 weeks to 6 weeks.

Due to the changes in the study, statistical analyses planned *a priori* were not carried out. Instead, visual analysis of the data is complemented with descriptive statistics, which are presented as raw values at each timepoint for each participant (41), as well as percentage changes from

baseline to completion of the intervention. In pooled analyses, where appropriate, descriptive statistics are presented as unadjusted means ± standard deviation. All data analysis was performed using the R software (R Core Team, 2021, https://www.R-project.org) and RStudio, an Integrated Development Environment for R, version 2022.7.1.554 (RStudio, Boston, MA, USA).

STR001: By completion of the 6-week intervention, the participant had attended 71% of training sessions. It was reported by the participant that illness not related to the training was the primary reason for missing the sessions.

STR003: The participant reported that she was struggling with treatment motivation, and that the only treatment sessions she was attending were sessions that were scheduled on the same day as the intervention training session. This situation became more problematic when the participant failed to meet weight gain requirements for two consecutive weeks. Upon further discussion with her attending physician, STR003 applied to be admitted to the inpatient unit at PCB at the end of intervention week 4 (prior to starting week 5), which enabled closer monitoring of the individual, facilitating her continued participation in the intervention. Nutrition intake requirements changed because of enrolment in different unit.

STR004: As a result of scheduling clashes between her treatment and the intervention, 1RM testing for participant STR004 had to be rescheduled from Week 6 to Week 7. This had to occur as STR004's regular treatment schedule could not be altered. This resulted in STR004 completing a further three resistance training sessions, utilising progressive overload, before completing the final 1RM test. In contrast, STR001 and STR003 did not complete extra sessions prior to Week 6 1RM testing.

RESULTS

A total of 4 participants were recruited, with data obtained from 3 (STR001, STR003 & STR004). One participant removed herself from the study prior to baseline testing. Patient baseline characteristics are presented in Table 1.

Table 1. Patient Baseline Characteristics.

Characteristics	STR001	STR003	STR004
Age, years	18	29	20
Initial Diagnosis, ICD-10 code	F50.9	F50.02	F50.01
Disorder Duration, years	3	7	1
Menstrual Cycle (previous 6 months)	No	No	Yes
BMI, kg/m^2	14.53	15.82	16.31

BMI: Body Mass Index, ICD: International Statistical Classification of Diseases and Related Health Problems, ICD-10 codes: F50.01: Anorexia Nervosa-restricting type, F50.02: Anorexia Nervosa-binge eating/purging type, F50.9: Eating disorder, unspecified

The percentage of completed training sessions was 71%, 94% and 95% for STR001, 003 and 004, respectively. No physical training-related physical injuries were reported. Primary outcome results are displayed in Figure 2 while secondary outcome results are presented in Table 2.

Individual training data is presented in Figure 3. As described elsewhere, Sessions 1-3 were utilised as an adjustment period.

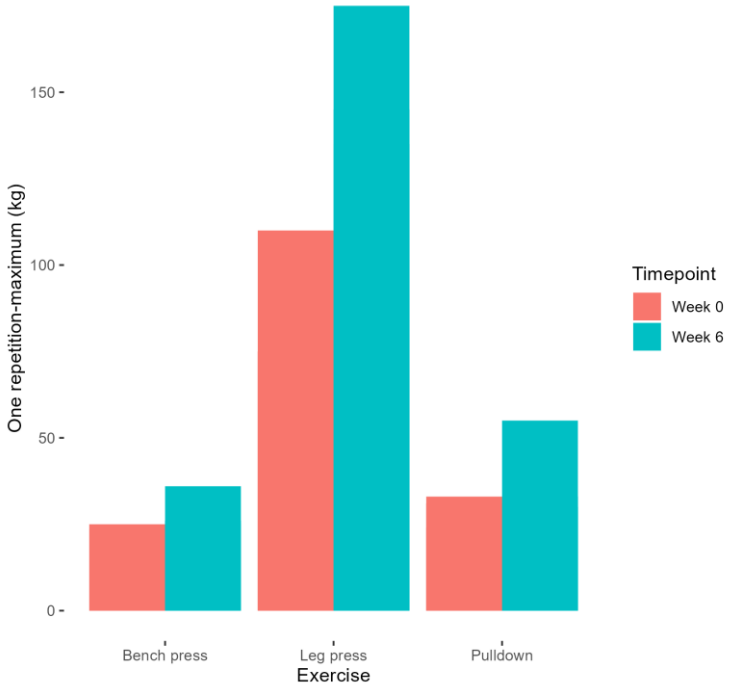

Figure 2. Mean change in 1-repetition maximum strength test from baseline to post-intervention for all participants (STR001, STR003, STR004) for each exercise.

Table 2. Secondary outcome results from 6-week maximal resistance training intervention for three participants (STR001, STR003 & STR004).

	Baseline			Week 6		
Outcome	STR001	STR003	STR004	STR001	STR003	STR004
BMI, kg/m^2	14.53	15.82	16.31	15.71	14.98	18.21
Weight, kg	44.5	45.7	48.8	48.8	44.0	53.0
EDI	127	206	32	97	231	16
EDI-DT	2	25	0	3	27	0
EDI-BD	15	35	17	8	34	16
EAI	13	22	6	10	22	6
VAS	30	52	4	13	39	0
CPM	894	677	1158	994	703	1186
Steps per 24 hours	15783	10280	20468	15599	12133	24192

BMI: Body Mass Index, BD: Body Dissatisfaction, DT: Drive for thinness, EAI: Exercise Addiction Inventory, EDI: Eating Disorder Inventory, VAS: Visual Analogue Scale, CPM: Counts Per Minute. Counts per minute represent a measure of acceleration in a specified time interval (60s)

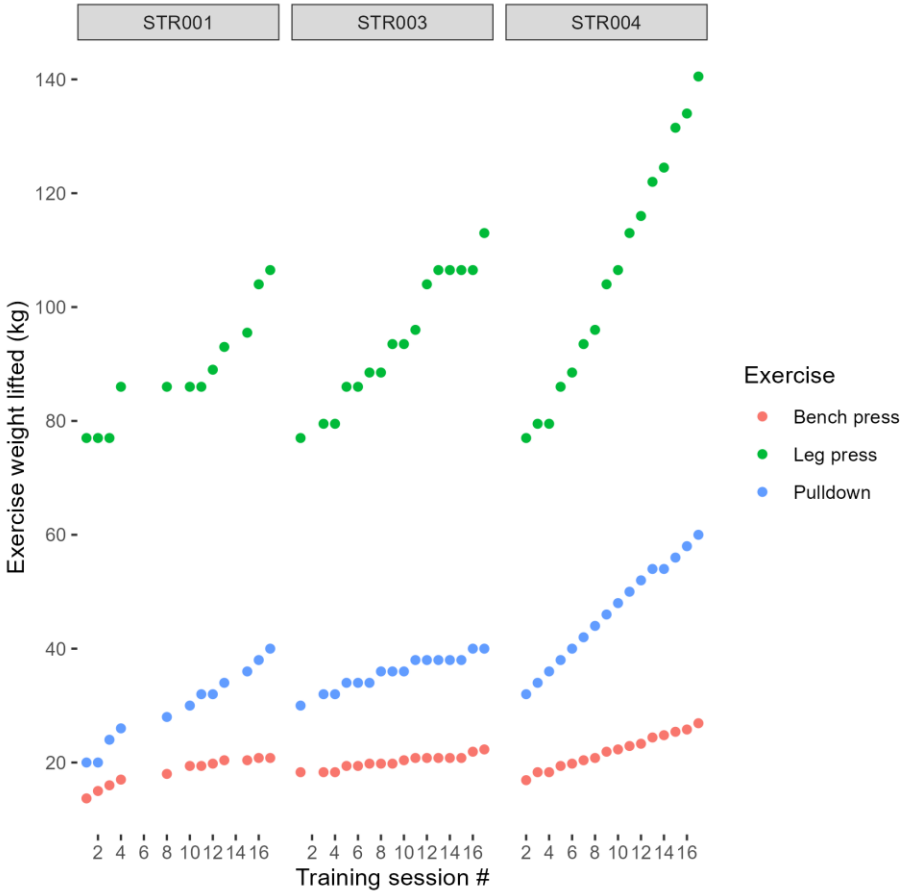

Figure 3. Exercise Training Progression Data.
Spaces in the data represent participant absences.

STR001 case presentation: A woman who met the ICD-10 criteria for AN (64) and was further classified as "atypical" and "restrictive" type of AN by her attending physician. Her current AN severity was rated as "severe", but with no secondary symptoms. At her current height, her maximum weight was 60 kg (2015), and lowest weight was 35 kg (2019).

Physiological outcomes: The primary outcome of skeletal muscle strength increased as indicated by increases of all measures of 1RM from baseline to completion of the intervention, with an increase in incline leg press from 110kg to 145kg, bench press from 20kg to 25kg and pulldown from 24kg to 33kg. STR001 missed Sessions 5, 6, 7, 9 and 14 out of a total of 17 sessions. From Session 4 onward (not including adjustment period), increases from first to last training session in the weight lifted for five repetitions for the Leg Press, Bench Press and Pulldown were 20.5kg (24%), 4.8kg (22%) and 14kg (54%), respectively. The participant increased BMI by 1.18 kg/m^2 (8.1%). Over the 6-week period, weight increased by 4.3 kg, an increase of 1.3 kg over expected. Minimal difference in Steps/24H was noted, with a change from 15783 steps per 24 hours at baseline to 15599 steps per 24 hours post-intervention. Counts per minute by 100 (11.2%) from baseline to post-intervention.

Psychological outcomes: An improvement in eating disorder psychopathology was observed as indicated by a decreased of 30 points in the EDI questionnaire (23.6%). STR001 had low a baseline EDI-DT score with EDI-BD being similar to normal controls (14). The respective changes in the DT and BD subscales of the EDI questionnaire after the training intervention were +1 and -7 respectively. VAS mood score decreased by 17 points (56.7%), reflecting a decrease in meal-based anxiety. EAI decreased by 3 points (23.1%).

STR003 case presentation**:** A woman who met the ICD-10 criteria for AN (64), and was further classified as "typical" and "binge/purge" type of AN by her attending physician. Her current AN severity was rated as "severe", and secondary symptoms include anxious (avoidant) personality disorder. Her maximum weight at her current height was reported as 75 kg in 2012, and her lowest recorded weight was 38 kg in 2019. In the past 6 month she has been overeating/binging, dieting and used vomiting ≤ 1 time per week coupled with maladaptive exercise 1 time per week (duration not recorded/reported).

Physiological outcomes: Two out of three measures of 1RM increased from baseline to completion of the intervention, with an increase in incline leg press from 75kg to 145kg. A minor increase was observed in the bench press (from 25kg to 26kg), while a decrease was observed in pulldown, with a change from 31kg at baseline to 30kg post-intervention. STR003 missed Session 2 out of a total of 17 sessions. From Session 4 onward (not including adjustment period), increases from first to last training session in the weight lifted for five repetitions for the Leg Press, Bench Press and Pulldown were 33.5kg (42%), 4kg (22%) and 8kg (25%), respectively. The BMI of the participant decreased by -0.84 kg/m^2 (5.3%). Over the 6-week period, weight decreased by 1.7 kg, a difference of 4.7 kg below expected. An increase in Steps/24H was noted, with a change from 10280 steps per 24 hours at baseline to 12133 steps per day post-intervention. Counts per minute by 26 (3.8%) from baseline to post-intervention.

Psychological outcomes: The EDI score increased by 25 points (12.1%), reflecting a worsened eating disorder psychopathology. At baseline, STR003 had higher-than-normal EDI-DT and EDI-BD scores compared to Danish patients with eating disorders (14). The worsening of the participant's eating disorder psychopathology was not reflected within the EDI-DT and EDI-BD subscales, with minor changes observed (DT: +2, BD: -1). VAS mood score decreased by 13 points (25.0%), reflecting a decrease in meal-based anxiety. There was no change in overall EAI score.

STR004 case presentation**:** A woman who met the ICD-10 criteria for AN (64), and was further classified as "typical" and "restrictive" type of AN by her attending physician. Her AN severity was rated as "moderate", and she had no secondary symptoms. At her current height, her maximum weight was 75 kg (2015), and lowest weight was 37 kg (2019).

Physiological outcomes: All measures of 1RM increased from baseline to completion of the intervention, with an increase in incline leg press from 75kg to 175kg, bench press from 23.5kg

to 55kg and pulldown from 33kg to 36kg. STR004 missed Session 1 out of a total of 20 sessions (due to scheduling conflicts with standard of care, STR004 completed the post-intervention 1RM test in Week 7, which resulted in her partaking in an extra 3 training sessions). From Session 4 onward (not including adjustment period), increases from first to last training session in the weight lifted for five repetitions for the Leg Press, Bench Press and Pulldown were 86kg (91%), 10kg (55%) and 28kg (78%), respectively. The participant increased BMI of 1.9 kg/m^2 (11.6%). Over the 6-week period, weight increased by 4.2 kg, a difference of 0.2 kg above expected (the individual was moved to the daycare unit after two weeks by clinicians following improvement due to treatment success). An increase in Steps/24H was noted, with a change from 20468 steps per day at baseline to 24192 steps per day post-intervention. Counts per minute increased by 28 (2.4%) from baseline to post-intervention.

Psychological outcomes: The EDI score decreased by 16 points (50.0%), reflecting an improved eating disorder psychopathology. STR004 had low baseline EDI-DT score with EDI-BD being similar to normal controls (14). The respective changes in the DT and BD subscales of the EDI questionnaire after the training intervention were 0 and -1 respectively. VAS mood score decreased by 4 (100%) points, reflecting a decrease in meal-based anxiety. EAI showed no change, with the participant showing very low exercise dependence at both baseline and week 6.

DISCUSSION

The primary finding of this study was that participation in a maximal resistance training intervention resulted in improvements in lower body muscle strength in three patients with AN. Increases in 1RM were also observed in upper body muscle strength, however this differed by patient and by exercise (bench press vs. pulldown). No injuries were observed or reported, and the maximal resistance training was well-tolerated by participants. Furthermore, despite participation in three weekly exercise sessions for a period of six weeks, maladaptive exercise attitudes and behaviours, as measured by EAI, did not increase.

Following a 6-week maximal resistance training intervention, increases in muscle strength, as measured by 1RM, were observed, with the largest magnitude of change observed in the lower body exercise. Early changes in muscle strength appear to be explained by neural adaptations with an increase in muscle size observed after a longer period of resistance training (5, 24), while neural adaptations are greater following high-load training than low-load training (36). Thus, it is difficult to determine how much of the improvements in muscle strength can be attributed to hypertrophy. Furthermore, although no measures of bone health were obtained in this study, the large strength increases observed suggests that high strain rates and magnitude have been imposed on the bone, supported by cross-sectional findings of a relationship between 1RM and bone mineral density (31). Given that AN is associated with increased risk of osteoporosis (3, 35) and fracture risk (40), in addition to reduced muscle mass (22, 39), there is a need to explore other approaches to help improve long-term bone and muscle health. It would be expected that participation in maximal resistance training would stimulate a more favourable osteogenic

environment, promoting improved bone health. Long-term participation in a maximal resistance training program, coupled with optimal energy availability as per standard treatment could be a viable approach to try to improve long-term bone and lean body mass outcomes. Moderate-to-high levels of activity were observed in the three participants in this case report series according to the assessed steps/24 hours, and thus it is crucial to ensure adequate energy availability to ensure patients with AN to resolve undernutrition issues and help stimulate an anabolic environment hypertrophy and improvements in bone mineral density.

The impact of exercise on psychological behaviours present in AN is equivocal. Firstly, there are concerns that the use of exercise training by patients with AN may trigger maladaptive exercise tendencies to control body weight and shape (46) or to avoid some dreaded consequence of not exercising (18), which may be problematic given the prevalence of maladaptive exercise in patients with AN (16). In this study, improvements in the EDI total score were observed in two patients, while a third reported a worsening of eating disorder psychopathology. Upon further inspection of the EDI questionnaire subscales, there were minimal changes in the EDI-DT and EDI-BD subscales except for one patient who reported improvements in body dissatisfaction. While no consistent impact on EDI-DT and EDI-BD were found in this study, other studies have found positive changes following completion of an exercise intervention. Szabo and Green found the EDI total score significantly decreased for patients with AN upon completion of an exercise intervention (58), while Sundgot-Borgen et al. reported decreased body dissatisfaction and a reduced drive for thinness with participation in a supervised exercise program as part of the treatment of bulimic patients (57). Vancampfort et al. conducted a systematic review which concluded that exposure to supervised exercise led to improvements in attitude towards body weight and shape, while participation in a resistance training program was also suggested to improvement the perception of exercise, (62). Given the concerns that surround the addition of exercise to standard treatment of AN, this improvement in the perception of exercise is particularly interesting, as the participation in an resistance training program may reduce the tendency to partake in maladaptive exercise. Furthermore, while little change was observed in maladaptive exercise tendencies in this study as reported by EAI, this is not surprising given that the intervention did not incorporate a specific psychological component to address participation in the intervention. However, the lack of adverse events, such as a triggering of maladaptive exercise attitudes and behaviours, caused by maximal resistance training should be considered a positive outcome due to the proposed risks associated with patients with AN participating in an exercise regimen.

The two participants with the improvements in total EDI score were those who were progressing in their treatment according to their attending physician and had improved their BMI. As has been noted in *Complicating Factors*, the worsened eating disorder psychopathology was observed in the individual who was regressing in her treatment and was admitted to the inpatient ward. From one perspective, the addition of maximal resistance training in this participant's standard of care could be considered a positive in that it ensured she attended the clinic for treatment at least three days a week (on days that the intervention was taking place), and this was noted by the participant's attending physician. Another perspective, however, should consider the risk of

this positive aspect developing into maladaptive exercise tendencies. The addition of exercise to standard of care may not be suitable for all patients with AN, and so it is necessary to identify factors that may help determine which individuals may be considered eligible to incorporate maximal resistance training into their standard of care. In our study, the individual who reported a worsening of eating disorder psychopathology and weight status had a longer disorder duration, presented with binge/purge subtype of AN and had secondary symptoms. In some studies, studies it was observed that individuals with AN-R were more likely to partake in problematic physical activity (44). Looking at specific dimensions of maladaptive exercise however, it was observed that restrictive eating was only correlated with maladaptive exercise, whereas binge eating correlated with compensatory exercise and exercise to control weight/shape, in addition to maladaptive exercise (42). Another factor to consider is disorder duration, with disorder duration associated with habit strength (17). It is possible that individuals with a longer disorder duration may find it more difficult, or require more time, to reframe how they think of and perceive exercise. If this is the case, it is possible that STR003 used participation in the intervention as a way of controlling weight gain as a result of their treatment, whereas STR001 and STR004 may have been able to adopt a healthier attitude towards exercise more successfully/quickly. The addition of maximal resistance training may not be suitable for all individuals with AN. There may be a certain level of recovery required prior to partaking in maximal resistance training sessions. It has been suggested that individuals below 80% of an ideal body weight or engaging in purging exercise with caution to avoid complications that may present in individuals with bradycardia, while it is recommended that individuals with functional hypothalamic amenorrhea should avoid high impact exercise (52). There may be aspects of an individuals' disorder that may indicate whether they would be a suitable candidate to partake in maximal resistance training, such as attitudes towards exercise or eating disorder psychopathology. However, some studies have noticed improvements in maladaptive exercise tendencies and eating disorder psychopathology following an exercise intervention. As such, it may not be ideal to simply consider certain individuals unsuitable for participation in maximal resistance training programs – instead it may be the case that the addition of maximal resistance training to standard of care requires dynamic evaluation throughout an individuals' treatment, and there may be periods where regular training sessions are deemed more or less beneficial to overall treatment success. While not within the scope of this paper, further research (which is adequately powered) should consider the different aspects of the AN disorder that may predict the response of certain groups of individuals to the addition of maximal resistance training to their overall treatment plan, and also consider at which stages of recovery from AN is the addition of maximal resistance training most beneficial to the individual. One of the benefits of maximal resistance training is its positive impact on bone and muscle strength. However, if a patient is not interested in resistance training, alternative types of exercise should be explored to improve the ability to tailor physical training interventions to the patient.

The health benefits of resistance training are well known, however there are concerns about the incorporation of exercise in the treatment of patients with AN. In this study, maximal resistance training was shown to improve muscle strength in individuals with AN. Furthermore, despite

concerns about impaired bone and muscle health in this population, no injuries were reported, indicating that maximal resistance training was well-tolerated by the three participants in this study. However, concerns surrounding participation in a maximal resistance training program for patients with AN are understandable, such as the potential risk physical injuries or the presence of maladaptive exercise behaviours. Future studies therefore need to both address basic science, such as epigenetic and cellular acute responses and systematic adaptations from resistance and applied approaches on how best to implement such training together with standard of care. This is necessary to determine optimal implementation protocols, not only in a controlled experimental setup but in real-world treatment settings, with the aim of improving long-term prognoses of individuals with AN. Another practical implication of the findings in this study is to ensure proper exercise competence in eating disorder clinic staff to safely supervise maximal resistance training in this patient group. Others have suggested that clinical exercise physiologists are excellent providers of such competence (6). Finally, with a focus on patient-centred care, there is a need to consider the individual; for each individual, the success of the addition of resistance training to their treatment may depend on the stage of their recovery process when it is introduced. It must also be acknowledged that not every individual with AN may benefit from resistance exercise, and an emphasis should be placed on reframing attitudes towards exercise instead of just the physical act of carrying out resistance training. Future studies should incorporate a psychological component of a resistance training intervention with the aim of targeted maladaptive exercise-related psychopathologies. Various eating disorder diagnoses might require adapted approaches to supervised maximal resistance training to ensure it is safe for the patient. This should be a collaborative approach between clinicians, patients and, ideally, clinical exercise physiologists to design a suitable maximal resistance training program to aid the individual with AN on their recovery journey and improve long-term prognosis.

The main limitation of this study is the transition from a controlled experimental trial to a case series because of the COVID-19 pandemic. This resulted in reduced recruitment, resulting in power not being satisfied and the lack of a control group, along with violations of the original study protocol. As a result, planned statistical analyses were not carried out; it is not possible to rule out the possibility of observed changes in individuals with AN who participated in a maximal resistance training intervention happening by chance. There were also differences within study procedures which may have influenced changes in outcomes from baseline to post-intervention due to scheduling conflicts and participant absences. As a result of the interruption in the study, participants only completed 6-7 weeks of the maximal resistance training intervention out of the intended 12 weeks. Future research should consider longer interventions to assess the long-term impact of maximal resistance training as an add-on to standard of care in the treatment of AN. Despite the major limitations of this study, there were several strengths which may help inform future research. Firstly, the researchers who conducted the intervention had prior experience in coaching resistance training exercises and were able to ensure safe and controlled participation in a maximal resistance training intervention. The study also utilised a participatory design, integrating clinical staff and patients with AN into the wider project.

In conclusion, the addition of maximal resistance training to standard of care of AN may be one viable approach to improve muscle strength in individuals with AN. However, careful consideration is needed of the suitability of maximal resistance training for each individual, as well as the individual's treatment. Larger clinical trials are required to assess and validate the addition of maximal resistance training to standard of care compared to just standard treatment. Future research should also consider if there are certain disorder or individual characteristics that may indicate if an individual would be a suitable candidate for the addition of maximal resistance training to their treatment plan.

REFERENCES

1. Agne A, Quesnel DA, Larumbe-Zabala E, Olmedillas H, Graell-Berna M, Pérez-Ruiz M, et al. Progressive resistance exercise as complementary therapy improves quality of life and body composition in anorexia nervosa: A randomized controlled trial. Complement Ther Clin Pract 48: 101576, 2022.

2. Arcelus J, Mitchell AJ, Wales J, Nielsen S. Mortality rates in patients With anorexia nervosa and other eating disorders: A meta-analysis of 36 studies. Arch Gen Psychiatry 68(7): 724–31, 2011.

3. Bachrach LK, Katzman DK, Litt IF, Guido D, Marcus R. Recovery from osteopenia in adolescent girls with anorexia nervosa. J Clin Endocrinol Metab 72(3): 602–6, 1991.

4. Bahrainy S, Levy WC, Busey JM, Caldwell JH, Stratton JR. Exercise training bradycardia is largely explained by reduced intrinsic heart rate. Int J Cardiol 222: 213–6, 2016.

5. Balshaw TG, Massey GJ, Maden-Wilkinson TM, Lanza MB, Folland JP. Neural adaptations after 4 years vs 12 weeks of resistance training vs untrained. Scand J Med Sci Sports 29(3): 348–59, 2019.

6. Bergmeier HJ, Morris H, Mundell N, Skouteris H. What role can accredited exercise physiologists play in the treatment of eating disorders? A descriptive study. Eat Disord 29(6): 561–79, 2021.

7. Billman GE, Cagnoli KL, Csepe T, Li N, Wright P, Mohler PJ, et al. Exercise training-induced bradycardia: Evidence for enhanced parasympathetic regulation without changes in intrinsic sinoatrial node function. J Appl Physiol 118(11): 1344–55, 2015.

8. Bratland-Sanda S, Martinsen EW, Sundgot-Borgen J. Changes in physical fitness, bone mineral density, and body composition during inpatient treatment of underweight and normal weight females with longstanding eating disorders. Int J Environ Res Public Health 9(1): 315–30, 2012.

9. Bulik CM, Sullivan PF, Tozzi F, Furberg H, Lichtenstein P, Pedersen NL. Prevalence, heritability, and prospective risk factors for anorexia nervosa. Arch General Psychiatry 63(3): 305–12, 2006.

10. Calogero RM, Pedrotty KN. The practice and process of healthy exercise: An investigation of the treatment of exercise abuse in women with eating disorders. Eat Disord 12(4): 273–91, 2004.

11. Do Carmo I, Mascarenhas M, Macedo A, Silva A, Santos I, Bouça D, et al. A study of bone density change in patients with anorexia nervosa. Eur Eating Disord Rev 15(6): 457–62, 2007.

12. Catalan-Matamoros D, Helvik-Skjaerven L, Labajos-Manzanares MT, Martínez-de-Salazar-Arboleas A, Sánchez-Guerrero E. A pilot study on the effect of Basic Body Awareness Therapy in patients with eating disorders: A randomized controlled trial. Clin Rehabil 25(7): 617–26, 2011.

13. Chantler I, Szabo CP, Green K. Muscular strength changes in hospitalized anorexic patients after an eight week resistance training program. Int J Sports Med 27(8): 660–5, 2006.

14. Clausen L, Rosenvinge JH, Friborg O, Rokkedal K. Validating the Eating Disorder Inventory-3 (EDI-3): A comparison between 561 female eating disorders patients and 878 females from the general population. J Psychopathol Behav Assess 33(1): 101–10, 2011.

15. Cook B, Engel S, Crosby R, Hausenblas H, Wonderlich S, Mitchell J. Pathological motivations for exercise and eating disorder specific health-related quality of life. Int J Eat Disord 47(3): 268–72, 2014.

16. Davis C, Katzman DK, Kaptein S, Kirsh C, Brewer H, Kalmbach K, et al. The prevalence of high-level exercise in the eating disorders: Etiological implications. Compr Psychiatry 38(6): 321–6, 1997.

17. Davis L, Walsh BT, Schebendach J, Glasofer DR, Steinglass JE. Habits are stronger with longer duration of illness and greater severity in anorexia nervosa. Int J Eat Disord 53(5): 683–9, 2020.

18. Dittmer N, Jacobi C, Voderholzer U. Compulsive exercise in eating disorders: Proposal for a definition and a clinical assessment. J Eat Disord 6(1): 1–9, 2018.

19. Eddy KT, Tabri N, Thomas JJ, Murray HB, Keshaviah A, Hastings E, et al. Recovery from anorexia nervosa and bulimia nervosa at 22-year follow-up. J Clin Psychiatry 78(2): 184–9, 2017.

20. van Eeden AE, van Hoeken D, Hoek HW. Incidence, prevalence, and mortality of anorexia nervosa and bulimia nervosa. Curr Opin Psychiatry 34(6): 515-24, 2021.

21. El Ghoch M, Pourhassan M, Milanese C, Müller MJ, Calugi S, Bazzani PV, et al. Changes in lean and skeletal muscle body mass in adult females with anorexia nervosa before and after weight restoration. Clin Nutr 36(1): 170–8, 2017.

22. Errichiello L, Iodice D, Bruzzese D, Gherghi M, Senatore I. Prognostic factors and outcome in anorexia nervosa: A follow-up study. Eat Weight Disord 21(1): 73–82, 2016.

23. Erskine RM, Fletcher G, Folland JP. The contribution of muscle hypertrophy to strength changes following resistance training. Eur J Appl Physiol 114(6): 1239–49, 2014.

24. Faje AT, Fazeli PK, Miller KK, Katzman DK, Ebrahimi S, Lee H, et al. Fracture risk and areal bone mineral density in adolescent females with anorexia nervosa. Int J Eat Disord 47(5): 458–66, 2014.

25. Fernandez-del-Valle M, Larumbe-Zabala E, Villaseñor-Montarroso A, Cardona Gonzalez C, Diez-Vega I, Lopez Mojares LM, et al. Resistance training enhances muscular performance in patients with anorexia nervosa: A randomized controlled trial. Int J Eat Disord 47(6): 601–9, 2014.

26. Galusca B, Bossu C, Germain N, Kadem M, Frere D, Lafage-Proust MH, et al. Age-related differences in hormonal and nutritional impact on lean anorexia nervosa bone turnover uncoupling. Osteoporos Int 17(6): 888–96, 2006.

27. Garber CE, Blissmer B, Deschenes MR, Franklin BA, Lamonte MJ, Lee IM, et al. American College of Sports Medicine position stand. Quantity and quality of exercise for developing and maintaining cardiorespiratory, musculoskeletal, and neuromotor fitness in apparently healthy adults: Guidance for prescribing exercise. Med Sci Sports Exerc 43(7): 1334–59, 2011.

28. Giovinazzo S, Sukkar SG, Rosa GM, Zappi A, Bezante GP, Balbi M, et al. Anorexia nervosa and heart disease: A systematic review. Eat Weight Disord 24(2): 199–207, 2019.

29. Granziol U, Griffiths MD, Zou L, Yang P, Herschel HK, Junker A, et al. The Expanded Exercise Addiction Inventory (EAI-3): Towards reliable and international screening of exercise-related dysfunction. Int J Ment Health Addict Epub ahead of print: doi: 10.1007/s11469-023-01066-2, 2023.

30. Griffiths MD, Szabo A, Terry A. The exercise addiction inventory: A quick and easy screening tool for health practitioners. Br J Sports Med 39(6): e30–e30, 2005.

31. Guimarães BR, Pimenta LD, Massini DA, Dos Santos D, Da Cruz Siqueira LO, Simionato AR, et al. Muscle strength and regional lean body mass influence on mineral bone health in young male adults. PLoS One 13(1): e0191769, 2018.

32. Hartman D, Crisp A, Rooney B, Rackow C, Atkinson R, Patel S. Bone density of women who have recovered from anorexia nervosa. Int J Eat Disord 28: 107–12, 2000.

33. Hausenblas HA, Fallon EA. Exercise and body image: A meta-analysis. Psychol Health 21(1): 33–47, 2006.

34. Hotta M, Shibasaki T, Sato K, Demura H. The importance of body weight history in the occurrence and recovery of osteoporosis in patients with anorexia nervosa: Evaluation by dual X-ray absorptiometry and bone metabolic markers. Eur J Endocrinol 139(3): 276–83, 1998.

35. Iwajomo T, Bondy SJ, Oliveira C de, Colton P, Trottier K, Kurdyak P. Excess mortality associated with eating disorders: Population-based cohort study. Br J Psychiatry 219(3): 487–93, 2021.

36. Jenkins NDM, Miramonti AA, Hill EC, Smith CM, Cochrane-Snyman KC, Housh TJ, et al. Greater neural adaptations following high- vs. low-load resistance training. Front Physiol 8: 331, 2017.

37. Kandemir N, Slattery M, Ackerman KE, Tulsiani S, Bose A, Singhal V, et al. Bone parameters in anorexia nervosa and athletic amenorrhea: Comparison of two hypothalamic amenorrhea states. J Clin Endocrinol Metab 103(6): 2392–402, 2018.

38. Kosmiski L, Schmiege SJ, Mascolo M, Gaudiani J, Mehler PS. Chronic starvation secondary to anorexia nervosa is associated with an adaptive suppression of resting energy expenditure. J Clin Endocrinol Metab 99(3): 908–14, 2014.

39. Lloyd EC, Powell C, Schebendach J, Walsh BT, Posner J, Steinglass JE. Associations between mealtime anxiety and food intake in anorexia nervosa. Int J Eat Disord 54(9): 1711–6, 2021.

40. Lucas AR, Melton LJ, Crowson CS, O'Fallon WM. Long-term fracture risk among women with anorexia nervosa: A population-based cohort study. Mayo Clin Proc 74(10): 972–7, 1999.

41. Manolov R, Gast DL, Perdices M, Evans JJ. Single-case experimental designs: Reflections on conduct and analysis. Neuropsychol Rehabil 24(3–4): 634–60, 2014.

42. Martin SJ, Schell SE, Srivastav A, Racine SE. Dimensions of unhealthy exercise and their associations with restrictive eating and binge eating. Eat Behav 39: 101436, 2020.

43. Meczekalski B, Podfigurna-Stopa A, Katulski K. Long-term consequences of anorexia nervosa. Maturitas 75(3): 215–20, 2013.

44. Melissa R, Lama M, Laurence K, Sylvie B, Jeanne D, Odile V, et al. Physical activity in eating disorders: A systematic review. Nutrients 12(1): 183, 2020.

45. Misra M, Miller KK, Bjornson J, Hackman A, Aggarwal A, Chung J, et al. Alterations in growth hormone secretory dynamics in adolescent girls with anorexia nervosa and effects on bone metabolism. J Clin Endocrinol Metab 88(12): 5615–23, 2003.

46. Mond JM, Calogero RM. Excessive exercise in eating disorder patients and in healthy women. Aust N Z J Psychiatry 43(3): 227–34, 2009.

47. Mountjoy M, Ackerman KE, Bailey DM, Burke LM, Constantini N, Hackney AC, et al. 2023 International Olympic Committee's (IOC) consensus statement on Relative Energy Deficiency in Sport (REDs). Br J Sports Med 57(17): 1073–97, 2023.

48. Mueller SM, Immoos M, Anliker E, Drobnjak S, Boutellier U, Toigo M. Reduced bone strength and muscle force in women 27 years after anorexia nervosa. J Clin Endocrinol Metab 100(8): 2927–33, 2015.

49. Navalta JW, Stone WJ, Lyons TS. Ethical issues relating to scientific discovery in exercise science. Int J Exerc Sci 12(1): 1-8, 2019.

50. Ng LWC, Ng DP, Wong WP. Is supervised exercise training safe in patients with anorexia nervosa? A meta-analysis. Physiotherapy 99(1): 1–11, 2013.

51. Pettersson C, Svedlund A, Wallengren O, Swolin-Eide D, Paulson Karlsson G, Ellegård L. Dietary intake and nutritional status in adolescents and young adults with anorexia nervosa: A 3-year follow-up study. Clin Nutr 40(10): 5391–8, 2021.

52. Quesnel DA, Cooper M, Fernandez-del-Valle M, Reilly A, Calogero RM. Medical and physiological complications of exercise for individuals with an eating disorder: A narrative review. J Eat Disord 11(1): 1–18, 2023.

53. Rizk M, Lalanne C, Berthoz S, Kern L, Godart N. Problematic exercise in anorexia nervosa: Testing potential risk factors against different definitions. PloS One 10(11): e0143352, 2015.

54. Schmerler J, Chiu AK, Agarwal AR, Kreulen RT, Srikumaran U, Best MJ. Increased prevalence of lower extremity soft tissue injuries and surgeries in patients with anorexia nervosa and bulimia nervosa. Phys Sportsmed 20: 1–7, 2023.

55. Smith AR, Zuromski KL, Dodd DR. Eating disorders and suicidality: What we know, what we don't know, and suggestions for future research. Curr Opin Psychol 22: 63–7, 2018.

56. Springall GAC, Caughey M, Zannino D, Kyprianou K, Mynard JP, Rudolph S, et al. Long-term cardiovascular consequences of adolescent anorexia nervosa. Pediatr Res 94(4): 1457–64, 2023.

57. Sundgot-Borgen J, Rosenvinge JH, Bahr R, Schneider LS. The effect of exercise, cognitive therapy, and nutritional counseling in treating bulimia nervosa. Med Sci Sports Exerc 34(2): 190–5, 2002.

58. Szabo CP, Green K. Hospitalized anorexics and resistance training: Impact on body composition and psychological well-being. A preliminary study. Eat Weight Disord 7(4): 293–7, 2002.

59. Thien V, Thomas A, Markin D, Birmingham CL. Pilot study of a graded exercise program for the treatment of anorexia nervosa. Int J Eat Disord 28(1): 101–6, 2000.

60. Toutain M, Gauthier A, Leconte P. Exercise therapy in the treatment of anorexia nervosa: Its effects depending on the type of physical exercise—A systematic review. Front Psychiatry 13: 939856, 2022.

61. del Valle MF, Pérez M, Santana-Sosa E, Fiuza-Luces C, Bustamante-Ara N, Gallardo C, et al. Does resistance training improve the functional capacity and well being of very young anorexic patients? A randomized controlled trial. J Adolesc Health 46(4): 352–8, 2010.

62. Vancampfort D, Vanderlinden J, De Hert M, Soundy A, Adámkova M, Skjaerven LH, et al. A systematic review of physical therapy interventions for patients with anorexia and bulemia nervosa. Disabil Rehabil 36(8): 628–34, 2014.

63. ICD-11 for mortality and morbidity statistics. Retrieved from: https://icd.who.int/browse/2024-01/mms/en#263852475; 2024.

64. ICD-10 Classification of mental and behavioural disorders: Clinical descriptions and diagnostic guidelines. Retrieved from: https://www.who.int/publications/i/item/9241544228; 1992.