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BEV2900 - Spring 2022

Bachelor's thesis in Human Movement Science
Supervisor: Xiao-Mei Mai
May 2022

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Norwegian University of Science and Technology
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Abstrakt

Bakgrunn: Kvinner har større risiko for å utvikle bein- og muskelsykdommer i løpet av livet, særlig etter menopause. Grunnet dette problemet, er hensikten med denne studien å kartlegge hvordan unge kvinner kan forebygge disse sykdommene og hva som potensielt kan øke sjansen for utvikling av sykdom ved å undersøke effektene av fysisk aktivitet og lav energitilgjengelighet. **Metode:** Studiene ble hentet gjennom databasene PubMed, Oria og Google Scholar. Deltakerne var sunne premenopausale kvinner mellom 18-40 år. Artiklene måtte være publisert mellom 2002 og 2022. **Resultat:** Totalt 8 studier ble brukt, der 5 representerte fysisk aktivitet, og 3 lav energitilgjengelighet. Samtlige så at intervensjonene påvirket bein- og muskelhelse. **Konklusjon:** Basert på resultatene, var det tydelig at fysisk aktivitet påvirker bein- og muskelhelse positivt og at lav energitilgjengelighet muligens har motsatt effekt og fører til amenoré og forstyrrelser i ernæringsnivåer, beinresorpsjon og beinformasjon.

Abstract

Purpose: Women have a higher risk of developing bone and muscular diseases in life, especially after menopause. Based on this problem, the purpose of this study is to explore how young women can prevent these diseases and what potentially may increase the chance of developing diseases by examining the effects of physical activity and low energy availability. **Methods:** Studies were found through databases PubMed, Oria and Google Scholar. Subjects were healthy premenopausal women between 18-40 years old. Articles had to be published between 2002 and 2022. **Results:** A total of 8 studies where used, with 5 representing physical activity, and 3 low energy availability. All the studies saw that the interventions impacted bone and muscular health. **Conclusion:** Based on the results, it was clear that physical activity positively affects bone and muscular health, and that low energy availability may have the opposite effect, leading to amenorrhea and disturbances in nutrition levels, bone resorption and bone formation.

Keywords: *physical activity, low energy availability, premenstrual women, bone health, muscular health*

Introduction

The occurrence of osteoporosis and osteopenia is higher in older people, particularly in Nordic countries (Meyer, 2004). The reduction in bone mineral density (BMD) contributes to an increase in bone fractures, most commonly in the femoral neck (FN) and in the lumbar spine column (LS), due to weakened bone structure (Kishimoto et al., 2012). With age, it is also common for the body to lose muscle mass (sarcopenia), often combined with a decrease in physical activity (PA), which in turn can lead to a decline in daily function (Callréus et al., 2012). Due to the physiological differences between men and women, there is a higher occurrence of osteoporosis, osteopenia, and sarcopenia amongst women (Kato et al., 2020). It is therefore reasonable to assume that preventing an early reduction in BMD and muscle mass, particularly in women, is beneficial, both for society and quality of life.

Women's bodies are constantly changing during the three first decades of their lives, and during the third decade they reach peak bone mass, muscle mass and strength, as well as still being premenopausal (Manolagas et al., 2013). Some of the factors that physiologically separates women from men are their high levels of estrogen and an increased growth of bone mass and strength relative to muscle mass (Lang, 2011). Women produce three different types of estrogen: *estradiol*, *estrone*, and *estriol*. *Estradiol* is produced during their fertile years, *estrone* is located mostly in adipose and muscle tissue, and *estriol* is mostly involved in pregnancy (Berg, 2021). With higher levels of estrogen the female body will maintain skeletal integrity and be able to grow skeletal mass (Lang, 2011). When a woman goes through menopause, *estrone* is the only hormone, of the three, left in the body. As a result of the low amount of estrogen after menopause, the bone tissue weakens, and the chance of developing osteoporosis is higher.

PA is important throughout life, especially today in a time where many have sedentary lives, as it has many benefits regarding cardiovascular, muscular, bone, mental, and reproductive health, to list a few (Duckham et al., 2014; Kato et al., 2020; Troy et al., 2018). The female body is interestingly intricate, with many interrelating processes that affect each other, especially the relationship between bone and reproductive health (Babatunde & Forsyth, 2016; Lang, 2011). With the knowledge of how muscular health also can affect bone health, it is therefore of interest to investigate the bone and muscular health of young women, considering the risk of osteopenia and sarcopenia later in life.

Women will have a functioning, healthy body when the physiological conditions are optimal, particularly in relation to the balance between energy intake and expenditure over time, due to energy availability (EA) (Slater et al., 2017). The basal metabolic rate (BMR) sets a minimum intake requirement based on the amount of energy expended from the basal physiological functions throughout the day (*NNR Nordic Nutrition Recommendations 2012*, 2014). A long-term imbalance with an emphasis on low intake in relation to the expenditure creates low energy availability (LEA) and will skew the homeostasis and greatly impact both the bone, muscular and reproductive health as these systems heavily affect each other (Papageorgiou et al., 2017). LEA has been studied both in women with eating disorders (ED) and in female elite athletes, as these groups are more likely to have a higher expenditure compared to intake, either as a result of restricted diet, excessive expenditure or both (Mathisen et al., 2020; Papageorgiou et al., 2018). In the latter group, LEA has been studied as a part of an interrelationship called "the female athlete triad" (FAT), and later the Relative Energy Deficiency in Sport (RED-S) (Areta et al., 2021). LEA has the potential to induce temporary menstrual dysfunction, which in turn can impact the bone health in a similar manner menopause does, as aforementioned (Slater et al., 2016). In addition, inadequate food intake may result in nutritional deficiencies (e.g., insufficient intake of carbohydrates, fat, calcium (Ca), and vitamin D), which also affect bone, muscular and reproductive health (Márquez & Molinero, 2013; *NNR Nordic Nutrition Recommendations 2012*, 2014).

The positive effects of physical activity are many. Specifically for bone and muscular health, resistance training can strengthen both bone and muscle mass, as well as improving cardiovascular and muscular endurance (Nickols-Richardson et al., 2007; Omi, 2014). However, for PA to benefit the body, it is crucial that it is receptive to the added and necessary strain it provides to maintain a healthy and functioning body (Ihle & Loucks, 2009). A stabile long-term energy balance over time is therefore essential, as LEA impacts both the anabolic and catabolic processes, affecting the bone accrual, muscle protein synthesis and production of estrogen (James & Carroll, 2010; Márquez & Molinero, 2013). The main purpose of this literature study is therefore to explore if physical activity has positive effects, as well as if low energy availability has negative effects, on bone and muscular health in young women.

Method

The process of the literature search is presented in the flow charts below (figure 1 and 2). The databases used in the research where PubMed, Oria and Google Scholar. When searching for relevant articles suitable for the aim of the study, it was necessary to use two sets of keywords. The keywords "premenopausal", "young women" and "women" were utilised for both sets, but it was necessary to distinguish "physical activity" and "low energy availability" to find articles that would provide an adequate amount of relevant literature. Further it was also necessary to use the keywords "bone health" and "muscular health" to evaluate the relevance of the articles. The keywords gave thousands of articles in the different databases, but through filtering the results, both regarding the relevance and the compliance between keywords and the title or abstract of the articles, a total of 45 articles were of interest, 27 and 18 articles for "physical activity" and "low energy availability", respectively. Based on the inclusion and exclusion criteria that were established, a total of 8 articles were deemed relevant to the literature study, with 5 articles for "physical activity" and 3 articles for "low energy availability", respectively.

Inclusion and exclusion criteria

Inclusion criteria that were chosen for the original articles were that articles had to include premenopausal women in the age range of 18-40, and they needed to be published between 2002 and 2022. Articles written as systematic reviews or meta-analyses, in addition to animal studies and articles including peri- or postmenopausal women, were excluded.

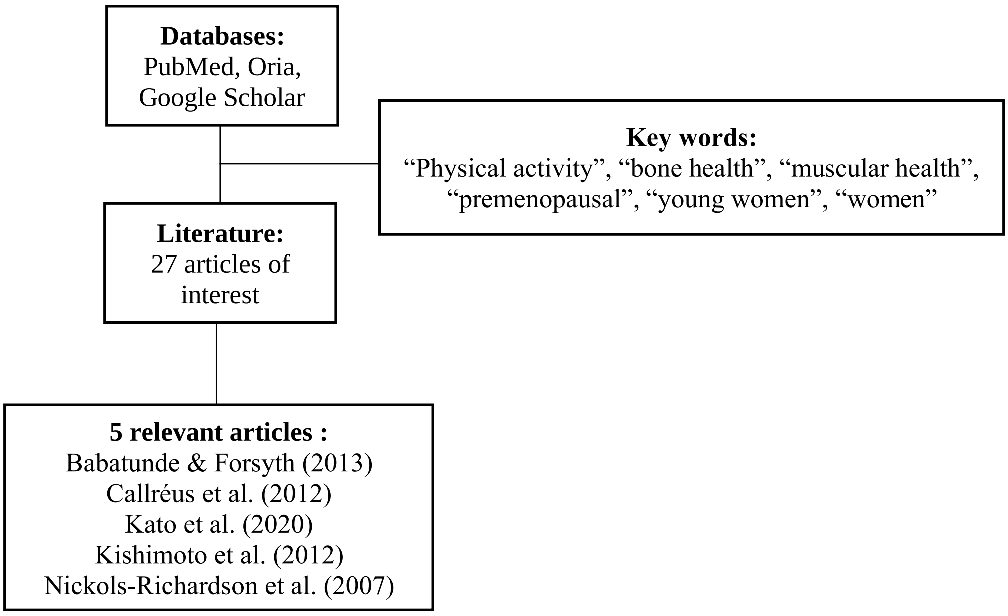

Figure 1*: Flow chart for literature search on the effect of physical activity on bone and muscular health.*

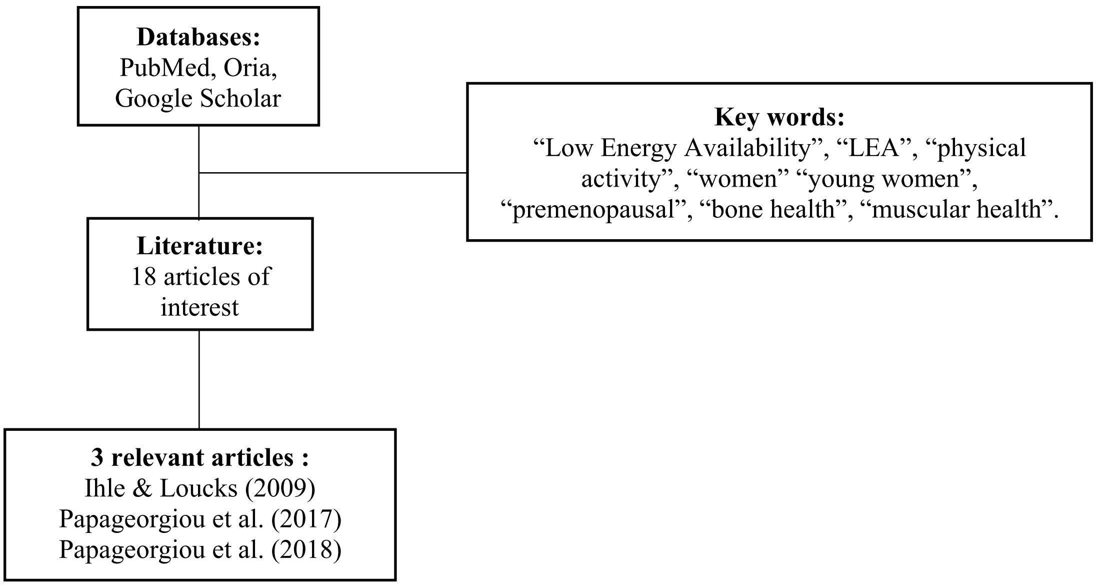

Figure 2: *Flow chart for literature search on the effect of low energy availability on bone and muscular health.*

Results

This study focused on the effects of physical activity and low energy availability on bone and muscular health in young women, with a total of eight primary studies. By including articles on both PA and LEA, they covered a wide range of factors, both positively and negatively affecting the female body. The eight primary studies consisted of primarily clinical trial studies, such as randomized controlled trials (RCT) and randomized crossover studies (crossover RCT), and a population-based study, as shown in table 1. Table 1 depicts the characteristics of the original articles that were used in this literature study, and table 2 provides the main findings of these articles.

Table 1: *Characteristics for the primary studies used in this report*

Study	Study design	Population and sample size (n)	Age (years)	Study purpose
Physical activity				
Babatunde & Forsyth (2013)	RCT	Total *n* = 96 women Intervention group: 48 - Hormonal: 24 - Non-hormonal: 24 Control group: 48 - Hormonal: 23 - Non-hormonal: 25	18-35 Mean age: 22.25 ± 3.5	Examine the effect high-impact lifestyle exercise may have on bone health in premenopausal women.
Callréus (2012)	Population-based questionnaire study	Total *n* = 1061 women	Only 25 Mean age: 25 ± 0.2	Describe how exercise patterns change over time in a population of normal young women and evaluate how much recreational exercise affects BMD.
Kato (2020)	RCT	Total *n* = 41 women Intervention group: 21 Control group: 20	Mean age: 21.5 ± 1.8	Examine if pole push-off movement of NW influences BMC and aBMD of the distal radius and muscle CSA at mid-femoral and mid-humeral levels.
Kishimoto (2012)	RCT	Total *n* = 26 Intervention group: 13 Control group: 13	19-24 Mean age: 20.5 ± 1.5	Examine if short-term high impact jump activity has an effect on bone metabolism in non-athlete college-aged women.
Nickols-Richardson (2007)	RCT	Total *n* = 70 Unilateral concentric: 37 Eccentric: 33	18-26 Mean age: 20.1 ± 1.9	Test their hypothesis if high-load eccentric versus concentric mode of IRT would produce greater increase in muscular strength, FFSTM, BMD and BMC in trained legs and arms.

Table 1 *(continued)*

Low energy availability				
Ihle & Loucks (2004)	Clinical trial study	Total n = 29 women	Mean age: 21.4 ± 0.6	Assessing bone turnover after manipulating LEA in young women.
Papageorgiou (2017)	Crossover RCT	Total n = 22 Women: n = 11 Men: n = 11	18-35 Mean age: 26 ± 5	How LEA affects BTMs in cohorts of women and men and compare the effects between sexes.
Papageorgiou (2018)	Crossover RCT	Total n = 10	18-40 Mean age: 24 ± 3	Achieving LEA through diet or exercise, and the effect it has on BTMs in active young women.

See appendix 1 for abbreviations.

Table 2: *Results from the primary studies with reported outcome measures*

Study	Intervention	Type of reported outcome measures	Outcome measures
Physical activity			
Babatunde & Forsyth (2013)	**Intervention group:** 6 months with 10 two-legged max. vertical jumps using an arm swing in CMJ style 3 days per week. **Control group:** Sham stretching exercises.	*Calcaneal BUA*	Preliminary analysis indicated that there was no significant difference in the relationship between the pre- and post-intervention BUA scores, or BMI and post-intervention BUA. Factorial analysis indicated that BMI and pre-intervention bone health as covariates were significantly related to post-intervention BUA scores, and of a significant effect on bone health in the intervention group (mean increase in BUA of 3.28 dB/MHz) compared to the control group.

***Table 2** (continued)*

Callréus (2012)	Group was divided into different levels of RAL (1-6), PSS (0-16) and COMB-RP based on answers from questionnaire.	*FN-BMD* *TR-BMD* *LS-BMD* *TB-BMD* *TB-BMC*	Women in RAL 4-6 (highly active), PSS ≥5 (high impact load) and high-COMB-RP had significantly higher FN-, TR- and LS-BMD than women in RAL 1-3 (less active), PSS (0-4) and low-COMB-RP. Adjusting for weight and for the covariates resulted in further confirmation that TB-BMD and TB-BMC was greater in high-COMB-RP women vs. low-COMB-RP. Some activities indicated a higher BMD, both total and site-specific, compared to non-active women.
Kato (2020)	**Intervention group:** 6 months with NW 3 times per week at a target rating of perceived exertion of 10-11; min. 30 min the first month, increasing 5-10 min in the second month and an additional 5-10 min the third month, with a max. of 60 min. **Control group:** Perform normal daily activities similar to those they performed before the study.	*BMC* *aBMD* *CSA*	No significant changes in BMC or aBMD at 1/3, 1/6 and 1/10 bone length from the distal radius, except for at the 1/10 site in the NW group, where there was a significant increase after intervention. No significant changes in muscular or adipose CSA both mid-humeral and mid-femoral from baseline to post-intervention.
Kishimoto (2012)	**Intervention group:** 2 weeks with 1 jumping session, consisting of 10 two-legged DJ with a 30-second rest interval between jumps, 5 days per week. **Control group:** Did not perform the jumping protocol.	*Bone serum markers* <u>*Bone resorption*</u> *TRAP5b:* *CTX:* <u>*Bone formation*</u> *OC:* *BAP:*	 Significant change in jump group compared to control, but non-significantly lower post- than pre-intervention. Non-significant change in jump group compared to control, but a significant decrease from pre- to post-intervention. No significant changes in jump group compared to control or in pre- to post-intervention Significant change in jump group compared to no change in control, and a significant decrease from pre- to post-intervention

***Table 2** (continued)*

<table>
<tr>
<td>Nickols-Richardson (2007)</td>
<td>Intervention:
5 months with sets of six reciprocal knee and elbow extensions and flexions at $60°\cdot s^{-1}$, with 1-min recovery between each set. From weeks 1 through 5, number of sets increased with one from 1 to 5 sets for each exercise.

The non-dominant arm and leg was assigned to undergo training, and participants were randomly assigned to either concentric or eccentric training.

Control:
The dominant limbs served as control.</td>
<td>Muscular strength

Bone mineral (TB-BMC, TB-FFSTM, TPF BMD, DT-BMD, DT-BMC)</td>
<td>Significantly higher after both concentric (CONC) and eccentric (ECC) training, and significant gains in trained vs. untrained limbs. ECC was also superior to CONC in terms of improved muscular strength in arms.

Isokinetic resistance training increased muscular strength, but small gains were detected in the control limbs as well.

TB BMC and TB FFSTM significantly increased with training in both intervention groups.

TPF and TF BMD and BMC significantly increased in trained limbs when controlled against untrained limbs.

DT BMD only significantly increased in the CONC untrained leg, and DT BMC significantly decreased in ECC trained leg. FFSTM and FM of ECC trained leg was significantly greater than in untrained leg (FM of untrained leg was reduced).

TF BMC of CONC untrained arm significantly increased. Arm FFSTM of trained limbs also significantly increased in both training groups, with a significantly greater gain in ECC trained limb than in the untrained limb.</td>
</tr>
<tr>
<td colspan="4">Low energy availability</td>
</tr>
<tr>
<td>Ihle & Loucks (2004)</td>
<td>Intervention:
Over 2 menstrual cycles, the participants were administered to a balanced EA treatment (45 kcal/kgLBM/day) in the first cycle, and one of three different restricted EA treatments (either 30, 20, or 10 kcal/kgLBM/day) in the second cycle.

All participants expended 15 kcal/kgLBM/day of 70% VO_{2max} exercise for 30-40 min.</td>
<td>Bone markers</td>
<td>For the 45 kcal/kgLBM/day treatment, the bone markers indicated a mean concentration of:

<table>
<tr><td>OC (ng/ml)</td><td>9.8 ± 0.6</td></tr>
<tr><td>PICP (ng/ml)</td><td>168 ± 11</td></tr>
<tr><td>NTX (nM BCE/mM Cr)</td><td>58 ± 4</td></tr>
</table>

Compared to the balanced EA treatment, the restricted EA treatments showed the following concentration changes:

<table>
<tr><th>kcal/ kgLBM/ day</th><th>OC</th><th>PICP</th><th>NTX</th></tr>
<tr><td>10</td><td>↓28%</td><td>↓26%</td><td>↑34%</td></tr>
<tr><td>20</td><td>↓32%</td><td>↓19%</td><td>No effect</td></tr>
<tr><td>30</td><td>↓11%</td><td>↓12%</td><td>No effect</td></tr>
</table>
</td>
</tr>
</table>

***Table 2** (continued)*

Papageorgiou (2017)	All participants completed both interventions over 2 separate menstrual cycles: 1) controlled (CON) balanced EA (45 kcal/kgLBM/day), consuming a diet of 60 kcal/kgLBM/day 2) restricted (RES) EA (15 kcal/kgLBM/day), achieved by diet and exercise manipulation, consuming a diet of 30 kcal/kgLBM/day All participants expended an EEE of 15 kcal/kgLBM/day at 70% VO_{2peak} exercise.	*BTMs:* *Calcium metabolism markers:* *Regulatory and reproductive hormones:* *Altered bone turnover:*	β-CTX increased and P1NP and BT ratio decreased in RES compared to CON. No significant differences in either of the calcium metabolism markers (PTH, ACa, Mg and PO_4) in RES compared to CON. No significant differences in sclerostin, IGF-1, T_3, GLP-2 or 17β-estradiol in RES compared to CON. There was a decrease in leptin and insulin in RES compared to CON. 10 out of 11 women had altered bone turnover as a result of the changes in bone resorption, bone formation or both, compared to 6 out of 11 men.
Papageorgiou (2018)	**Intervention:** All participants completed all three 3-day interventions in randomized order over 3 consecutive menstrual cycles: 1) energy-balanced, controlled EA (CON), 45 kcal/kgLBM/day achieved through intake and no exercise 2) diet-induced low EA (D-RES), diet intake restricted to 15 kcal/kgLBM/day and no exercise 3) training-induced low EA (E-RES), obtained low EA of 15 kcal/kgLBM/day through exercise energy expenditure at an intensity of 70% of VO_{2peak} to 30 kcal/kgLBM/day and intake of 45 kcal/kgLBM/day.	*BTMs:* *Calcium metabolism markers:* *Regulatory and reproductive hormones:* *Altered bone turnover:*	β-CTX increased and P1NP decreased from baseline (BASE) to day 6 (D6) but showed difference across conditions. No significant changes in [ACa], [Mg] and [PO_4], except a decrease in mean [PTH] over time and a 9% decrease in [PO_4] from BASE to E-RES. Over time, mean IGF-1 decreased in D-RES (13%) and E-RES (23%) compared to CON, and mean [T_3] decreased 16% in D-RES with no significant change in E-RES. No changes in mean insulin concentrations over time or across conditions, whilst mean leptin concentrations decreased over time and showed differences across all conditions. Mean [17β-estradiol] increased over time in natural progression with the menstrual cycle but were not different between conditions. 8 and 5 women responded to altered bone metabolism due to increased β-CTX, decreased P1NP or both, and 2 and 2 women responded to altered bone metabolism due to simultaneous increase of β-CTX and decrease of P1NP, in D-RES and E-RES respectively.

See appendix 1 for abbreviations.

Based on table 2, for PA both Babatunde and Forsyth (2013) and Nickols-Richardson et al. (2007) found a significant difference between the intervention group and control group. Callréus et al. (2012) supported the theory but concluded that it may have an influence. Kato et al. (2020) concluded with a significant difference in BMD in the intervention group, but small differences in muscular strength. Kishimoto et al. (2012) found difference in intervention group vs. control group. Regarding LEA, Papageorgiou et al. (2017), Ihle and Loucks (2009) and Papageorgiou et al. (2018) found a decrease in bone formation markers.

Discussion

The aim of this study was to explore the effects of physical activity and low energy availability on the bone and muscular health of young women. Based on the results, it is possible to conclude that effects are evident, with PA promoting growth and strengthening of bone and muscle mass and LEA promoting bone resorption.

Physical activity

All of the studies about physical activity concluded that PA had a positive effect on bone health. Babatunde and Forsyth (2013) concluded that women who exercise regularly in their everyday life may prevent potential public health intervention, as their results indicate that a high level of recreational activity strengthens bone mass. Callréus et al. (2012) found that women who maintained an everyday habit of physical activity from adolescence into adulthood, had a higher BMD and BMC than those who did not, as well as having a lower risk of potential lifestyle diseases. With the Nordic walking experiment, Kato et al. (2020) concluded with an increase in BMC, aBMD and muscle cross sectional area at the mid-humeral level after six months. Kishimoto et al. (2012) also concluded that daily bouts of jump activities short-term would decrease bone resorption. Nickols-Richardson et al. (2007) found that high-intensity, slow-velocity isokinetic resistance training positively affected the BMD and BMC in young women and increased the muscle strength in specific areas.

Low energy availability

The studies about LEA concluded that energy restrictions, both from diet and exercise, will affect the bone health. Ihle and Loucks (2009) found that LEA may have a preventative effect on young women trying to reach their peak bone mass. The main findings in Papageorgiou et al. (2017) concluded that five days of energy restriction decreased women’s bone formation and increased bone resorption, meaning that more bone deteriorated than was rebuilt in a short-term LEA. As there were two crossover interventions with both women and men, they also saw that these results were exclusive to the female participants. Papageorgiou et al. (2018) concluded that LEA negatively affected bone formation, but there were minimal changes in bone resorption.

Based on the findings, there is a clear consensus that PA and LEA affect bone and muscular health, PA positively and LEA negatively, which is consistent with other studies and reviews. Looking at the PA aspect, it was clear that moderate to high intensity training is beneficial to maintain a healthy bone and muscular health. Also, activities with mechanical loading increases BMD and BMC in load-bearing sites, which are more prone to injuries and fractures that reduce quality of life when BMD and BMC are reduced (Kato et al., 2020; Kishimoto et al., 2012). The LEA aspect shows that having a severely reduced EA long-term reduces bone mass and increases risk of osteoporotic fractures and bone stress injuries (Márquez & Molinero, 2013). In addition, it may cause irreversible effects if left untreated for a long time, increasing the risk of osteoporosis and issues regarding fertility, but it may be reversible if identified early (Hutson et al., 2021; Mathisen et al., 2020; Slater et al., 2016).

Reproductive health

When investigating female physiology, it is necessary to take menstrual cycles and contraceptives into consideration. Therefore, pregnant women were excluded.

Babatunde and Forsyth (2013) found a small, but non-significant, difference between hormonal and non-hormonal contraceptive users, meaning that the osteogenic responses to the intervention were comparable for both groups. Callréus et al. (2012) did not impart contraception use or menstrual function in their study. Kato et al. (2020) and Nickols-Richardson et al. (2007) documented use before and after the experiment, but saw no changes regarding the hormonal levels. Kishimoto et al. (2012) included women with oral-contraceptives and non-hormonal contraceptive users but saw no significant difference between the groups. None of them investigated the effects of PA on menstrual function directly.

Ihle and Loucks (2009), Papageorgiou et al. (2017) and Papageorgiou et al. (2018) all adapted their study around the menstruation cycle. Ihle and Loucks (2009) concluded that bone resorption increased and bone formation was suppressed when EA was restricted severely enough to suppress *estradiol*. Papageorgiou et al. (2017) found non-significant differences related to reproductive hormones, whilst Papageorgiou et al. (2018) concluded that LEA evoked changes in women's hormone concentrations.

Body mass

It was also important to measure the women's weight and BMI. In either of the PA studies, there were no significantly big differences in weight at the beginning of the research and at the end. Callréus et al. (2012) was the only study with a significant difference in BMI and body weight in women having a high PSS score compared with those having a low PSS score.

In the articles about LEA there was a bigger difference. All three articles started off with all subjects having no significant difference in weight, but throughout the experiments they concluded that the intervention groups lost weight as the experiments went on.

Methodological discussions

Most of the studies were RCTs or crossover RCTs, which bodes well for the validity, reliability, and data precision due to objective data collection, less subjective biases, experiments over a long time, and control groups or intervention groups with sufficient washout periods in-between. Unfortunately do many of the studies have small sample sizes, which is less than desirable for the sake of true statistical significance. However, in the studies exploring LEA, a small sample size in a crossover RCT design is beneficial, as it minimizes the risk of confounding covariates, as well as making follow-up easier. It is also worth arguing that inducing LEA in healthy, young women is unethical due to the negative effects it seems to have long term, making it reasonable to limit the extent of the experiment to a short time span, although it limits the studies to only investigate short-term effects. It was difficult to define a specific study design for the Ihle and Loucks (2009) study as there was a disagreement as to whether it fit the definition of a prospective cohort study or a crossover RCT. It was therefore defined only as a clinical trial study without further elaboration.

The population-based study, an epidemiologic cohort study, used a questionnaire to collect data. The number of participants is beneficial for the validity and reliability of the study, due to the larger sample size. Simultaneously, questionnaires are more subjective and may provide less accurate data due to recall bias and/or errors in reporting (e.g., under- or overestimation).

In contrast, the study design seemed fitting for the cohort and provided a variety of data that was well supported by verifiable scientific literature.

A source of error is that most of the studies primarily focus on bone health, meaning that the effects on muscular health can only be interpreted indirectly and does not allow this literature study to fully explore both, especially in relation to LEA.

Physiological explanatory mechanisms

Physical activity has obvious benefits to the overall health of humans, specifically by strengthening, improving and/or maintaining cardiovascular, muscular and bone health, which in turn provides a healthy basis for many of the other physiological processes in the body (Kato et al., 2020). Movement of the body is dependent upon the concentric, eccentric, and isometric contractions of the skeletal muscles, which are attached to the skeleton, facilitating the extension and flexion of joints, as well as the ability to carry weight (Nickols-Richardson et al., 2007). Resistance training is good for the bones and muscles due to the added force of external weight, which encourages the accrual and strengthening of bone and an increase in size and/or strength of the muscle cells (Nickols-Richardson et al., 2007). It is also evident that activities such as Nordic walking and high-impact training ought to elevate the BMD, as several of the primary articles state. As a woman reaches peak bone and muscle mass by the end of the third decade of her life, PA from early age can contribute to a better foundation and possibly delay the inevitable atrophy of old age (Troy et al., 2018).

However, the body of a young woman affected by LEA may have unfavourable physiological conditions which will affect their ability to reach peak bone and muscle mass compared to a healthy woman (Weaver et al., 2019). LEA is a result of the intake being insufficient in comparison to the expenditure long term, regardless of whether the intake is restricted, the expenditure is excessive, or there is a combination (Papageorgiou et al., 2017). The lack of energy surplus above the limit of BMR inhibits physiological processes, which in this case can negate performance, capacity, and recovery. The body runs on glycogen, converted from macronutrients through gluconeogenesis, stored in the muscle glycogen depots and the intramuscular triglycerides (Weaver et al., 2019). When the depots are depleted, gluconeogenesis or glucose from diet is used to restore the depots. If the intake is restricted, it inhibits the resynthesis of muscle glycogen and encourages the body to use protein, usually from muscle tissue, as a substitute, instigating muscle atrophy (Weaver et al., 2019). Weaver et al. (2019) also stated that a restricted diet may also impact which nutrients are present, such as calcium and vitamin D, which are essential for bone and muscular health.

Practical implications

To examine the status of the bones, muscles and reproductive system, high-quality imaging, diagnostics, and blood analysis equipment, such as dual energy X-ray absorptiometry (DXA) and high resolution peripheral quantitative computed tomography (HR-pQCT) are needed to get high-quality data with minimally invasive and painful procedures. Unfortunately, these forms of clinical tests are costly and considering how many participants these trials should include for the sake of validity and reliability, it is more cost-effective to use questionnaires, which are more subjective and possibly biased, or keep the sample sizes at a minimum, risking statistical significance.

A clinical trial is the preferred study design due to the high level of objectivity. However, it is necessary to consider that trials in a test lab are different from implementing the interventions in everyday life. Especially regarding LEA, as it is a condition that occurs after long-term exposure and has a higher degree of varied individual repercussions, as studies on FAT and RED-S show (Mathisen et al., 2020; Papageorgiou et al., 2017). The day-to-day levels of energy restriction are seldom as consistent as they are in an experiment.

It is also notable, as aforementioned, that the scarcity of studies investigating muscular health in addition to bone health significantly affects the overall ability to draw any properly justified conclusions on that topic in this study.

Future studies

This study finds it necessary to further study the effects PA and LEA have on bone and muscular health combined, specifically in premenstrual, recreationally active women, due to the physiological ramifications of inactivity or energy restriction. Within this field it is also imperative to continue to study female physiology with reproductive health in mind, to further promote the exploration of the hormonal changes throughout a menstrual cycle and how that can work in women’s favour in contrast to being a monthly disadvantage. It is important to investigate LEA in men as well, but due to the extended consequences it has in women, it is considered fair to prioritize women.

In this study, it was deemed unethical to induce LEA with long-term experiments in young women because of the effects it has. It is therefore necessary to find women who already fit one or more of the criteria of FAT (menstrual disturbance, low BMD, and/or disordered eating) to study the long-term effects and possibly the reversibility of the condition.

Conclusion

Based on the findings, it is evident that PA, both resistance training and high-impact training, is beneficial for both bone and muscular health, as well as the overall health in general, considering how it aids in strengthening and maintaining the skeleton and the muscles in young women. By contrast, LEA seems to negate the benefits of PA and induces disturbances in the physiological processes pertaining to the bone remodelling cycle, as the body is deprived of sufficient levels of nutrients, impacting both bone resorption, bone formation and menstrual function.

References

Areta, J. L., Taylor, H. L., & Koehler, K. (2021). Low energy availability: history, definition and evidence of its endocrine, metabolic and physiological effects in prospective studies in females and males. *European Journal of Applied Physiology*, *121*(1), 1-21.

Babatunde, O., & Forsyth, J. (2013). Effects of lifestyle exercise on premenopausal bone health: a randomised controlled trial. *Journal of bone and mineral metabolism*, *32*(5), 563-572.

Babatunde, O., & Forsyth, J. (2016). Lifestyle exercises for bone health and health-related quality of life among premenopausal women: a randomised controlled trial. *Promot Educ*, *23*(3), 63-71. https://doi.org/10.1177/1757975914568901

Berg, J. P. (2021). Østrogener. In J. P. Berg (Ed.), *Store Norske Leksikon*.

Callréus, M., McGuigan, F., Ringsberg, K., & Åkesson, K. (2012). Self-reported recreational exercise combining regularity and impact is necessary to maximize bone mineral density in young adult women: A population-based study of 1,061 women 25 years of age. *Osteoporos Int*, *23*(10), 2517-2526. https://doi.org/10.1007/s00198-011-1886-5

Duckham, R. L., Baxter-Jones, A. D. G., Johnston, J. D., Vatanparast, H., Cooper, D., & Kontulainen, S. (2014). Does Physical Activity in Adolescence Have Site-Specific and Sex-Specific Benefits on Young Adult Bone Size, Content, and Estimated Strength? *J Bone Miner Res*, *29*(2), 479-486. https://doi.org/10.1002/jbmr.2055

Hutson, M. J., O'Donnell, E., Brooke-Wavell, K., Sale, C., & Blagrove, R. C. (2021). Effects of Low Energy Availability on Bone Health in Endurance Athletes and High-Impact Exercise as A Potential Countermeasure: A Narrative Review. *Sports Medicine*, *51*(3), 391-403. https://doi.org/10.1007/s40279-020-01396-4

Ihle, R., & Loucks, A. B. (2009). Dose-response relationships between energy availability and bone turnover in young exercising women [Randomized crossover study]. 10. https://asbmr.onlinelibrary.wiley.com/doi/full/10.1359/JBMR.040410

James, M.-S., & Carroll, S. (2010). Effects of different impact exercise modalities on bone mineral density in premenopausal women: a meta-analysis. *Journal of bone and mineral metabolism*, *28*(3), 251-267.

Kato, T., Tomioka, T., Yamashita, T., Yamamoto, H., Sugajima, Y., & Ohnishi, N. (2020). Nordic Walking Increases Distal Radius Bone Mineral Content in Young Women. *J Sports Sci Med*, *19*(2), 237-244.

Kishimoto, K., Lynch, R. P., Reiger, J., & Yingling, V. R. (2012). Short-term jump activity on bone metabolism in female college-aged nonathletes. *Journal of sports science & medicine, 11*(1), 31.

Lang, T. F. (2011). The Bone-Muscle Relationship in Men and Women. *J Osteoporos, 2011*, 702735-702734. https://doi.org/10.4061/2011/702735

Manolagas, S. C., O'Brien, C. A., & Almeida, M. (2013). The role of estrogen and androgen receptors in bone health and disease. *Nat Rev Endocrinol, 9*(12), 699-712. https://doi.org/10.1038/nrendo.2013.179

Márquez, S., & Molinero, O. (2013). Energy availability, menstrual dysfunction and bone health in sports; an overview of the female athlete triad. *Nutricion hospitalaria, 28*(4), 1010-1017.

Mathisen, T. F., Heia, J., Raustøl, M., Sandeggen, M., Fjellestad, I., & Sundgot-Borgen, J. (2020). Physical health and symptoms of relative energy deficiency in female fitness athletes. *Scandinavian journal of medicine & science in sports, 30*(1), 135-147.

Meyer, H. E. (2004, 20.10.2016). *Fakta om beinskjørhet og brudd (osteoporose og osteoporotiske brudd)*. Folkehelseinstituttet. https://www.fhi.no/fp/folkesykdommer/beinskjorhet/beinskjorhet-og-brudd---fakta-om-os/

Nickols-Richardson, S., Miller, L., Wootten, D., Ramp, W., & Herbert, W. (2007). Concentric and eccentric isokinetic resistance training similarly increases muscular strength, fat-free soft tissue mass, and specific bone mineral measurements in young women. *Osteoporosis international, 18*(6), 789-796.

NNR Nordic Nutrition Recommendations 2012. (2014). (N. Ministerråd, Ed. 5th ed.). Nordic Council of Ministers. https://doi.org/10.26530/OAPEN_483279

Omi, N. (2014). Influence of exercise and sports on bone. *The Journal of Physical Fitness and Sports Medicine, 3*(2), 241-248.

Papageorgiou, M., Elliott-Sale, K. J., Parsons, A., Tang, J. C., Greeves, J. P., Fraser, W. D., & Sale, C. (2017). Effects of reduced energy availability on bone metabolism in women and men. *Bone, 105*, 191-199.

Papageorgiou, M., Martin, D., Colgan, H., Cooper, S., Greeves, J. P., Tang, J. C., Fraser, W. D., Elliott-Sale, K. J., & Sale, C. (2018). Bone metabolic responses to low energy availability achieved by diet or exercise in active eumenorrheic women. *Bone, 114*, 181-188.

Slater, J., Brown, R., McLay-Cooke, R., & Black, K. (2017). Low Energy Availability in Exercising Women: Historical Perspectives and Future Directions. *Sports Med*, *47*(2), 207-220. https://doi.org/10.1007/s40279-016-0583-0

Slater, J., McLay-Cooke, R., Brown, R., & Black, K. (2016). Female Recreational Exercisers at Risk for Low Energy Availability. *International Journal of Sport Nutrition & Exercise Metabolism*, *26*(5).

Troy, K. L., Mancuso, M. E., Butler, T. A., & Johnson, J. E. (2018). Exercise Early and Often: Effects of Physical Activity and Exercise on Women's Bone Health. *Int J Environ Res Public Health*, *15*(5), 878. https://doi.org/10.3390/ijerph15050878

Weaver, C. M., Bischoff-Ferrari, H., Daly, R. M., & Wong, M.-S. (2019). *Nutritional Influences on Bone Health : 10th International Symposium* (1st 2019. ed.). Springer International Publishing : Imprint: Springer.

Appendix 1: Glossary of abbreviations

aBMD =Areal bone mineral density
ACa = albumin-adjusted calcium
BAP = Bone-specific Alkaline Phosphatase
β-CTX = β-carboxylic terminal cross-linked telopeptide of type I collagen
BMC = Bone mineral content
BMD = Bone mineral density,
BMR= The basal metabolic rate
BTM = Bone turnover markers
BT ratio = Bone turnover ratio
BUA = Broadband Ultrasound Attenuation
CMJ = Countermovement Jump
COMB-RP = Combined RAL and PSS score
CON = Control group
CONC = Concentric training
CSA = Cross-sectional area
CTX = C-Terminal Telopeptides of Type I Collagen
DJ = Drop Jumps
D-RES = Diet restricted group
DT = Distal Tibia
DXA = Dual energy X-ray absorptiometry
EA = Energy availability
ECC = Eccentric training
ED = Eating disorders
EEE = Exercise energy expenditure
E-RES = Exercise restricted group
FAT = Female athlete triad
FFSTM = Fat-free soft tissue mass
FN-BMD = Femoral neck BMD
FN =Femoral neck
GLP-2 = Glucagon-like-peptide-2
HR-pQCT = High Resolution Peripheral Quantitative Computed Tomography
IGF-1= Insulin-like growth factor 1
IRT = Isokinetic resistance training
kg/LBM = kg Lean Body Mass
LEA = Low energy availability
LS = Lumar spine columm
LS-BMD = Lumbar spine (L1-L4) BMD
Mg = Magnesium
NTX = Urinary N-telopeptide
NW = Nordic walking
OC = Osteocalcin
P1NP = Amino-terminal propeptide of type 1 procollagen
PA = Physical activity
PICP = Serum type I procollagen carboxy-terminal propeptide
PO_4 = Phosphate
PSS = Peak Strain Score
PTH = Parathyroid hormone
RAL = Recreational Activity Level
RCT = Randomized controlled trial
RED-S = The Relative Energy Deficiency in Sport
RES = Restricted intake group
T_3 = triiodothyronine
TB-BMD = Total body BMD
TB-BMC = Total body BMC
TF = Total forearm
TPF = Total proximal femur
TR-BMD = Trochanter BMD
TRAP5b = Tartrate-Resistant Acid Phosphatase

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