Contents lists available at ScienceDirect

# **Bone Reports**

journal homepage: www.elsevier.com/locate/bonr

# Effect of a pulse-based diet and aerobic exercise on bone measures and body composition in women with polycystic ovary syndrome: A randomized controlled trial

Laura E. McBreairty<sup>a</sup>, Maryam Kazemi<sup>a</sup>, Philip D. Chilibeck<sup>b</sup>, Julianne J. Gordon<sup>b</sup>, Donna R. Chizen<sup>c</sup>, Gordon A. Zello<sup>a,\*</sup>

<sup>a</sup> College of Pharmacy and Nutrition, 104 Clinic Place, University of Saskatchewan, Saskatoon, SK S7N 2Z4, Canada

<sup>b</sup> College of Kinesiology, Physical Activity Complex, University of Saskatchewan, 87 Campus Drive, Saskatoon, SK S7N 5B2, Canada

<sup>c</sup> Obstetrics and Gynecology, College of Medicine, 103 Hospital Drive, Saskatoon, SK S7N 0W8, Canada

#### ARTICLE INFO

Keywords: Polycystic ovary syndrome Randomized controlled trial Hip geometry Bone mineral density

#### ABSTRACT

Polycystic ovary syndrome (PCOS) is the most common endocrine disorder in women of reproductive age, with clinical symptoms including menstrual dysfunction and hyperandrogenemia, as well as insulin resistance which is thought to be a key contributing factor to symptoms. Insulin is also thought to positively affect bone while oligo- and amenorrhea are known to negatively affect bone. Lifestyle modification is the first recommendation to treat symptoms of PCOS; however, little is known about the effect of lifestyle interventions on bone measures in this population. Pulses (e.g., chickpeas, beans, split peas, lentils) have been shown to lower fasting insulin, and the objective of this study was to determine the effect of a pulse-based diet compared to the therapeutic lifestyle changes (TLC) diet on bone measures and body composition in women with PCOS. Women aged 18-35 years with PCOS were randomized to either a pulse-based diet or the TLC diet for 16-weeks while following an aerobic exercise program. Thirty-one in the TLC group and 29 in the pulse group completed dual-energy X-ray absorptiometry analysis following the intervention. After 16-weeks, both groups had a lower BMI, whole body fat mass, and % fat (p < 0.005), with no difference in lean mass. In both groups, lumbar spine bone mineral content (BMC) and density were higher following the intervention (p < 0.05) while femoral neck bone mineral density (BMD) was lower (p < 0.05). Intertrochanteric section modulus improved in both groups while there was a group x time interaction in femoral shaft subperiosteal width which was more favorable in the pulse group (p < 0.05). This study demonstrates that the femoral neck may be compromised during a lifestyle intervention in women with PCOS. Research is warranted to preserve bone health during lifestyle change in women with PCOS

#### 1. Introduction

Polycystic ovary syndrome (PCOS) is a common endocrine disorder in women of reproductive age with a prevalence estimated at 5–20% of premenopausal women (March et al., 2010; Yildiz et al., 2012). Characteristics of the syndrome include menstrual and ovulatory dysfunction, hyperandrogenemia, hirsutism, and polycystic ovaries (Azziz et al., 2009). Furthermore, insulin resistance and associated hyperinsulinemia affect 50–70% of women with PCOS, which is thought to be a contributing factor to the pathogenesis of the syndrome (Douglas,

#### 2006; Moran and Norman, 2004).

Oligomenorrhea or amenorrhea are present in approximately 65–80% of women with PCOS (Hart et al., 2004) and these menstrual disturbances have been associated with low bone mineral density (BMD) in conditions associated with low estrogen such as eating disorders (Solmi et al., 2016). Some studies have suggested a protective effect of hyperinsulinemia associated with PCOS on BMD (McBreairty et al., 2018; Yüksel et al., 2001). Others have demonstrated lean women with PCOS have lower BMD compared to controls, while obese women with PCOS are not different from either group (Katulski et al., 2014).

\* Corresponding author.

https://doi.org/10.1016/j.bonr.2020.100248

Received 30 August 2019; Received in revised form 19 December 2019; Accepted 21 January 2020

Available online 23 January 2020





Abbreviations: AUC, area under the curve; BMC, bone mineral content; BMD, bone mineral density; BMI, body mass index; CSA, cross-sectional area; CSMI, cross-sectional moment of inertia; DXA, dual-energy X-ray absorptiometry; FS, femoral shaft; NN, narrow neck; PCOS, polycystic ovary syndrome; SPW, subperiosteal width; TLC, therapeutic lifestyle changes; Z, section modulus

E-mail address: gordon.zello@usask.ca (G.A. Zello).

<sup>2352-1872/ © 2020</sup> University of Saskatchewan, Saskatchewan, Canada. Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/BY-NC-ND/4.0/).

Furthermore, no difference in BMD between women with PCOS and healthy controls has also been demonstrated (Ganie et al., 2018).

The first line treatment for PCOS is lifestyle change aimed at weight management, and it has been shown that a 5–10% weight reduction can lead to significant clinical improvements in symptoms of PCOS (Teede et al., 2018). Although weight loss is beneficial in PCOS, BMD is positively associated with body weight (McBreairty et al., 2018) and little is known about the risk of negatively affecting BMD following weight loss in this population. Furthermore, there is increasing evidence for the importance of using bone geometry to assess bone strength (Bonnick, 2007) and there are currently no studies determining the effect of a diet and exercise intervention on measures of hip geometry in women with PCOS. This is particularly important considering the demonstration that normal-weight women with PCOS appear to have compromised BMD (Katulski et al., 2014).

Pulses (e.g., lentils, chickpeas, beans, split peas) have a low-glycemic index and have been shown to lower fasting blood insulin (Sievenpiper et al., 2009). While many plant-based protein sources, such as pulses, are low in sulfur amino acids, it has been suggested that foods high in sulfur amino acids, such as animal-based proteins, may lead to sulfuric acid production and subsequent bone resorption (Zwart et al., 2005). The present study is part of a larger study determining the effects of a pulse-based diet in women with PCOS. We previously demonstrated the benefits of a low-glycemic-index pulse-based diet including split peas, lentils, beans, and chickpeas over the Therapeutic Lifestyle Changes (TLC) diet on the cardiometabolic health of women with PCOS (Kazemi et al., 2018). In this secondary outcome analysis of the trial, we compared changes in the bone and body composition markers of women with PCOS who participated in the pulse-based or the TLC diet interventions. We hypothesized that the detrimental effect of weight loss on bone may in part be mitigated by a pulse-based diet compared to the TLC diet.

#### 2. Methods

## 2.1. Study design

The present study is part of a larger study investigating the effects of a 16-week pulse-based diet and exercise intervention in women with PCOS and has been described elsewhere (McBreairty et al., 2017). The study was a single-blind, parallel, stratified-randomized clinical trial carried out between April 2011 and June 2016. The study was approved by the University of Saskatchewan Biomedical Research Ethics Board (BIO-REB 10-98), and all women gave written informed consent before participation in the study. All procedures were conducted in compliance with the World Medical Association Declaration of Helsinki, the Guidelines of the International Conference on Harmonization on Good Clinical Practice, and the Canadian Tri-Council Policy Statement on the Ethical Conduct for Research Involving Humans (Canadian Institute of Health Research). We adhered to the Consolidated Standards of Reporting Trials (CONSORT) guidelines for reporting on randomized clinical trials. The trial was registered at ClinicalTrials.gov (https:// clinicaltrials.gov/, NCT01288638. Lifestyle Intervention for Polycystic Ovary Syndrome: Pulse-Based Diet and Exercise).

# 2.2. Participants

Women aged 18 to 35 years old and experiencing missed or irregular periods, unwanted male-pattern facial and/or body hair growth, and/or infertility were recruited via posters, contacting doctors' offices and postings on the University of Saskatchewan website. For diagnosis of PCOS women met with an obstetrics-gynecologist and were assessed using criteria specified in the PCOS report of the Androgen Excess and PCOS Society (Azziz et al., 2006). A diagnosis of PCOS required 1) either oligo-amenorrhea and/or polycystic ovaries defined as > 25 follicles visualized by transvaginal ultrasonography to reflect the newest

guidelines for polycystic ovaries recommended by the Androgen Excess and PCOS Society (Dewailly et al., 2014), and 2) hyperandrogenism as defined by a Ferriman and Gallwey score of > 6 and/or biochemical hyperandrogenemia. Hirsutism was scored using the modified Ferriman-Gallwey Index, adjusted for ethnicity (Yildiz et al., 2010). Exclusion criteria included the use of hormonal birth control methods or fertility medications during the 3 months prior to diagnosis. Women taking medications that are known or suspected to interfere with cardiometabolic and reproductive function, weight, and/or appetite, or having a medical condition limiting exercise or consumption of a pulsebased diet were also excluded. A diagnosis of PCOS was excluded in women with the following conditions: Taking anti-seizure or anti-psychotic medications known to induce development of polycystic ovaries: untreated hyperprolactinemia or thyroid disease; or, excessive adrenal androgen production confirmed by a diagnosis of congenital adrenal hyperplasia or an adrenal tumor. Women were also excluded from the study if they had an uncontrolled medical condition that interfered with ovarian or systemic hormone production, were pregnant or breastfeeding, or resided outside of the local geographic area.

#### 2.3. Study setting

The study was conducted in Saskatoon, SK Canada. Diagnostic appointments were completed at the Royal University Hospital in Saskatoon. Other assessments took place at the College of Kinesiology research facility on the University of Saskatchewan campus.

## 2.4. Intervention

Following the diagnosis of PCOS, participants underwent baseline testing as described previously (McBreairty et al., 2017) and is further detailed below. Participants then met with a registered dietitian for 1.5 h where the TLC diet guidelines were explained. These guidelines were developed by the National Cholesterol Education Program Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (National Cholesterol Education Program (Adult Treatment Panel III), 2002). Details of the TLC diet and counseling were previously published (Kazemi et al., 2018; McBreairty et al., 2017). Participants were provided with handouts about TLC guidelines and were also given Canada's Food Guide. The dietitian explained healthy choices based on the TLC guidelines and participants were encouraged to consume lean meats such as chicken or fish as a protein source. Participants also received approximately 4-h of education and counseling about PCOS and the benefits of lifestyle change to manage PCOS which was delivered by a gynecologist and researchers who were knowledgeable about reproductive endocrinology and clinical nutrition.

All participants followed the TLC diet for 2-weeks which was followed by a repeat of baseline clinical blood measures. Participants were then randomized to either the TLC or pulse-based diet using a computer-generated allocation schedule with a block size of four and a permuted block design. Randomization was stratified based on the use of the insulin-sensitizing drug Metformin and was performed by an investigator not involved in obtaining or entering participant data. Participants were notified of diet allocation via email and were not blind to randomization. Both intervention groups participated in an aerobic exercise program during the 16-week intervention which is further described below. Baseline measures were repeated at the end of the 16-week intervention, with clinical bloodwork repeated both at 9weeks and at the end of the 16-weeks.

#### 2.5. Diet

The pulse based-diet included meals prepared with dry peas, lentils, chickpeas, and beans. Two daily meals were supplied to participants weekly (i.e., 14 lunch and dinner meals) and contained approximately



Fig. 1. CONSORT (Consolidated Standards of Reporting Trials) diagram outlining study progression.

150 g per day of pulses dry weight (250 g per day wet weight) which has been shown to be beneficial for lowering blood glucose and lipids (Abeysekara et al., 2012; Schäfer et al., 2003). The meals included frozen and fresh options and participants provided input for meal preferences as well as allergies. Subjects were counseled to replace foods normally eaten for lunch and supper with the pulse-based food so as not to increase daily caloric intakes and were instructed to follow the TLC guidelines for breakfast and snacks. Those randomized to the TLCdiet were instructed to continue to follow the TLC-diet guidelines and to limit pulse consumption. Compliance to diet and exercise were determined via a daily log book where both groups recorded daily exercise. The pulse group recorded which pulse meals were consumed each day and whether TLC guidelines were followed for breakfast and snacks, and the TLC group recorded whether the TLC guidelines were followed.

## 2.6. Exercise

All participants were instructed to participate in aerobic exercise 5 days per week for 45 min per day with 3 required sessions at a University of Saskatchewan research exercise facility. Participants were able to choose which exercise equipment to use among the options of treadmill, cycling, elliptical, or rowing machine. Participants were given a gym orientation by a research assistant and were instructed to exercise at an intensity of at least 60% of their age-predicted maximal heart rate (i.e., 220-age).

#### 2.7. Dual-energy X-ray absorptiometry (DXA)

Dual-energy X-ray absorptiometry (Hologic© Discovery Wi; Bedford, MA) was used to determine bone measures and body composition and was performed and analyzed by a certified radiology technologist as described previously (Beck et al., 2011; Chilibeck et al., 2013). A quality-control phantom scan was performed daily. Geometric measures were determined at the narrow neck (NN) region, the intertrochanteric region, and the femoral shaft (FS), and included the subperiosteal width (SPW), bone cross-sectional area (CSA), cross-sectional moment of inertia (CSMI), and section modulus (Z). Bone CSA represents BMC and expresses the amount of bone within a cross-section in terms of cortical equivalent surface area opposed to mineral mass. Z accounts for mass distribution and CSMI further accounts for the maximum distance of mass distribution. The CSA indicates the compressive strength of bone with CSMI and Z indicating bone bending strength. SPW indicates bone outer diameter and contributes to section modulus, therefore increasing the bending strength of bone (LaCroix et al., 2010). Coefficients of variation for whole body, lumbar spine and

#### Table 1

	TLC		Pulse		p-Values	
	Baseline	16-weeks	Baseline	16-weeks	Time	Group x time
BMI (kg/m <sup>2</sup> )	$34.0 \pm 8.5$	$32.2 \pm 8.5$	$30.8 \pm 6.2$	$29.4 \pm 5.7$	0.005	ns
Weight (kg)	$92.7 \pm 24.5$	87.8 ± 22.1	$83.1 \pm 16.1$	79.3 ± 14.7	0.004	ns
Fat mass (kg)	$38.9 \pm 17.5$	37.6 ± 15.6	$33.5 \pm 11.6$	$31.3 \pm 11.4$	0.0016	ns
Lean mass (kg)	47.9 ± 8.4	$48.0 \pm 8.6$	$46.5 \pm 6.0$	45.7 ± 5.6	ns	ns
% Fat	$42.2 \pm 9.5$	$41.1 \pm 9.0$	$39.7 \pm 7.4$	$38.5 \pm 7.8$	0.0003	ns
BMC (kg)	$2.315 \pm 0.278$	$2.331 \pm 0.285$	$2.265 \pm 0.265$	$2.261 \pm 0.248$	ns	ns

Comparison of whole body anthropometric measures in women with PCOS following either a pulse-based or therapeutic lifestyle changes (TLC) diet.

Data are expressed as mean ± SD and analyzed using repeated measures 2-factor ANOVA. BMC, bone mineral content; BMI, body mass index.

proximal femur BMD were 0.5%, 0.7%, and 1.0%, respectively. Coefficients of variation for NN, intertrochanteric, and FS, respectively, were 5.3%, 1.8%, and 1.2% for SPW; 2.6%, 2.2%, and 1.8% for CSA; 7.2%, 4.3%, and 3.7% for CSMI; and 3.5%, 3.4%, and 2.1% for Z. Coefficients of variation for fat and bone mineral-free lean tissue mass (lean mass) were 3% and 0.5% respectively. Body mass was determined with a calibrated scale and height determined with a stadiometer. Body mass index (BMI) was calculated as mass (kg) divided by height squared  $(m^2)$ .

#### 2.8. Clinical measures

Total testosterone and estradiol were measured in a clinical laboratory at the Saskatoon Health Region in Saskatoon, Saskatchewan. Testosterone was determined using the IMMULITE 2000 Systems Analyzers (Tarrytown, NY) solid-phase, competitive chemiluminescent enzyme immunoassay. Estradiol was determined via electrochemiluminescence immunoassay. The intra-assay % coefficient of variation was < 7% for both assays.

#### 2.9. Statistics

Students *t*-test was used to compare mean age between groups. A 2-factor ANOVA was used to compare the two groups over time (i.e., before vs. after the 16-week intervention), with time as a repeated-measures factor. All data were analyzed using Statistica version 12 (Statsoft, Chicago IL). Data are presented as mean  $\pm$  SD. A p-value < 0.05 was considered significant. Determination of sample size has been previously reported (McBreairty et al., 2017)

#### 3. Results

#### 3.1. Study compliance

The study outline can be seen in Fig. 1. The intervention was completed by 31 and 30 women in the TLC and pulse group, respectively. Thirty-one and 29 women completed the end of intervention DXA assessment in the TLC and pulse groups, respectively, with all presented analysis performed on this sub-group. The mean age of the TLC and pulse groups were  $26.8 \pm 4.5$  years and  $26.6 \pm 5.0$  years, respectively, with no difference between groups. Compliance to the exercise program was  $53.1 \pm 22.2 \text{ min/day}$  and  $42.5 \pm 8.6 \text{ min/day}$  over 5 days/week for the pulse-based and TLC diet groups, respectively, with no difference between the groups. Out of the 14 weekly meals, women in the pulse group consumed  $11.2 \pm 0.2$  meals per week and followed the TLC guidelines for breakfast and snacks  $5.48 \pm 0.36$  days per week. The TLC group followed the TLC guidelines a mean of  $5.30 \pm 0.26$  days/week. The compliance to dietary interventions was comparable between groups (p = 0.12).

#### 3.2. Clinical intervention measures

Testosterone was determined in 18 and 20 women in the TLC and pulse groups, respectively. Testosterone was  $1.73 \pm 0.86$  and  $1.54 \pm 0.79$  nmol/L pre- and post-intervention, respectively, for the TLC group, and  $1.75 \pm 0.56$  and  $1.50 \pm 0.42$  nmol/L pre- and post-intervention, respectively, for the pulse group. There was a time main effect for testosterone (p = 0.02) with no difference between groups. There were no differences found in estradiol which was  $214.1 \pm 175.9$  and  $223.4 \pm 216.4$  pmol/L pre- and post-intervention, respectively, in the TLC group (n = 17), and  $161.9 \pm 111.6$  and  $244.8 \pm 177.1$  pmol/L pre- and post-intervention, respectively, in the pulse group (n = 17).

#### 3.3. Bone and body composition measures

Hip structural analysis measures for SPW, CSA, CSMI, and Z were determined in 26 and 24 women in the TLC and pulse groups, respectively, while all other measures were determined in all women who completed the end of intervention DXA. There was a time main effect for BMI (p = 0.005), body weight (p = 0.004), whole body fat mass (p = 0.0016), and % fat (p = 0.0003), with all measures lower following the intervention and no differences between groups. There were no differences in whole-body lean mass (Table 1).

There was a time main effect for LS BMD (p = 0.032), LS BMC (p = 0.012), and IT Z (p = 0.042), which were higher following the intervention. There was also a time main effect for femoral neck BMD (p = 0.016) which was lower at the end of the intervention. There was a group x time interaction in FS SPW (p = 0.032) (3.03  $\pm$  0.2 and 2.98  $\pm$  0.25 cm baseline and 16-weeks, respectively in the TLC group versus 2.91  $\pm$  0.22 and 2.93  $\pm$  0.23 cm baseline and 16-weeks, respectively, in the pulse group) (Table 2).

#### 3.4. Adverse events

Four adverse events were reported by three participants in the pulse-based diet group who withdrew from the study. The adverse events of upset stomach (n = 2), flatulence (n = 1), and bloating (n = 1) were rated as mild to moderate severity.

#### 4. Discussion

Many studies have assessed BMD in women with PCOS due to the characteristics associated with the syndrome that are known to affect bone such as amenorrhea, obesity, hyperandrogenemia, and hyperinsulinemia (Good et al., 1999; Katulski et al., 2014; Noyan et al., 2004). Although little is known about the effect of lifestyle interventions and weight loss on bone measures in women with PCOS, this study demonstrates that when combined with exercise, both a pulse-based diet and TLC diet for 16-weeks lead to ~5% weight reduction with improved bone measures in the lumbar spine but reduced BMD in femoral neck. Both groups also improved IT Z following the intervention

#### Table 2

Comparison of lumbar spine and hip bone measures in women with PCOS following either a pulse-based or therapeutic lifestyle changes (TLC) diet.

	TLC		Pulse		p-Values	
	Baseline	16-weeks	Baseline	16-weeks	Time	Group x time
Total hip BMD (g/cm <sup>2</sup> )	$0.978 \pm 0.143$	$1.010 \pm 0.130$	$0.990 \pm 0.114$	$0.984 \pm 0.109$	ns	ns
Total hip BMC (g)	$33.00 \pm 6.19$	$33.16 \pm 6.31$	$31.8 \pm 5.10$	$31.6 \pm 5.5$	ns	ns
FN BMD (g/cm <sup>2</sup> )	$0.873 \pm 0.105$	$0.863 \pm 0.107$	$0.872 \pm 0.117$	$0.856 \pm 0.112$	0.016	ns
FN BMC (g)	$4.375 \pm 0.650$	$4.296 \pm 0.893$	$4.275 \pm 0.732$	$4.254 \pm 0.735$	ns	ns
LS BMD (g/cm <sup>2</sup> )	$1.022 \pm 0.097$	$1.036 \pm 0.099$	$1.045 \pm 0.102$	$1.049 \pm 0.103$	0.032	ns
LS BMC (g)	$58.70 \pm 8.01$	59.95 ± 8.64	59.6 ± 9.3	$60.2 \pm 9.6$	0.012	ns
Troc BMD (g/cm <sup>2</sup> )	$0.772 \pm 0.140$	$0.757 \pm 0.119$	$0.753 \pm 0.088$	$0.739 \pm 0.099$	ns	ns
IT BMD (g/cm <sup>2</sup> )	$1.174 \pm 0.132$	$1.175 \pm 0.149$	$1.138 \pm 0.136$	$1.146 \pm 0.137$	ns	ns
NN SPW (cm)	$3.36 \pm 0.31$	$3.23 \pm 0.33$	$3.185 \pm 0.340$	$3.317 \pm 0.403$	ns	ns
NN CSA (cm <sup>2</sup> )	$3.31 \pm 0.44$	$3.36 \pm 0.60$	$3.227 \pm 0.522$	$3.225 \pm 0.474$	ns	ns
NN CSMI (cm <sup>4</sup> )	$2.83 \pm 0.71$	$2.88 \pm 0.74$	$2.512 \pm 0.711$	$2.643 \pm 0.671$	ns	ns
NN Z (cm <sup>3</sup> )	$1.59 \pm 0.37$	$1.73 \pm 0.66$	$1.490 \pm 0.394$	$1.475 \pm 0.320$	ns	ns
IT SPW (cm)	$5.74 \pm 0.48$	$5.71 \pm 0.55$	$5.492 \pm 0.519$	$5.522 \pm 0.511$	ns	ns
IT CSA (cm <sup>2</sup> )	$5.82 \pm 1.12$	$5.89 \pm 1.21$	$5.608 \pm 0.853$	$5.676 \pm 0.889$	ns	ns
IT CSMI (cm <sup>4</sup> )	$16.44 \pm 4.81$	$17.01 \pm 5.53$	$14.56 \pm 4.22$	$15.03 \pm 4.35$	ns	ns
IT Z (cm <sup>3</sup> )	$5.03 \pm 1.28$	$5.19 \pm 1.45$	$4.56 \pm 1.14$	$4.74 \pm 1.04$	0.042	ns
FS SPW (cm)	$3.03 \pm 0.2$	$2.98 \pm 0.25$	$2.91 \pm 0.22$	$2.93 \pm 0.23$	ns	0.032
FS CSA (cm <sup>2</sup> )	$4.64 \pm 0.83$	$4.61 \pm 0.98$	$4.41 \pm 0.62$	$4.42 \pm 0.62$	ns	ns
FS CSMI (cm <sup>4</sup> )	$3.90 \pm 1.07$	$3.87 \pm 0.95$	$3.52 \pm 0.90$	$3.94 \pm 2.05$	ns	ns
FS Z (cm <sup>3</sup> )	$2.48~\pm~0.55$	$2.52 ~\pm~ 0.48$	$2.31 ~\pm~ 0.44$	$2.38 ~\pm~ 0.52$	ns	ns

Data are expressed as mean  $\pm$  SD and analyzed using repeated measures 2-factor ANOVA. CSA, cross-sectional area; CSMI, cross-sectional moment of inertia; FS, femoral shaft; IT, intertrochanteric; NN, narrow neck; SPW, subperiosteal width; Troc, trochanter; WB, whole body; Z, section modulus.

and the pulse group had more favorable FS SPW after 16-weeks. These findings highlight that diet and exercise leading to weight loss can have opposing effects on bone in women with PCOS.

Weight loss in premenopausal women is associated with reduced BMD (Fogelholm et al., 2001); however, including aerobic exercise during diet interventions has been shown to offset the deleterious effects on bone. Hosny et al. (2012) demonstrated that in premenopausal women, the addition of aerobic exercise to a calorie restricted diet for 3 months led to higher BMD in the lumbar spine and hip as well as higher lean mass, while both groups lost weight. A systematic review determining the effect of exercise on femoral neck and lumbar spine BMD in pre- and post-menopausal women concluded that exercise slows bone loss from the lumbar spine while studies in the femoral neck were less consistent (Wallace and Cumming, 2000); however, a systematic review by Kelley et al. (2013) concluded that exercise improved both lumbar spine and femoral neck BMD.

Interestingly, although estradiol was not different following the intervention, it has been suggested that the lumbar spine is more sensitive to reproductive hormones such as estrogen and age of menarche while both BMD and geometry of the femoral neck are more sensitive to body composition, with lean mass as the strongest predictor (Mallinson et al., 2013). In the study by Hosny et al. (2012) lean body mass was significantly higher following an aerobic exercise intervention, which was not found in this study despite a similar exercise regimen. It is possible that solely high-impact exercise aimed at increasing lean mass would be necessary to mitigate the effects of weight loss on femoral neck BMD in women with PCOS. In addition, both interventions in this study led to lower testosterone, and the lower BMD in the femoral neck may in part be due to the association of testosterone with femoral neck BMD and not lumbar spine BMD in women with PCOS (McBreairty et al., 2017). Further research is required to elucidate the impact of lifestyle interventions on bone health across BMI classes and PCOS variants in reproductive age women.

Compared to BMD, less is known about geometric measures of bone in pre-menopausal women (Kelley et al., 2013). Despite the lower femoral neck BMD following the intervention, intertrochanteric Z improved in both groups after 16 weeks. These results are supported by Vainionpää et al. (2007) who have suggested that redistribution of bone mass can be achieved via low-impact exercise while increasing bone mass may require a higher threshold in pre-menopausal women. Consequently, the aerobic exercise program used in this study may have been sufficient to prevent negative impacts on hip bone geometry while being insufficient to prevent loss in femoral neck density.

Although there were no differences in adherence to exercise between groups, FS SPW was more favorable in the pulse group following the intervention. This finding is contradictory to the association of FS SPW with insulin in women with PCOS (McBreairty et al., 2018), as insulin area under the curve following a 2-hour glucose tolerance test was previously shown to be lower in the pulse group following the intervention (Kazemi et al., 2018). It is possible that the plant-based protein source provided in the pulse group resulted in more favorable FS SPW as the more acidic animal-based protein TLC diet may have led to more bone resorption; however, the remaining measures were similar between groups and results were not adjusted for the many secondary measures.

One of the primary limitations of this study is the lack of a nonexercise control group to differentiate between the effects of diet and exercise. One of the strengths of this study is the inclusion of a well define PCOS population. Furthermore, this study addresses the current gap in research evaluating lifestyle interventions in women with PCOS. The recent international guidelines on PCOS do not address exercise in relation to bone health and exercise recommendations are consistent with international physical activity guidelines and include no PCOS specific evidence-based recommendations (Teede et al., 2018).

#### 5. Conclusions

This study demonstrates that both a pulse-based and TLC diet when combined with exercise lead to loss of body weight and fat mass, with improvements in lumbar spine BMD and BMC as well as intertrochanteric Z; however, both interventions also lead to a loss in femoral neck BMD. There were no differences in bone outcomes between diet groups, with the exception of FS SPW which was more favorable in the pulse group. Future studies should determine whether inclusion of high impact exercise can prevent loss of femoral neck BMD in women with PCOS and mitigate the potential negative effect on the bone from improved insulin sensitivity.

#### Funding

This research was funded by Agriculture and Agri-Food Canada through the Growing Forward II Pulse Science Cluster (G00011676), Saskatchewan Pulse Growers (G00014962), the Canada Foundation for Innovation (29638), and Saskatchewan Health Research Foundation. Funders were not involved in study design, the collection, analysis, and interpretation of data, in the writing of the report or in the decision to submit the article for publication.

# **Transparency document**

The Transparency document associated with this article can be found, in online version.

#### Declaration of competing interest

None.

#### Acknowledgements

We would like to thank the participants of this study. As well we would like to thank the nutrition students who prepared meals and Deborah Michel for her technical assistance.

#### References

- Abeysekara, S., Chilibeck, P.D., Vatanparast, H., Zello, G.A., 2012. A pulse-based diet is effective for reducing total and low density lipoprotein-cholesterol in older adults. Br. J. Nutr. 108, S103.
- Azziz, R., Carmina, E., Dewailly, D., Diamanti-Kandarakis, E., Escobar-Morreale, H.F., Futterweit, W., et al., 2006. Criteria for defining polycystic ovary syndrome as a predominantly hyperandrogenic syndrome: an Androgen Excess Society guideline. J. Clin. Endocrinol. Metab. 91 (11), 4237–4245.
- Azziz, R., Carmina, E., Dewailly, D., Diamanti-Kandarakis, E., Escobar-Morreale, H.F., Futterweit, W., et al., 2009. The Androgen Excess and PCOS Society criteria for the polycystic ovary syndrome: the complete task force report. Fertil. Steril. 91, 456.
- Beck, T.J., Kohlmeier, L.A., Petit, M.A., Wu, G., Leboff, M.S., Cauley, J.A., et al., 2011. Confounders in the association between exercise and femur bone in postmenopausal women. Med. Sci. Sports Exerc. 43, 80.

Bonnick, S.L., 2007. HSA: beyond BMD with DXA. Bone 41, S9-S12.

- Chilibeck, P.D., Vatanparast, H., Pierson, R., Case, A., Olatunbosun, O., Whiting, S.J., et al., 2013. Effect of exercise training combined with isoflavone supplementation on bone and lipids in postmenopausal women: a randomized clinical trial. J. Bone Miner. Res. 28, 780.
- Dewailly, D., Lujan, M.E., Carmina, E., Cedars, M.I., Laven, J., Norman, R.J., et al., 2014. Definition and significance of polycystic ovarian morphology: a task force report from the Androgen Excess and Polycystic Ovary Syndrome Society. Hum. Reprod. Update 20, 334.
- Douglas, C.C., 2006. Role of diet in the treatment of polycystic ovary syndrome. Fertil. Steril. 85, 679.
- Fogelholm, G.M., Sievänen, H.T., Kukkonen-Harjula, T.K., Pasanen, M.E., 2001. Bone mineral density during reduction, maintenance and regain of body weight in premenopausal, obese women. Osteoporos. Int. 12, 199.
- Ganie, M.A., Chakraborty, S., Sehgal, A., Sreejith, M., Kandasamy, D., Jana, M., Rashid, A., 2018. Bone mineral density is unaltered in women with polycystic ovary syndrome. Horm. Metab. Res. 50 (10), 754–760.
- Good, C., Tulchinsky, M., Mauger, D., Demers, L.M., Legro, R.S., 1999. Bone mineral density and body composition in lean women with polycystic ovary syndrome. Fertil. Steril. 72, 21.
- Hart, R., Hickey, M., Franks, S., 2004. Definitions, prevalence and symptoms of polycystic ovaries and polycystic ovary syndrome. Best Pract. Res. Clin. Obstet. Gynaecol. 18, 671.

- Hosny, I.A., Elghawabi, H.S., Younan, W.B., Sabbour, A.A., Gobrial, M.A., 2012. Beneficial impact of aerobic exercises on bone mineral density in obese premenopausal women under caloric restriction. Skelet. Radiol. 41, 423.
- Katulski, K., Slawek, S., Czyzyk, A., Podfigurna-Stopa, A., Paczkowska, K., Ignaszak, N., et al., 2014. Bone mineral density in women with polycystic ovary syndrome. J. Endocrinol. Investig. 37, 1219.
- Kazemi, M., McBreairty, L.E., Chizen, D.R., Pierson, R.A., Chilibeck, P.D., Zello, G.A., 2018. A comparison of a pulse-based diet and the therapeutic lifestyle changes diet in combination with exercise and health Counselling on the cardio-metabolic risk profile in women with polycystic ovary syndrome: a randomized controlled trial. Nutrients 30 (10), 10.
- Kelley, G.A., Kelley, K.S., Kohrt, W.M., 2013. Exercise and bone mineral density in premenopausal women: a meta-analysis of randomized controlled trials. Int. J. Endocrinol. 2013, 741639.
- LaCroix, A.Z., Beck, T.J., Cauley, J.A., Lewis, C.E., Bassford, T., Jackson, R., et al., 2010. Hip structural geometry and incidence of hip fracture in postmenopausal women: what does it add to conventional bone mineral density? Osteoporos. Int. 21, 919.
- Mallinson, R.J., Williams, N.I., Hill, B.R., De Souza, M.J., 2013. Body composition and reproductive function exert unique influences on indices of bone health in exercising women. Bone 56, 91.
- March, W.A., Moore, V.M., Willson, K.J., Phillips, D.I., Norman, R.J., Davies, M.J., 2010. The prevalence of polycystic ovary syndrome in a community sample assessed under contrasting diagnostic criteria. Hum. Reprod. 25, 544.
- McBreairty, L.E., Chilibeck, P.D., Chizen, D.R., Pierson, R.A., Tumback, L., Sherar, L.B., et al., 2017. BMC Nutr. 3, 23.
- McBreairty, L.E., Zello, G.A., Gordon, J.J., Serrao, S.B., Pierson, R.A., Chizen, D.R., et al., 2018. Women with polycystic ovary syndrome have comparable hip bone geometry to age-matched control women. J. Clin. Densitom. 21 (1), 54–60.
- Moran, L., Norman, R.J., 2004. Understanding and managing disturbances in insulin metabolism and body weight in women with polycystic ovary syndrome. Best Pract. Res. Clin. Obstet. Gynaecol. 18, 719.
- National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III), 2002. Third report of the national cholesterol education program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults. Circulation 106, 3143.
- Noyan, V., Yucel, A., Sagsoz, N., 2004. The association of bone mineral density with insulin resistance in patients with polycystic ovary syndrome. Eur. J. Obstet. Gynecol. Reprod. Biol. 115, 200.
- Schäfer, G., Schenk, U., Ritzel, U., Ramadori, G., Leonhardt, U., 2003. Comparison of the effects of dried peas with those of potatoes in mixed meals on postprandial glucose and insulin concentrations in patients with type 2 diabetes. Am. J. Clin. Nutr. 78, 99.
- Sievenpiper, J.L., Kendall, C.W., Esfahani, A., Wong, J.M., Carleton, A.J., Jiang, H.Y., et al., 2009. Effect of non-oil-seed pulses on glycaemic control: a systematic review and meta-analysis of randomised controlled experimental trials in people with and without diabetes. Diabetologia 52, 1479.
- Solmi, M., Veronese, N., Correll, C.U., Favaro, A., Santonastaso, P., Caregaro, L., et al., 2016. Bone mineral density, osteoporosis, and fractures among people with eating disorders: a systematic review and meta-analysis. Acta Psychiatr. Scand. 133, 341 May.
- Teede, H.J., Misso, M.L., Costello, M.F., Dokras, A., Laven, J., Moran, L., Piltonen, T., Norman, R.J., 2018. International PCOS Network. Recommendations from the international evidence-based guideline for the assessment and management of polycystic ovary syndrome. Hum. Reprod. 33 (9), 1602–1618.
- Vainionpää, A., Korpelainen, R., Sievänen, H., Vihriälä, E., Leppäluoto, J., Jämsä, T., 2007. Effect of impact exercise and its intensity on bone geometry at weight-bearing tibia and femur. Bone 40, 604.
- Wallace, B.A., Cumming, R.G., 2000. Systematic review of randomized trials of the effect of exercise on bone mass in pre- and postmenopausal women. Calcif. Tissue Int. 67, 10.
- Yildiz, B.O., Bolour, S., Woods, K., Moore, A., Azziz, R., 2010. Visually scoring hirsutism. Hum. Reprod. Update 16 (1), 51–64.
- Yildiz, B.O., Bozdag, G., Yapici, Z., Esinler, I., Yarali, H., 2012. Prevalence, phenotype and cardiometabolic risk of polycystic ovary syndrome under different diagnostic criteria. Hum. Reprod. 27, 3067.
- Yüksel, O., Dökmetaş, H.S., Topcu, S., Erselcan, T., Sencan, M., 2001. Relationship between bone mineral density and insulin resistance in polycystic ovary syndrome. J. Bone Miner. Metab. 19, 257.
- Zwart, S.R., Davis-Street, J.E., Paddon-Jones, D., Ferrando, A.A., Wolfe, R.R., Smith, S.M., 2005. Amino acid supplementation alters bone metabolism during simulated weightlessness. J. Appl. Physiol. (1985) 99, 134.