

## INFORMATION TO USERS

This manuscript has been reproduced from the microfilm master. UMI films the text directly from the original or copy submitted. Thus, some thesis and dissertation copies are in typewriter face, while others may be from any type of computer printer.

**The quality of this reproduction is dependent upon the quality of the copy submitted.** Broken or indistinct print, colored or poor quality illustrations and photographs, print bleedthrough, substandard margins, and improper alignment can adversely affect reproduction.

In the unlikely event that the author did not send UMI a complete manuscript and there are missing pages, these will be noted. Also, if unauthorized copyright material had to be removed, a note will indicate the deletion.

Oversize materials (e.g., maps, drawings, charts) are reproduced by sectioning the original, beginning at the upper left-hand corner and continuing from left to right in equal sections with small overlaps.

Photographs included in the original manuscript have been reproduced xerographically in this copy. Higher quality 6" x 9" black and white photographic prints are available for any photographs or illustrations appearing in this copy for an additional charge. Contact UMI directly to order.

ProQuest Information and Learning  
300 North Zeeb Road, Ann Arbor, MI 48106-1346 USA  
800-521-0600

UMI<sup>®</sup>



WEIGHT MOVED IN ONE YEAR OF STRENGTH TRAINING  
AND FEMUR TROCHANTER BONE DENSITY CHANGE  
IN 140 POST-MENOPAUSAL WOMEN:  
A DOSE-RESPONSE RELATIONSHIP

by

Eleanor Christine Cussler

Copyright © Eleanor Christine Cussler 2000

A Thesis Submitted to the Faculty of the  
GRADUATE INTERDISCIPLINARY PROGRAM IN EPIDEMIOLOGY  
In Partial Fulfillment of the Requirements  
For the Degree of

MASTER OF SCIENCE

In the Graduate College  
THE UNIVERSITY OF ARIZONA

2 0 0 0

UMI Number: 1403183

Copyright 2000 by  
Cussler, Eleanor Christine

All rights reserved.

UMI<sup>®</sup>

---

UMI Microform 1403183

Copyright 2001 by Bell & Howell Information and Learning Company.

All rights reserved. This microform edition is protected against  
unauthorized copying under Title 17, United States Code.

---

Bell & Howell Information and Learning Company  
300 North Zeeb Road  
P.O. Box 1346  
Ann Arbor, MI 48106-1346

## STATEMENT BY AUTHOR

This thesis has been submitted in partial fulfillment of requirements for an advanced degree at the University of Arizona and is deposited in the University Library to be made available to borrowers under rules of the Library.

Brief quotations from this thesis are allowable without special permission, provided that accurate acknowledgment of source is made. Requests for permission for extended quotation from or reproduction of this manuscript in whole or in part may be granted by the copyright holder.

SIGNED: Ermano C Cusler

## APPROVAL BY THESIS DIRECTOR

This thesis has been approved on the date shown below:

Robin B Harris

Robin B. Harris, Ph.D., MPH  
Assistant Professor of Public Health

12/4/2000

Date

## ACKNOWLEDGMENTS

I would like to thank Dr. Robin Harris, Ph.D., MPH, for her assistance and support throughout my graduate studies and as head of my thesis committee, Dr. Timothy Lohman, Ph.D., for providing me with the idea and the encouragement, and Dr. Zhao Chen, Ph.D. MPH, for her clarity and insights into methodology. Further, I would like to thank and the B.E.S.T. Study investigators and staff for their years of work and answers to all my questions and the B.E.S.T. Study participants without whom this thesis would not have been possible.

## DEDICATION

I dedicate this thesis to my family, for their help, patience, and encouragement.

## TABLE OF CONTENTS

LIST OF TABLES.....	8
LIST OF ILLUSTRATIONS.....	9
ABSTRACT.....	10
CHAPTER 1: INTRODUCTION.....	11
1.1 Definition and Epidemiology of Osteoporosis..	11
1.2 Relationship of Bone Mineral Density to Osteoporosis.....	13
1.3 BMD and its Relationship to Hip Fracture.....	13
1.4 Hip Structure and Fracture Sites.....	14
1.5 Other Risk Factors for Osteoporosis and Hip Fracture.....	14
1.6 Study Objectives.....	16
1.6.1 Introduction.....	16
1.6.2 Hypothesis.....	17
1.6.3 Study Questions.....	17
1.6.3.1 Objective 1.....	17
1.6.3.2 Objective 2.....	18
CHAPTER 2: BACKGROUND.....	19
2.1 Bone Response to Exercise.....	19
2.2 Trochanter BMD and Strength Training Exercise: The Evidence for an Association.....	20
2.2.1 Animal Studies.....	20
2.2.2 Cross-sectional and Case-control Studies.....	21
2.2.3 Longitudinal and Intervention or Prevention Studies.....	23
2.3 The Bone Estrogen Strength Training Study: A Brief Overview.....	30
CHAPTER 3: MATERIALS AND METHODS.....	33
3.1 Introduction.....	33
3.2 Study Population.....	33
3.3 Subject Consent.....	34
3.4 Inclusion/Exclusion Criteria.....	34
3.5 Other Interventions and Measurements.....	35
3.5.1 Bone Mineral Density: DXA.....	36
3.5.2 Demographics and Anthropometry.....	37
3.5.3 Intervention Progressive Strength Training.....	38
3.5.3.1 Strength Training Components.....	38
3.5.3.2 Training Facilities.....	40
3.5.3.3 Exercise Protocol and.....	41
the BEST Book	

TABLE OF CONTENTS - *Continued*

3.5.3.4	Exercise Logging.....	41
3.5.3.5	Exercise Awards and Incentives....	42
3.6	Data Management.....	42
3.6.1	Subject Demographics.....	43
3.6.2	Subject Anthropometrics.....	44
3.6.3	Strength Training Weight Calculations and Adjustment.....	45
3.7	Statistical Analysis.....	46
3.7.1	Selection of Subjects for Analysis.....	46
3.7.2	Fitness Center Coding and Adjustment....	47
3.7.3	Cohort, Age, HRT Status, and Other Covariates.....	48
3.7.4	Statistical Analyses.....	49
3.7.5	Multiple Linear Regression.....	51
3.7.6	Specific Analyses for Objective 1.....	53
3.7.7	Specific Analyses for Objective 2.....	54
CHAPTER 4:	RESULTS.....	56
4.1	Baseline Characteristics .....	56
4.2	One Year Changes.....	56
4.3	Weights moved.....	59
4.4	Correlations between Weight Moved and BMD Change.....	62
4.5	Description of Potential Confounders.....	65
4.5.1	Cohort or Entry into the Study.....	65
4.5.2	Fitness Center.....	68
4.5.3	HRT Status.....	74
4.5.4	Weight Change.....	74
4.5.5	Regression Models Examining Potential Confounders.....	76
4.5.6	Summary of Potential Confounders.....	81
4.6	Does Strength Training Exercise Increase Trochanter BMD?.....	82
4.7	What is the Relationship between Amount of Weight Moved and Change in Trochanter BMD?...	82
CHAPTER 5:	DISCUSSION.....	89
5.1	Strength Training Exercise and BMD Change....	89
5.2	Confounding Effects.....	94
5.3	Strengths of Study.....	99
5.3.1	Introduction.....	99
5.3.2	Size.....	100
5.3.3	Study Design.....	100
5.3.3.1	Subject Selection.....	100

TABLE OF CONTENTS - *Continued*

5.3.3.2	Choice of Intervention.....	101
5.3.3.3	Retention and Compliance.....	103
5.3.4	Adjustment for Covariates.....	103
5.3.5	Consistency.....	104
5.3.6	Biological Plausibility.....	104
5.3.7	Specificity.....	105
5.3.8	Dose-Response.....	105
5.3.9	Strength of Association.....	106
5.4	Limitations of Study.....	107
5.4.1	Selection Bias.....	107
5.4.2	Measurement and Information Bias.....	109
5.4.3	Statistical Considerations.....	110
5.4.4	Generalizability.....	111
CHAPTER 6:	SUMMARY AND CONCLUSIONS.....	113
6.1	Introduction.....	113
6.2	Materials and Methods.....	114
6.3	Results.....	115
6.4	Discussion.....	116
6.5	Conclusions.....	117
APPENDIX.....		118
REFERENCES.....		130

## LIST OF TABLES

TABLE 1,	Selected Baseline Characteristics of 140 Exercising Women.....	57
TABLE 2,	Selected Characteristics of 140 Exercising Women at 1 Year.....	58
TABLE 3,	Selected Exercise Statistics and Mean Weights Moved in 1 Year by 140 Exercisers....	61
TABLE 4,	Correlations of Baseline Trochanter BMD And Trochanter BMD Change with Amount Of Weight Moved in Specific Exercises.....	64
TABLE 5,	Selected Baseline Characteristics By Cohort.....	66
TABLE 6,	Selected 1-Year Characteristics By Cohort.....	67
TABLE 7,	Mean Weight Moved in Specific Exercises By Cohort.....	69
TABLE 8,	Selected Baseline and 1-Year Characteristics By Fitness Facility.....	71
TABLE 9,	Mean Weight Moved Overall and for Individual Exercises by Fitness Facility.....	73
TABLE 10,	Selected Baseline and 1-Year Characteristics By HRT Status.....	75
TABLE 11,	Selected Baseline and 1-Year Characteristics By Body Weight Change Groups.....	77
TABLE 12,	Coefficients and Statistical Test Results From Regression Analysis for Selected Exercises: Full Models and Models Minus Potential Confounding Variables.....	78
Table 13,	Coefficients and Statistical Test Results From Regression Analysis for Total Weight: Base Model and Models Plus Potential Confounding Variables.....	80
TABLE 14,	Regression Coefficients and Statistics for Change in Trochanter BMD by Weight Moved In Individual Exercises and Total Weight....	83
TABLE 15,	Predicted Change in Trochanter BMD for Each 1,000 lbs Moved per Week and for Total Weight Moved.....	88

## LIST OF ILLUSTRATIONS

FIGURE 1, One-Year Mean Trochanter BMD Change For 142 Exercisers.....	60
FIGURE 2, Total Weight Moved in 1 Year By 142 Exercisers.....	63
FIGURE 3, Fitness Center Attendance by Cohort.....	70
FIGURE 4, Predicted Mean Change in Trochanter BMD With Standard Deviations of Total Weight Moved.....	85
FIGURE 5, Predicted Mean Change in Trochanter BMD With Standard Deviations of Weight Moved In Selected Exercises.....	86

## ABSTRACT

Osteoporosis or very low bone mineral density (BMD) has been shown to increase the risk of hip fracture in postmenopausal women. Exercise, particularly strength training, may increase BMD in older women and thus help prevent osteoporosis and hip fracture.

Change in femur trochanter BMD was examined in 140 postmenopausal women enrolled in the Bone Estrogen Strength Training (BEST) Study who performed a one-year progressive resistance training program.

A significant  $0.012 \pm 0.024$  g/cm<sup>2</sup> increase in femur trochanter BMD was found from baseline to 1 year for the entire group. In multiple linear regression, the increase was positively and linearly related to the total weight moved ( $p < .015$ ) even after adjustment for age, baseline trochanter BMD, HRT status, change in body weight, cohort, and fitness center. Among individual exercises, the squats showed the strongest while the back extension exhibited the weakest association with change in BMD.

## CHAPTER 1: INTRODUCTION

### 1.1 Definition and Epidemiology of Osteoporosis

Osteoporosis is a disease of normal bone defined by bone loss and increased porosity (microarchitectural deterioration) (1,2). It is often described as a silent disease because there are no apparent symptoms and it may be discovered only when a bone fractures. Fracture is often used, therefore, to define the disease in epidemiological studies of osteoporosis. For instance, the public health impact of the disease is measured by the costs of disability and death due to fracture.

By 2015, it is estimated that the prevalence of osteoporosis will reach 35 million persons in the United States (3). Osteoporosis affects more women than men and primarily post-menopausal, white or Asian women. Of the 28 million Americans at risk for osteoporosis, 80% are women (4). Forty to fifty percent of white women will have an osteoporosis-related hip fracture over their lifetime (4,5). Of these, 10% to 20% will die in the six months following the fracture (5), and 25% will require long-term care (4,5).

Osteoporosis is associated with 1.5 million fractures each year in the United States, of which 300,000 are hip fractures(5). Direct costs resulting from osteoporosis were placed at \$5-10 billion in 1994 (2,6) and estimated to rise to \$10-15 billion in 2000 (1). There is no estimate of indirect costs, such as lost wages and productivity, due to osteoporosis.

Projected worldwide hip fracture estimates for the year 2050 are 6.26 million (7,8). Of these diagnoses, 70% will occur outside of North America and Europe, as Asian, African, Middle Eastern and Latin American populations experience greater longevity (5). As the number of people 65 years and older increases to an estimated 1.6 billion by the middle of this century, hip fracture will become a global health concern.

Secular trends, however, show increased hip fracture rates even after adjusting for the increased numbers of older individuals (9,10). Because rates are rising among both men and women, postmenopausal bone loss cannot account for all of this increase. Greater height, harder fall impact surfaces, and decreased physical exercise are possible explanations for this trend (8,9).

## 1.2 Relationship of Bone Mineral Density to Osteoporosis

Bone mineral density (BMD) is the primary measurement used for bone loss and definition of osteoporosis. In order to set international screening standards, the World Health Organization (WHO) defined female osteoporosis as a BMD of 2.5 standard deviations (SD) or more below the mean BMD for young adult white women. Individuals with BMD between -1 and -2.5 SD are considered to have osteopenia (low bone density) and are at elevated risk for osteoporosis. One SD represents a difference of approximately 10% of BMD (11). WHO uses a standard measurement of BMD, the mineral content of an area of bone in grams per centimeter squared ( $\text{g}/\text{cm}^2$ ).

## 1.3 BMD and its Relationship to Hip Fracture

BMD accounts for 70% of bone's strength (12). Even though BMD is highly correlated with bone strength ( $r=0.85$ ), other factors may influence bone strength, including bone architecture.

Low BMD thus jeopardizes bone strength. When forces and strain on bone with low mineral content surpass bone strength, fracture results. Low BMD has been shown to increase fracture risk in the hip in women. Riggs et al.

have reported that the incidence of spine and hip fracture increases exponentially as BMD decreases (5). Cummings et al. determined that each SD decrease in BMD in a population of 9704 women 65 years or older increased the risk of hip fracture incidence 2.7 times (13,14). The high relative risk that was found by this longitudinal study confirmed low BMD as a major risk factor for hip fracture.

#### 1.4 Hip Structure and Fracture Sites

Hip fracture can occur in different areas of the hipbone. The femur trochanter is especially susceptible to fracture because of its position near the exterior of the body. In falls, it is often the bone to receive the impact since the outside of the hip touches the fall surface first. Maintaining or building bone strength and density in the trochanter region is of particular importance in reducing the risk of fall fracture.

#### 1.5 Other Risk Factors for Osteoporosis and Hip Fracture

Osteoporosis and hip fracture have complex etiologies. Among the more important factors influencing BMD levels in normal women are the following:

- Age (5),
- Ethnicity and other genetic characteristics, such as frame size and family history of osteoporosis or fracture (15),
- Alcohol, caffeine, and tobacco use (16,17),
- Estrogen Levels (including menstrual cycle normality and status) and hormone replacement therapy (HRT) (1),
- Nutritional status, levels of calcium and vitamin D intake and absorption (18),
- Anorexia nervosa or bulimia (4),
- Use of particular medications (16),
- Weight loss (19),
- Past levels physical activity (20).

Hip fracture risk can increase due to the risk factors listed above. In addition, it is associated with bone geometry and conditions determining the nature of the fall precipitating the bone breakage (21). Bone geometry results primarily from the particular genetic makeup of the individual (22). The outcome of a fall, to which large stature might contribute adversely (8), may depend on the

physical condition of the individual (23). General nutritional status and fitness plays an important role in whether a fall leads to a hip fracture (15). Thus, a woman's history of physical activity may predict her risk not only of osteoporosis but also of falling (23).

Lifelong exercise has been associated with a decrease in mortality in post-menopausal women (24). Muscle strength and increased balance derived through exercise may each independently contribute to lowering fall and fracture risk in older women (25). Exercise may reduce the risk of hip fracture by building bone density and strength. The effect of exercise on bone mineral density is the focus of this paper.

## 1.6 Study Objectives:

### 1.6.1 Introduction

To date, there have been few studies that have quantified the changes in trochanter BMD due to strength training. Two have reported on the effects of different strength training regimens (26,27). However, these studies focused on the quality of the exercise regimen. The effect of the amount of exercise was not evaluated. To measure

exercise quantity, an intervention program needs to be extensive and precise. The BEST study provided a unique opportunity to explore exercise quantity and BMD change, due to its size, the comprehensiveness of exercise intervention, and the extensive exercise documentation by subjects.

The aim of this thesis is to examine the dose-response relationship between femur trochanter BMD and weight moved in progressive strength training exercises performed by 140 post-menopausal women over a one-year period. Further, this paper will explore those factors influencing the bone/exercise association.

#### 1.6.2 Hypothesis

In this group of 140 post-menopausal women, the quantity of weight moved in strength training exercises over a 1-year period is positively and significantly associated with the amount of BMD change in the femur trochanter.

#### 1.6.3 Study Questions

##### 1.6.3.1 Objective 1:

What is the dose-response relationship between the amount of weight moved in one year of exercise and change in femur trochanter BMD in this group of post-menopausal women? Does the trochanter respond differently to different types of exercise?

1.6.3.2 Objective 2:

Is the association between amount of weight moved in one year of exercise and change in femur trochanter BMD independent of the potential confounding effects of time of study entry, fitness facility use, HRT status, and 1-year change in body weight?

## CHAPTER 2: BACKGROUND

### 2.1 Bone Response to Exercise

The role of exercise in bone building has long been accepted. More than a century ago, the German anatomist, Julius Wolff, proposed the law of bone remodeling in which bone changes its architecture in response to stressing (23). Mechanical loading constitutes a form of stressing and changes the density distribution of the bone. Gravity and muscle tightening also create strains within the skeleton. The skeleton responds to these forces by generating bone. The forces must exceed the normal or optimal level of stress in order to initiate the formation of bone. Activities that produce uncommon or atypical strains will build more new bone than routine activities. Lanyon calls this process "architectural adjustments" to compensate for the unexpected change in strain types (28).

Exercise is thought to produce these kinds of stress on bone. The bone responds by increasing in density and strength.

## 2.2 Trochanter BMD and Strength Training Exercise - The Evidence for an Association

### 2.2.1 Animal Studies

Most animal studies have been designed to examine BMD response to the quality and quantity of loading. These experimental models take advantage of the measurement precision that accompanies controlled laboratory conditions, and results must be interpreted with caution with respect to human physiology (29). Strain magnitude, rate, distribution, quality (static versus dynamic), and cycles have been examined in experiments with rats, roosters, turkeys, dogs, and pigs (29,30).

In addition to experiments that load bones, studies with animals have looked at under-loading, comparable to the under-use of the human body as found in bed-rest and weightlessness during space travel.

Most studies, particularly of growing animals (31), have shown elevations in BMD with intense, site-specific loading of short duration. Animal research has helped to refine the understanding of the type and amount of exercise that may be best suited for human intervention trials designed to increase BMD.

### 2.2.2 Cross-sectional and Case-control Studies

For the most part, cross-sectional studies in humans have examined habitual, lifetime physical activity and current bone mineral density in older populations (16,17,32-38). The results suggest a possible link between regular physical activity and bone health; however, the findings are often inconclusive. For example, in the Rancho Bernardo Study, lifelong exercise was associated with higher hip BMD but not decreased fracture (38). In a random sample of 122 men and women, Brahm et al. reported insignificant effects on bone density from higher lifetime physical activity levels (37). In contrast, Coupland et al. demonstrated positive associations between BMD level and history of stair climbing and walking pace in a sample of post-menopausal women (32).

Surveys have helped to identify exercise as a possible measure for preventing osteoporosis. However, this design fails to yield conclusive results based on the lack of initial bone measurements for comparison with later ones. It is not known if the study participants improved bone strength through exercise, or if they exercised more because their initial bone density permitted them to succeed in athletic efforts (23). Conroy et al. reported

femur neck densities 24% higher among weight lifters than non-weight lifters despite the fact that the weight lifters had been lifting weights an average of only 2.7 years (39). This change is far greater than that expected in intervention studies.

Furthermore, individuals with a more sedentary existence may also be more likely to lead a less healthy lifestyle, including those activities that are also risk factors for low BMD: smoking, excessive alcohol consumption, and poor nutrition. These factors can confound the true association between physical activity and BMD.

Some cross-sectional studies, resembling case-control studies, compared habitual lifetime exercisers or athletes with sedentary controls (40). In a 1998 study by Kano, the exposure, lifetime exercise, and the outcome, BMD, were assessed for more than 5000 women aged 40-69. The prevalence odds ratios showed a significant protective effect of increased exercise in the 50-59 age group (OR=0.82; CI<sub>95%</sub>: 0.65-1.04) and in the 60-69 age group (OR=0.78 CI<sub>95%</sub>: 0.61-0.99) but lost significance in the 70 and over group (OR=1.25; CI<sub>95%</sub>: 0.67-2.35) (34). This last result might reflect the sample size of the older age

group. A study of 1373 Italian women (aged 40-64 years) gathered physical activity recall information for specific periods of life: early and late teens and the period prior to the interview (41). For the teen years, those women with high BMD were 1.4 (CI<sub>95%</sub>: 0.8-2.4) times more likely to have been physically active than those women with low BMD. For the period prior to the interview, an OR of 1.7 (CI<sub>95%</sub>: 1.1-2.6) was reported. The non-significant results for the younger years might have been influenced by recall bias.

Case-control studies, like cross-sectional studies, are relatively inexpensive, but are still subject to recall bias and to inexact measurement of exercise history and preclude conclusions regarding causality because of temporality issues. While a few case-control studies are reported, most researchers have focused on intervention or prevention trials.

### 2.2.3 Longitudinal and Intervention or Prevention Studies

Prospective cohort studies are rare in the exercise/BMD literature. The statistical advantage of a large cohort is offset by the high costs of screening for BMD change over time or for the long follow-up needed to

accrue cases of hip fracture (42). Cohort studies in this field tend to have small participant numbers. Furthermore, selection (volunteer and attrition) bias may be substantial.

Michel et al. followed the two-year BMD change in a small sample of exercisers drawn from a larger cohort of older runners (43). Decreases in BMD were reported in the group of runners who reduced their activity over the two-year period. While the small sample size (12 female and 15 male volunteers) permitted the use of expensive tomographic scans of the lumbar spine, low numbers heightened the role of chance in the analyses and of selection bias. Five "over-exercisers" were identified and may have produced a volunteer effect.

Clinical trials remain the best tools to study the relationship between exercise and BMD and provide the best evidence to date of a link between physical activity and BMD. A MEDLINE search and the results of four meta-analytic reviews (44-47) identified intervention trials conducted within the past 10 years that focused on postmenopausal women, a strength (resistance) training program, and hip BMD as one outcome measure. Studies of premenopausal women (48), heart patients (49), aerobic or

weight bearing exercise (18,40,44,50-55), and the BMD of the spine (40,51,56) and the distal radius (57-59) have provided comparable evidence.

Of the eight intervention studies, one did not have a control group (60) and another did not randomize the intervention group (61). Also, the intervention periods for both studies were short (4 and 6 months, respectively). Of the six remaining studies, two reported positive relationships between strength training and hip BMD change (25,27) while four found little or no positive connection between the intervention and outcome (26,62-64).

In a randomized, controlled study of 39 postmenopausal white women, Nelson et al. reported a positive association between femur neck BMD 1-year change and high intensity strength training exercise (25). The neck BMD increased by  $0.9(\pm 4.5)\%$  in the exercising group and decreased by  $-2.5(\pm 3.8)\%$  in the control group.

Kerr et al. block-randomized 56 postmenopausal women to two groups: endurance and strength training regimens (27). Within each group, one limb was randomized to either the exercise or control group. Thus, the non-exercised leg served as a control for the exercised leg. In the strength training limbs, a  $1.7(\pm 4.1)\%$  increase was found in

the femur trochanter BMD compared to a  $0.6(\pm 2.2)\%$  decrease for the controls after one year.

Published in 1997, a study of 39 postmenopausal women compared the BMD changes associated with two types of exercise: ground reaction forces (GRF) and joint reaction forces (JRF) (26). The former entailed walking, jogging, and stair climbing; the latter involved weight lifting and rowing. After 11 months of intervention, GRF exercises showed significant increases in hip BMD:  $3.5(\pm 0.8)\%$ ; however, a loss of  $0.8(\pm 0.7)\%$  was reported for JRF exercise.

In 1991, Heikkinen conducted a study with 78 healthy, postmenopausal Finnish women to determine the effects of HRT and exercise on lumbar and femoral BMD (62). Three sets of women were randomized to two different doses of HRT or no HRT, and to exercise or no-exercise groups. Exercise involved one hour per week of warm-up and strength training exercises. At one year, exercise alone did not increase BMD. Because BMD increased for both the HRT intervention groups and for both non-exercisers and exercisers within those groups, it was concluded that the impact of HRT dominated that of exercise.

Pruitt et al. followed 26 postmenopausal white women over 12 months of resistance training (63). The subjects were randomized to either a high or low intensity exercise program or to a control group. Although there were significant changes in muscle strength among the exercisers in both the high and low exercise groups, no BMD change differences were found. However, almost all the participants in this study were taking HRT and the range of baseline BMD values was limited.

A study published in 2000 by Rhodes et al. reported similar results (64). Forty-four postmenopausal women (mean age: 68.8 years) were randomly assigned to either progressive resistance training or control groups for a 1-year period. The women performed three 1-hour sessions of progressive resistance training at 75% of one repetition maximum (1RM), the maximum weight that can be lifted in a single attempt. They received close supervision for the first three months and then moved to exercise facilities closer to home without supervision. The high mean age of the women (approximately, 69 years) and the lack of monitoring after three months may have accounted for the insignificant bone density results.

The evidence from intervention research suggests that strength training may help to maintain hip BMD or even to increase bone density. The results are inconsistent, however, and difficult to interpret. Reasons for this inconsistency may lie in the limitations of strength training/BMD trials.

Participant numbers in the eight intervention studies described above ranged from 26 to 78 and the randomized groups never exceeded 30 subjects. While inactive women of normal health might benefit most in bone strength from these intervention programs (23,65), they are also the most difficult to retain in the strenuous exercise trials (66). Furthermore, analysis did not usually include adjustment for potential confounding factors.

While the use of a control group is an almost universal element of the studies (60), randomization may not be included. Some studies (61) allow prospective participants to choose between exercise and control groups in order to try to maximize enthusiasm and retention. This self-selection process compromises the validity of the intervention effect.

Studies often randomize to interventions involving combinations of exercise, hormone replacement therapy

(HRT), and calcium supplements. For example, some studies examined women who were not taking HRT (60); others involved only subjects using HRT (63). Bone density change differences are thus difficult to describe and compare.

The duration of the intervention also differs. It is widely accepted that bone does not respond to exercise in less than 6 months and may take as long as one year to change (30,48). Interventions of short duration, therefore, will not show the same results as those involving longer exercise programs. A null outcome in a short study may be valid, whereas a positive outcome should be viewed with caution.

The type of training programs may load and stress bones in different ways and to different degrees. To take full advantage of their expensive participants, researchers may develop complex strength training programs that do not invite easy comparison (29). Although some studies attempt to design exercises to be site-specific and impact the bone region of interest, exercise routines are often general and utilize many muscle groups. General programs are developed with the intent to design a routine that is practical for average middle-aged and older women. While the intention

is good, interpretation of the intervention effects is difficult.

Bone measurement equipment and bone site choice for the measurements differ as well. Bone density can be measured in several ways. Single-photon absorptiometry (SPA) is noninvasive and is most appropriate for measuring arm and leg bone. Quantitative computed tomography (QCT) permits 3-dimensional images and thus measures bone volume (23). QCT is most valuable in accessing the BMD of spine bones (23). Dual-energy x-ray absorptiometry allows area measurement of BMD in all body locations and is also non-invasive (23). It is therefore a compromise between the limited SPA and the expensive QCT. Restricted by equipment choice and funding considerations, some researchers concentrate on one bone site and try to match the intervention to that site.

The Bone Estrogen Strength Training (BEST) Study was designed to minimize the limitations of previous studies. A brief description of the study follows.

### 2.3 The Bone Estrogen Strength Training Study: A Brief Overview

The BEST Study, funded by the National Institutes of Health in 1995 for five years, is a randomized, controlled clinical intervention trial involving postmenopausal women. The aim of the study was to examine the effect of physical training (aerobic, weight bearing, and resistance exercise) on BMD and other anthropometric and physiologic measurements in post-menopausal women as they relate to osteoporosis and cardiovascular disease risk. A primary hypothesis proposed that one year of progressive strength training exercise would result in a 2% increase in BMD (67).

Although the original proposal intended to randomize women to both HRT and exercise interventions in a 2X2 scheme, recruitment strategies required that those already on HRT be included in the study and that exercise be randomized (block randomization) within HRT groups (HRT use versus no HRT use). The final intervention groups thus included Exercise/HRT, No Exercise/HRT, Exercise/No HRT, and No Exercise/No HRT. All women received a daily calcium supplementation of 500mg ( $\text{CaCO}_3$ ).

This thesis will examine the trochanter bone response of those women in the BEST Study intervention group, both HRT users and non-users, to the strength training

exercises. Exercising women who completed bone measurement testing at both the beginning and end of the year are included in analysis regardless of their exercise compliance.

## CHAPTER 3 - MATERIALS AND METHODS

### 3.1 Introduction

Beginning in 1995, 429 post-menopausal women were recruited into the BEST study cohorts every six months. Each cohort was block-randomized into four intervention groups based on their entry HRT use: 1. Exercise/HRT; 2. No exercise/HRT; 3. Exercise/No HRT; 4. No Exercise/No HRT. Of these women, 320 completed baseline DXA measurements, and 266 women returned at the end of one year for laboratory testing. One hundred forty-two exercisers completed the 1-year intervention. All participants completed questionnaires and laboratory testing at baseline, six months, and one year. The exercisers were asked to participate in cardio-fitness and progressive strength training sessions three times per week.

### 3.2 Study Population

The BEST Study targeted post-menopausal women, primarily white, Hispanic American, and Asian American. The source population included the approximately 40,000 females, aged 50 to 65, residing in Tucson, Arizona and nearby communities as determined by the 1990 United States

Census. Subjects were recruited using selected zip codes for direct mailing, medical clinics, community organizations, and media advertisement.

### 3.3 Subject Consent

At an initial recruitment meeting, written and verbal descriptions of all procedures were given out. Participants signed consent forms, which were then locked in a storage area of the University of Arizona Department of Exercise and Sports Medicine. Subjects consented to BMD measurements, blood draws, urine sampling, body composition assessment, stress tests, medical history, lifestyle, physical activity, and dietary intake questionnaires. Personal data remained confidential to all except the study investigators. Individualized reports were given out annually to each participant.

### 3.4 Inclusion/Exclusion Criteria

Participants were non-smoking females between 50 and 65 years of age and 5 to 10 years post-menopausal. In order to increase enrollment, this last criterion was modified in 1997, to include 3 to 10 years post-menopausal. Participants in the Tamoxifen Trial (University of Arizona

Cancer Center) or in the Women's Health Initiative (University of Arizona Women's Health Initiative Vanguard Center) were excluded. A graded stress (treadmill) test was used to identify those women with risk or presence of serious cardiovascular or musculoskeletal disease. Those who failed the stress test, had received treatment for cancer, or had participated in regular physical training within one year of the study were excluded.

### 3.5 Other Interventions and Measurements:

Calcium supplementation was required for all study participants. Women received 500 milligrams of  $\text{CaCO}_3$  daily for the entire intervention with an average compliance of 91.3% among all study subjects at one year and 91.7% among the exercisers. A dietary assessment was administered at baseline, six months, and one year. This included four days of diet records as well as a diet history obtained through the Arizona Food Frequency Questionnaire.

Questionnaires, both self- and technician-administered, included several on lifestyle and psychological factors. A physician recorded a medical history at baseline, and women reported any changes in

their health status during the year to the study program coordinator.

Other measurements particularly relevant to this paper are described below.

### 3.5.1 Bone Mineral Density: DXA

Femur, lumbar spine, total body, and distal radius BMD were measured by dual energy x-ray absorptiometry (DXA) using a Lunar Radiation Corporation model DPX-1 whole body scanner. In this technique, a dual energy (40 and 70 KeV) beam of x-ray radiation passes at uniform speed across the subject's body, which lies prone on the scanning platform. Two sources of x-ray energy are used to maintain a consistent, stable beam and to reduce errors that occur when a beam crosses an irregular body contour.

The Lunar equipment was calibrated each day with calibration phantoms and weekly with a hydroxyapatite lumbar vertebra bone. The scan speed was uniform for all subjects, and total body scans were completed in 15-20 minutes. The precision of the femur scans is approximately 1.2-1.5%. Subject position was standardized. The same technician analyzed all scans throughout the study. Algorithms provided by Lunar Radiation Corporation

software, version 3.4, completed the analysis. If outlying values were found, a second opinion was sought from a study investigator.

At each study time period, each subject was measured twice. Appointments were usually within a week of each other. The difference between the two measurements was checked. The DXA technician reanalyzed all difference values of 5% or more. The pair of results was then averaged, and the average used in analysis.

### 3.5.2 Demographics and Anthropometry

A study intake questionnaire was given at baseline to assess age, ethnicity, menstrual history, and HRT status. Women were asked not to change their HRT use and to report any changes to the program coordinator.

Height, weight, and skinfold thickness were measured at baseline, six months, and one year. Study staff requested that the women maintain their weight and typical diet patterns for the duration of the study.

While a 7-day physical activity questionnaire was given during the DXA scanning at baseline, six months, and one year, these data have not been computerized and were not included in the present analysis.

An assessment of strength independent of the exercise training protocol was made. Muscle strength of the knee, hip, back, and elbow areas was evaluated using a Cybex II isokinetic dynamometer (LIDO). The data from the LIDO hip extension were included in this analysis as a measure of baseline strength. This measure was associated with the hip region and was representative of other LIDO measures.

### 3.5.3 Intervention: Progressive Strength Training

The BEST workout program was designed to include flexibility, aerobic endurance, and muscle strengthening components. Subjects were asked to exercise three times per week for 45 to 75 minutes per session. Exercise intensity was designed to increase progressively over the year. A session included a warm-up period of stretching, followed by around 20 minutes of aerobic activity, and 20-30 minutes of weightlifting followed by a cool-off period.

#### 3.5.3.1 Strength Training Components

Weightlifting exercises were chosen to stress the lumbar vertebrae, the femur neck and trochanter regions, and the distal radius. By standardizing the strength training program, exercises were kept uniform between

subjects with regard to the target muscles and intensity and direction of the stress. Individualization of exercise routines was used to some extent to reduce soreness, improve motivation, and promote compliance. Women began with one set of 6 to 8 repetitions of each exercise and then increased to 2 sets at the end of one week. Initial weights were set at 50% of one repetition maximum (1RM), the maximum weight that can be lifted safely. Women were encouraged to achieve 70% of 1RM by the end of 3 months and to work up to 80% of 1 RM for the remainder of the year. Every 8 weeks, the 1RM was re-evaluated to adjust weight levels.

The following weightlifting exercises were included in the core group (see Appendix for descriptions):

Exercise	Target Muscles
1. Seated Leg Press (Right and Left Legs)	Quadriceps, gluteus, hamstrings
2. Lat. Pull Down	<i>Latissimus dorsi</i> , biceps <i>brachii</i> , Forearm flexor, posterior deltoid
3. Weighted March	<i>Iliopsoas</i> (hip flexors)
4. Seated Row	<i>Latissimus dorsi</i> , trapezius, forearm flexors rhomboids, biceps, brachialis, posterior deltoid, forearm flexors

5. Back Extension	<i>Erector spinae, gluteus, hamstring</i>
6. Military Press (Right and Left Arms)	Front and middle deltoid, triceps, <i>erector spinae</i>
7. Squats (Wall, Hack, and Smith)	Quadriceps, hamstrings, gluteus
8. Rotary Torso (Both Sides)	Obliques

### 3.5.3.2 Training Facilities

Four training facilities were available to study participants over the 4-year period during which all exercisers from the 6 cohorts completed their first year of training. Initially, subjects visited the Fitness and Health Institute of Tucson (FIT) and the Naturally Women Fitness Center (NW). When FIT was not longer open to participants, women trained the Metro Fitness (Metro) location and the University Medical Center Fitness Center (UMC). All centers were located centrally and had adequate parking. Subject choice of fitness center was usually based on the proximity of the center to her home or place of work. Most women exercised at one or at most two facilities during their 1-year intervention.

For some exercises, equipment type varied depending on the fitness facility. This was especially true for the seated leg press. Women who started at another facility reported more difficulty pressing similar weights when they moved to the UMC facility. Most women who visited the NW center did the Hack squats, whereas more of the harder Smith squats were performed at the other three facilities. Finally, each facility had a different machine for the rotary torso (see Appendix).

#### 3.5.3.3 Exercise protocol and the BEST Book

Qualified exercise trainers supervised all exercise sessions. These professionals trained subjects in the exercise protocol and advised them on the course of their programs. The trainers were also responsible for documenting attendance and monitoring subject progress.

The exercise protocol was compiled into a book known as The BEST Book. A copy of this book was located at each fitness facility and could be referenced by subjects.

#### 3.5.3.4 Exercise logging

All subjects recorded their tri-weekly sessions on exercise cards kept at the exercise facility. The subject's

name, the month, and the year were written at the top of each monthly card. Each card contained 13 session columns. At the top of each column, subjects entered the exercise session date and then filled in the two sets of weights and repetitions for each exercise printed down the left side of the card. A sample of the exercise card can be found in the Appendix.

At baseline, trainers explained the procedure for filling out the cards. A detailed description of the session recording was included in the BEST Book.

#### 3.5.3.5 Exercise awards and incentives

Awards and incentives were given throughout the study at various stages in the exercise program. Benchmark points were awarded based on attendance at exercise sessions, lifestyle classes, and group events, for meeting personal goals, and for calcium compliance. Recognition meals, tee shirts, and pins were some of the honors given.

### 3.6 Data Management

Data for subject demographics and anthropometry were double entered into a Visual FoxPro entry and verification system. Strength training exercise data were entered into

a FoxPro entry system and visually checked for errors and inconsistencies. Further FoxPro programs checked for incorrect dates and duplicate entries.

### 3.6.1 Subject Demographics

The subject file included the following information used in this analysis:

1. Cohort and subject id numbers (nominal),
2. Intervention group status (categorical:  
1=Exercise/HRT; 2=No Exercise/HRT;  
3=Exercise/HRT; 4=No Exercise/No HRT),
3. HRT use (0=No; 1=Yes),
4. Age at baseline (calculated from date of birth to cohort start date; continuous),
5. Years postmenopausal at baseline (continuous),
6. Years of education (0 to 20+ in one-year increments),
7. Self-reported physical activity rating (1=inactive, 2=somewhat inactive, 3=somewhat active, 4=active),
8. Fitness center attended (categorical, coded F=FIT; M=Metro; N=Naturally Women; U=UMC; O=other.)

### 3.6.2 Subject Anthropometrics

The anthropometry file included baseline and one-year weight in kilograms (mean of two trials) used in the calculation of body mass index (BMI) and change in body weight. BMI was calculated as follows:

$$\text{BMI} = \text{body weight (kg)} / (\text{height in meters})^2.$$

Change in body weight (kg) was

$$\Delta\text{Weight} = \text{Weight at one year} - \text{Weight at baseline}.$$

Files of body composition and bone measurement data were transferred in Dbase format directly from the LUNAR software into FoxPro reformatting programs. Percent body fat and fat free mass (FFM) were calculated from DXA-generated values for soft tissue, fat, and bone mineral content (BMC) measured in grams. The formula for percent fat was as follows:

$$\text{Percent fat} = ((\text{soft tissue} + \text{fat} + \text{BMC}) / (\text{soft tissue} + \text{BMC})) * 100.$$

FFM was calculated in this manner:

$$\text{FFM (grams)} = \text{soft tissue} + \text{BMC} - \text{fat}.$$

The Lunar Dbase files also provided baseline and one-year femur trochanter density ( $\text{g}/\text{cm}^2$ ) measurements for calculation of change in bone density:

$$\Delta\text{BMD} = \text{BMD at one year} - \text{BMD at baseline.}$$

### 3.6.3 Strength training weight calculations and adjustment

Raw strength training data (~15,000 records) were processed to summarize the total amount of weight moved for each of the individual exercises and for total weight. These totals were adjusted by factors unique to the exercise facility. For example, different facilities had baseplates of different weight for the seated leg press. The facility-specific weight pressed in one set of repetitions for the seated leg press (SLP) was calculated with the following formula:

$$\text{SLP weight} = ([\text{Weight added by subject}] \times [\# \text{ of repetitions}]) + [\text{facility baseplate weight}].$$

Finally, total yearly weight for the seated leg press was calculated in this fashion:

$$\text{Total SLP weight} = [\text{SLP weight/session}] \times [\# \text{ of sessions}].$$

The weighted march and military press weight totals were calculated using the entries for the right leg and

arm, respectively. The total weight moved included only these right side weight amounts.

Subjects received no credit for bimonthly testing days and for sessions that did not include both the weight moved and the number of repetitions that the weight was moved. Subjects with individual exercise weight totals that deviated from the total weight moved were determined from two-way scatter plots of total weight moved versus total weight for the individual exercises to allow tracking of injuries. Injuries were also recorded in a comment box at the bottom of the exercise card (see sample exercise card in Appendix).

### 3.7 Statistical Analysis

After initial data validity checks in FoxPro, Dbase files were exported into the Statistical Program for the Social Sciences (SPSS) (68) for further editing and analysis. All descriptive, comparative statistics and regression analyses were conducted using SPSS. A two-sided alpha level of 0.05 was used to denote statistical significance.

#### 3.7.1 Selection of Subjects for Analysis

Of the 320 subjects who completed baseline DXA testing, 266 also completed DXA testing at one year. Of this group, 142 women were randomized to exercise. For the final analysis, two women were removed from analysis because both women had moved 30% more weight than the next highest weight lifters (2.6 versus 2.0 million pounds) and had lost bone over the year. It was thought that these women might have reached a level of exercise that was detrimental to their bone health and should be excluded. Cross-sectional studies have reported lower levels of BMD among athletes exercising at extreme levels of exertion (30). Furthermore, the very high levels of exercise exceeded those that would be feasible or recommended for this age group. (Preliminary analyses including these two women suggested a sizable influence in regression.)

### 3.7.2 Fitness center coding and adjustment

More than 88% of the 140 women attended a single fitness center throughout the year of exercise. Because FIT was not longer available after the summer of 1997, some women visited two or three different facilities during the intervention year. For analysis, women were categorized by the facility where they performed the majority of their

exercise. Only 0.2% of the total exercise was performed at places other than the four training facilities.

Fitness center was coded as follows, and the FIT facility was fixed as the reference group:

Facility	Variable Name		
	metro	nw	umc
FIT	1	1	1
Metro	-1	0	0
Naturally Women	0	-1	0
UMC	0	0	-1

### 3.7.3 Cohort, Age, HRT status, and other covariates

Cohort was coded as follows with Cohort 1 as the reference category:

Cohort	Variable Name				
	coh2	coh3	coh4	coh5	coh6
1	1	1	1	1	1
2	-1	0	0	0	0
3	0	-1	0	0	0
4	0	0	-1	0	0
5	0	0	0	-1	0
6	0	0	0	0	-1

Age was calculated by subtracting date of birth from the study start date and included as a covariate in multivariate analysis. HRT status, coded as 0 for no use at baseline and 1 for use at baseline, was used in the form -1 for no use and +1 for use in regression. Baseline femur trochanter BMD ( $\text{g}/\text{cm}^2$ ) was rounded to 3 decimal places.

Unpublished analyses of the exercise and control groups showed a significant curvilinear relationship between body weight change and femur trochanter BMD change (unpublished data). Weight in kilograms squared was calculated for use in analysis and rounded to 2 decimal places.

To compare the effects of weight change on the intervention and outcome variables, three weight change categories were developed: weight loss  $\leq 2.0$  kg; weight change  $< 2.0$  kg; and weight gain  $\geq 2.0$  kg.

#### 3.7.4 Statistical Analyses

Descriptive statistics and frequency distribution curves were produced for all relevant variables to check for normality and outlying values. Continuous variables were compared by correlation analyses to establish the presence of crude relationships.

Pearson's correlations between weight moved, change in trochanter BMD, and potential continuous covariates: age, years postmenopausal, baseline BMD, percent fat and lean tissue, body mass index (BMI), and body weight change, were performed. In addition, the variables for amount of weight moved for individual exercises and for total weight were

squared to allow for a possible curvilinear relationship between the intervention and outcome.

To compare potential categorical covariate differences with respect to continuous variables, Student T-tests and analysis of variance (ANOVA) were conducted. Bonferroni post-hoc tests were performed to identify differences between individual category pairs.

Chi square tests evaluated statistical significance between the categorical variables: cohort, fitness center, HRT status, and body weight change groups.

Multiple linear regression analysis was used to relate change in trochanter BMD to weight moved in individual exercises and to total weight moved. Confounding effects were examined with linear regression and will be discussed subsequently.

To identify appropriate candidates for inclusion in final regression analysis, Affifi and Clark suggest testing small subsets of interrelated independent variables for high correlation and the potential for collinearity (69). High correlations were found between various anthropometric measurements. Body weight, BMI, percent body fat, fat free mass, and lean soft tissue had correlation coefficients

between .70 to .80 and were excluded from regression to reduce the risk of collinearity.

### 3.7.5 Multiple Linear Regression

Selection of limited variables was needed to preserve power in the multiple linear regression. Greenland suggests that there should be no less than ten subjects for every variable added to the regression equation (70,71). The final models for each specific exercise weight variable included the following:

- Exercise Weight (pounds; squared; continuous)
- Age (in years; continuous);
- Baseline femur trochanter BMD ( $\text{g}/\text{cm}^2$ ; continuous);
- HRT status dummy variable;
- Body weight change (kilograms; squared; continuous);
- Five Cohort dummy variables.
- Three Fitness center dummy variables;

The relationship between change in femur trochanter BMD and exercise weight moved may be curvilinear (72). Therefore, weight moved, the primary independent variable, was squared and included in the regression model to evaluate the curvilinear relationship.

Because of the known impact of age on both exercise capacity (73) and BMD (74), age was considered a covariate

and included in the models. Baseline bone density was included because low initial bone levels have been associated with greater improvement in BMD through exercise than higher initial bone density levels (29,31).

Variables for HRT status, change in body weight, cohort, and fitness center were also included and are discussed in Section 3.7.7. These variables were specifically examined as potential confounders.

Interactions among the independent covariates were not evaluated due to low subject numbers in the subcategories.

The general model used the following form:

$$\Delta\text{BMD} = \alpha + \beta_1 * \text{Wt}^2 + \beta_2 * \text{Age} + \beta_3 * \text{BMD}_{\text{base}} + \beta_4 * \text{Wt Change}^2 + \beta_{5-9} * \text{Cohort}_{2...6} + \beta_{10-12} * (\text{Fit Center}_{\text{metro}, \text{nw}, \text{umc}}) + \varepsilon.$$

All variables were forced into the models. Residuals were tested for random patterns (heteroscedasticity) and normal distributions. The effect of outliers for the dependent and independent variables were examined. Analysis of residual leverage was performed to identify cases most likely to influence the nature of the regression curve. Four cases were found. Their exclusion from

regression analysis had either no or a strengthening effect on the models. In the interest of increased power, the cases were left in the analysis. Correlations between variables that may have been highly related were performed to identify variables that could be collinear in regression analysis. No such variables were used together in the final models.

### 3.7.6 Specific Analyses for Objective 1

A paired T-test with baseline and 1-year BMD was used to determine whether BMD change was significantly different from zero. The change in BMD measured at the end of the one-year intervention was calculated as the difference in  $\text{g/cm}^2$  from baseline BMD levels.

Since beta coefficients from multiple linear regression reflected the change in BMD for weight squared, coefficients were converted to provide a standardized unit to compare individual exercises. Change in BMD for a standard deviation of weight moved provided such a standardized form. The calculation was as follows:

$$\Delta\text{BMD} = \beta_1 * (\text{SD}_{\text{wt}})^2$$

Values for predicted change in BMD for several increments of standard deviation, e.g., 0.5, 1.0, 1.5, were graphed to produce a regression curve using quadratic trendline generating software (75). Curves for individual exercise types could then be compared visually with each other and with the curve for total weight moved.

Beta coefficients were additionally adjusted to produce trochanter percent BMD change for every 1000 pounds per week. To produce percents, the coefficients were multiplied by 52,000, divided by  $.745 \text{ g/cm}^2$ , and multiplied by 100.

### 3.7.7 Specific Analyses for Objective 2

Observed differences between BMD change and weight moved among the various cohorts and exercise facilities suggested confounding by these variables. Stratified analyses using the ANOVA were performed to examine these differences. Because body weight change and HRT status were thought to impact BMD change, BMD change was compared by HRT status and weight change using Student T-tests.

Special regression analyses were performed with these four variables to explore confounding effects. The main effect of full models for selected exercises and total

weight was first evaluated. A potential confounder was removed and further computations were conducted. The models were then reevaluated for the percent change in the beta coefficient for weight moved. A change in adjusted coefficient (71) of  $\pm 15\%$  was used to define confounding (76).

To examine the influence of cohort and fitness center confounding effects on each other, a base regression model adjusting for age and baseline trochanter was constructed. The cohort and fitness center variables were added independently to this model and then together. Percent changes in beta coefficients for total exercise weight between the base model and models with added variables provided further tests for confounding.

## 4. CHAPTER 4 - RESULTS

### 4.1 Baseline Characteristics

Women who completed DXA testing at one year and were randomized to the exercise group were included in these analyses. Of the 320 women who completed baseline DXA testing, 177 were randomized to exercise with 142 returning for 1-year testing. Two women were then excluded from analysis because their recorded weights moved were almost three standard deviations from the mean.

Baseline characteristics of the 140 women are shown in Table 1. The group is predominately non-Hispanic white (87.9%) with a mean age at entry of 55.5( $\pm$ 4.4) years. The women averaged 5.5( $\pm$ 2.7) years postmenopausal with a mean baseline trochanter BMD of 0.745( $\pm$ 0.117) g/cm<sup>2</sup>. Half of the women reported taking HRT.

### 4.2 One Year Changes

At one year, the mean change in femur trochanter BMD was 0.012( $\pm$ 0.024) g/cm<sup>2</sup>, a 1.68% increase over the baseline value (Table 2). Calcium compliance, part of the overall

Table 1. Selected Baseline Characteristics of 140 Exercising Women

Variable	Mean	SD
Age (years)	55.5	4.4
Years Post-menopausal	5.5	2.7
Years Education	15.3	2.7
Self-reported Activity Score (1=inactive - 4=active)	2.6	0.7
Body Mass Index (kg/m <sup>2</sup> )	25.6	3.7
% Body Fat	38.6	6.1
Fat Free Mass (kg)	40.8	4.7
Trochanter BMD (g/cm <sup>2</sup> )	0.745	0.117
% on HRT	50.0	

Table 2. Selected Characteristics of 140 Exercising Women at One Year

Variable	Mean	SD
Change in Trochanter BMD (g/cm <sup>2</sup> )	0.012	0.024
% Change in Trochanter BMD	1.68	3.39
Change in Body Weight (kg)	0.26	2.52
% Calcium Compliance	91.6	13.4
% on HRT	51.4	
% Retention in Study	80.4	

intervention, was 91.6( $\pm$ 13.4)% for the year. At yearend, two women not on HRT started taking estrogen.

In Figure 1, a frequency histogram of exercisers for change in BMD is shown. The distribution is normal but somewhat right skewed.

#### 4.3 Weights moved

Women complied with 71.5( $\pm$ 19.8)% of the required training regimen (Table 3). Compliance was measured as the percent of expected sessions attended for the year. On average over the year, women moved 11,282 ( $\pm$ 2,618) pounds per exercise session and attended a mean of around 2 sessions per week or 103.5 sessions per year.

Table 3 also lists weight moved in the first year by the 140 exercisers, both for individual exercises and for total weight moved for all exercises. The mean total amount of weight moved per woman during the 1-year intervention was 1,167,819 ( $\pm$ 452,896) pounds, of which 383,748 ( $\pm$ 175,632) pounds was from the seated leg press, almost one-third of the average total weight. The military press and the weighted march exercises involved the least amount of weight lifted.

**Figure 1. One-Year Mean Trochanter BMD Change for 142 Exercisers**

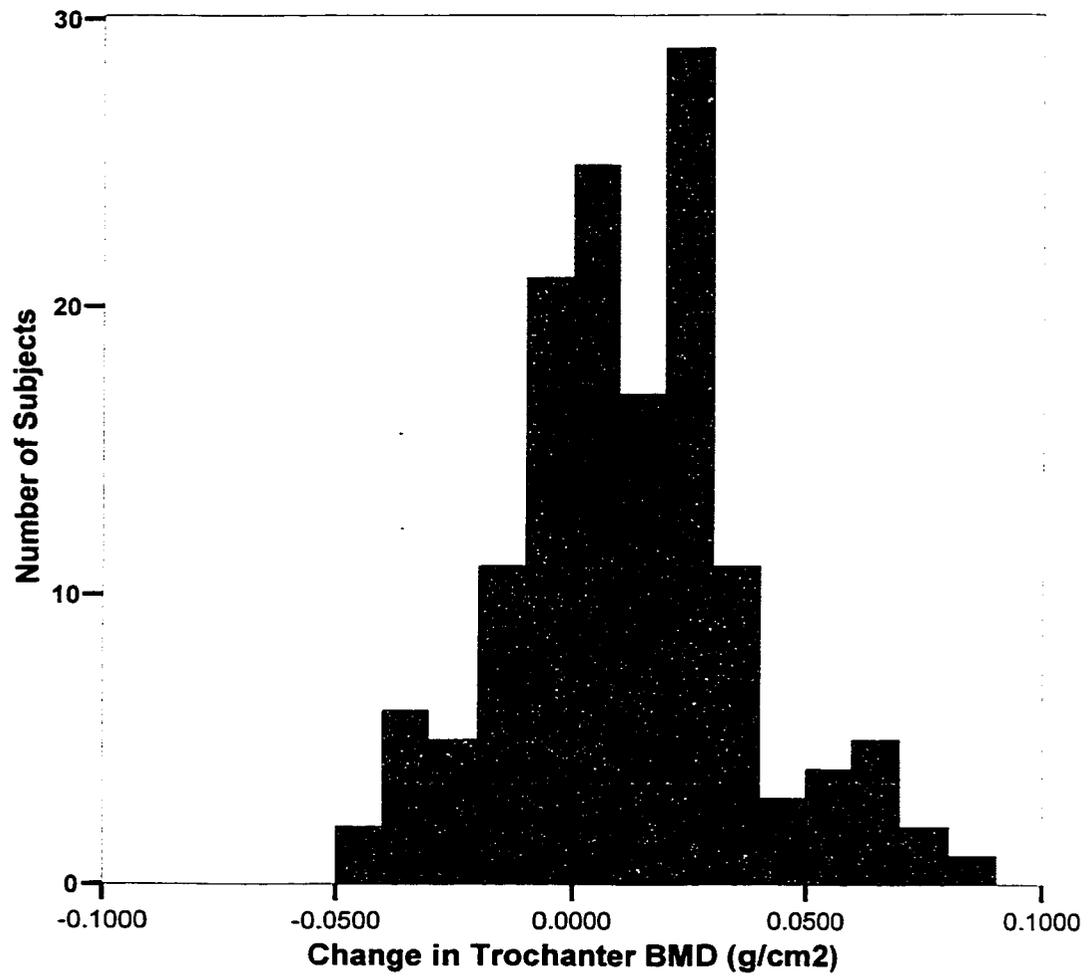


Table 3. Selected Statistics and Mean Weight Moved in One Year for Total and Specific Exercises (n=140 Exercisers)

	Mean	Standard Deviation
Exercise Compliance (%)	71.5	19.8
Number of sessions in 1 year per exerciser	103.5	29.0
Weight moved per session (lbs)	11,282	2,618
<b>Total weight (lbs)</b>	<b>1,167,819</b>	<b>452,896</b>
Seated leg press (lbs)	383,748	175,632
Latissimus dorsi pull (lbs)	122,958	45,858
Weighted march (r.) (lbs)	21,024	10,542
Seated row (lbs)	102,849	40,644
Back extension (lbs)	195,710	85,486
Military press (r.) (lbs)	19,019	7,851
Squats (lbs)	215,664	131,572
Rotary torso (lbs)	88,469	43,214

Figure 2 illustrates the frequency distribution for total weight moved of the 140 exercisers during the 1-year period. The eleven women who moved very little weight (5 histogram bars on the left) averaged only 24% exercise attendance.

#### 4.4 Correlations between Weight Moved and BMD Change

Table 4 reports Pearson's correlation coefficients for baseline BMD and BMD change with the weight moved in individual exercises as well as total weight moved. This table compares the relationships for two weight variables, not transformed and transformed (weight-squared).

The correlation between total weight moved and change in trochanter BMD was  $r=0.21$  ( $p<.05$ ) and increased to  $r=0.22$  ( $p<.01$ ) between BMD and weight squared. In general, correlations increased when the weight variables were squared. This was particularly evident for the *Latissimus dorsi* pull (lbs) exercise, where the correlation between trochanter change and *Latissimus dorsi* pull was 0.13 and 0.29 ( $p<.01$ ) between BMD change and *Latissimus dorsi* pull (lbs-squared).

**Figure 2. Total Weight Moved in One Year  
by 142 Exercisers**

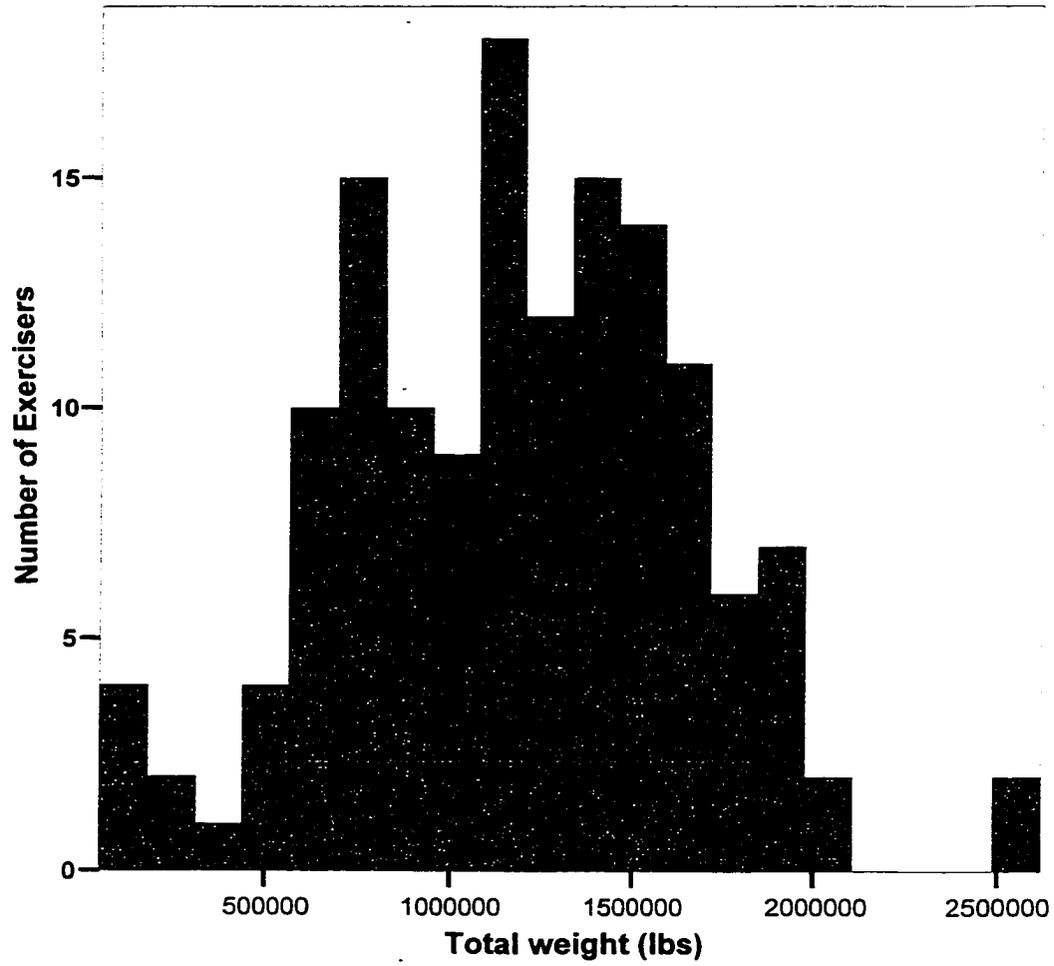


Table 4. Correlations of Baseline Trochanter BMD and Trochanter BMD Change with Amount of Weight Moved in Specific Exercises (n=140 Exercisers)

Exercise Type	Baseline Trochanter BMD		Change in Trochanter (1 year)	
	weight	weight <sup>2</sup>	weight	weight <sup>2</sup>
<b>Total Weight</b>	<b>0.18*</b>	<b>0.22**</b>	<b>0.21*</b>	<b>0.22**</b>
Seated Leg Press	0.14	0.17*	0.17*	0.17*
Lat. Pull	0.08	0.26**	0.13	0.29**
Weighted March	0.17*	0.21*	0.11	0.06
Seated Row	0.12	0.14	0.13	0.14
Back Extension	0.06	0.09	0.12	0.07
Military Press (right)	0.14	0.14	0.24**	0.27**
Squats	0.23**	0.26**	0.25**	0.29**
Rotary Torso	0.18*	0.22**	0.17*	0.12

\* p<.05

\*\*p<.01

## 4.5 Description of Potential Confounders

### 4.5.1 Cohort or Entry into the Study

Because of concern that date of entry into the study could potentially change how women exercised and complied, this variable was evaluated. Table 5 shows selected baseline characteristics of the 140 women by cohort (or date of entry). There were no significant baseline differences between the six cohorts of women in age, years since menopause, BMD, and baseline BMD. The lowest baseline BMD was in Cohort 6 with  $.726(\pm.114)$  g/cm<sup>2</sup> compared to Cohort 3 at  $.771(\pm.160)$  g/cm<sup>2</sup>. Statistically significant baseline differences were found in the LIDO hip extension and percent body fat with Cohorts 4 and 6 representing the range.

One-year characteristics between the cohorts are reported for both intervention and outcome in Table 6. Cohort 3 moved approximately 34% more weight than Cohort 5. Cohorts 2 and 6 showed smaller gains in femur trochanter BMD than the other four cohorts. Women in Cohort 2, with the smallest proportion of HRT users, gained on average  $0.005\pm 0.025$  g/cm<sup>2</sup> while Cohort 6 gained  $0.002\pm 0.021$  g/cm<sup>2</sup>. Cohort 1, with the greatest increase in BMD, gained  $0.028\pm 0.029$  g/cm<sup>2</sup>, ten times the gain for Cohort 6 ( $p<.002$ ).

Table 5. Selected Baseline Characteristics by Cohort (n=140 Exercisers)

Cohort	1	2	3	4	5	6
N	23	19	18	23	30	27
	Mean SD	Mean SD	Mean SD	Mean SD	Mean SD	Mean SD
Age (years)	55.9±3.5	56.3±4.7	56.0±4.3	53.9±5.7	54.4±4.5	55.5±3.5
Years Post-menopausal	5.5±2.8	6.9±3.2	6.2±3.7	5.2±2.7	4.9±1.9	4.8±1.8
Body Mass Index (kg/m <sup>2</sup> )	26.7±3.8	25.9±3.9	26.0±3.9	25.9±4.2	25.2±3.6	24.3±3.2
% Body Fat*	39±6.4	39.4±6.7	40.0±6.2	40.1±5.4	37.8±6	36.7±6
Fat Free Mass (kg)	42.8±5	39.6±4.4	40.5±3.9	41.0±5.5	41.3±5.1	39.4±3.9
Trochanter bmd (g/cm <sup>2</sup> )	0.732±.105	0.754±.112	0.771±.16	0.763±.129	0.736±.097	0.726±.114
LIDO hip extension** (lbs)	67.0±18.3	65.8±23.3	65.1±22.6	70.0±23.8	62.0±17.8	50.4±24.2

\*p<.055 (ANOVA)

\*\*p<.001 (ANOVA)

Table 6. Selected One-Year Characteristics by Cohort (n=140 Exercisers)

Cohort	1	2	3	4	5	6
N	23	19	18	23	30	27
	Percent	Percent	Percent	Percent	Percent	Percent
On HRT at 1 year	52.2	21.1	50.0	60.9	53.3	55.6
Retention in study	74.2	70.4	85.7	82.1	85.7	84.4
	Mean SD					
Weight change at 1 year (kg)	0.0±2.8	0.2±2.2	0.5±3.2	0.7±2.3	-0.2±2.3	0.4±2.6
Total Weight Moved (in 1000's of lbs)	1370±407	1116±447	1378±515	1066±502	1031±375	1130±417
Change in trochanter BMD (g/cm <sup>2</sup> )*	0.028±.029	0.005±.025	0.015±.023	0.012±.015	0.012±.023	0.002±.021

\* p<.002 (ANOVA) between Cohort 6 and Cohort 1

Table 7 suggests that women differed by cohort in the amount of weight they moved in the specific exercises. Statistically significant differences were found in the seated leg press between Cohorts 1 and Cohorts 2, 4, and 5. In the military press (r), Cohort 5 lifted less weight than Cohort 1 ( $p < .026$ ). For the squats, Cohort 3 moved more weight than Cohort 6 ( $p < .05$ ). For the rotary torso, Cohort 3 moved more weight than Cohorts 5 and 6 ( $p < .001$  and  $p < .002$ , respectively).

#### 4.5.2 Fitness Center

Figure 3 provides a breakdown of use of the exercise facilities by cohort. Cohorts 1-3 exercised primarily at FIT and NW, while Cohorts 4-6 used mostly Metro, NW, and UMC. Half or more of Cohorts 1-4 exercised at NW. Cohorts 5 and 6 attendance was split more equally among the three centers used by Cohorts 4-6. With the uneven distribution of the fitness centers among the cohorts, differences between cohorts in exercise weight moved might reflect, in part, differences in the fitness centers utilized.

Table 8 shows that, despite the large differences in the numbers of women using the fitness centers, the four

Table 7. Mean Weight Moved in Specific Exercises by Cohort (n=140 Exercisers)

Cohort	In 1000's of lbs	Total Weight Moved	Seated Leg Press*	Lat. Dorsi Pull	Weighted March (r.)	Seated Row	Back Extension	Military Press (r.)**	Squats^	Rotary Torso^^
1	Mean± SD	1370±407	492±162	137±45	191±68	119±38	201±61	24±8	274±98	81±34
2	Mean± SD	1116±447	332±155	117±42	211±100	94±35	173±65	19±8	235±140	108±44
3	Mean± SD	1378±515	451±173	127±48	252±109	110±44	216±110	20±10	285±133	123±49
4	Mean± SD	1066±502	341±177	112±56	206±115	92±49	188±102	18±8	189±146	89±44
5	Mean± SD	1031±375	321±155	116±41	183±89	97±36	198±82	17±6	177±139	72±31
6	Mean± SD	1130±417	389±177	130±44	233±135	106±39	198±89	19±7	172±94	76±42

\* p<.005 between Cohorts 1 & 5; p<.035 between Cohorts 1 & 2; p<.039 between Cohorts 1 & 4 (ANOVA)

\*\* p<.026 between Cohorts 1 & 5 (ANOVA)

^ p<.054 between Cohorts 3 & 6 (ANOVA)

^^ p<.018 between Cohorts 1 & 3; p<.037 between Cohorts 2 & 5; p<.001 between Cohorts 3 & 5; p<.002 between Cohorts 3 & 6 (ANOVA)

Figure 3. Fitness Center Attendance by Cohort

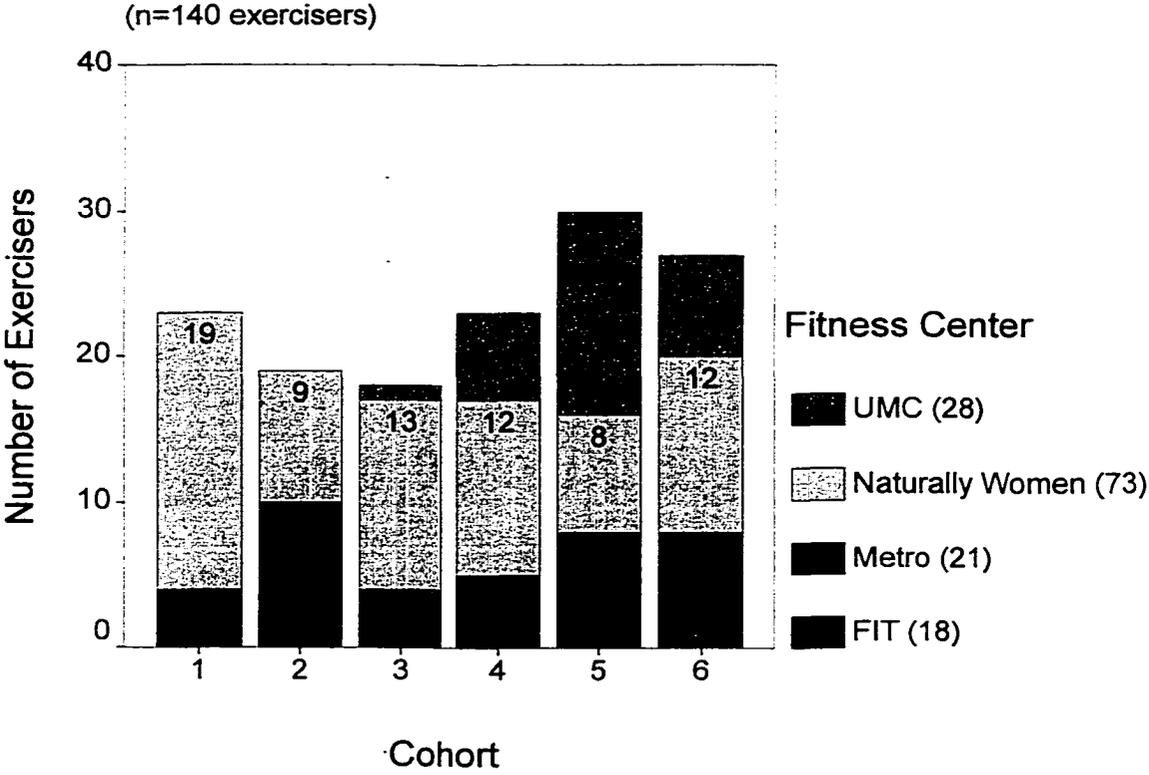


Table 8. Selected Baseline and 1-Year Characteristics by Fitness Facility (n=140 Exercisers)

Time Period	Fitness Center	FIT	Metro	NW	UMC
Baseline	N	18	23	73	28
		Mean SD	Mean SD	Mean SD	Mean SD
	Age (years)	55.7±4.3	55.5±4.0	55.1±4.6	55.2±4.4
	Years Post-menopausal	5.8±2.3	5.8±3.6	5.4±2.8	5.2±2.0
	Body Mass Index (kg/m <sup>2</sup> )	26.5±3.4	24.2±2.2	26.0±4.3	25.0±3.0
	% Body Fat	39.2±6.6	38.6±4.8	38.9±6.4	37.7±6.2
	Fat Free Mass (kg)	41.4±5.7	39.5±3.0	41.2±5.0	40.5±4.3
	Trochanter BMD (g/cm <sup>2</sup> )	.739±.10	.716±.1	.757±.1	.745±.1
	LIDO hip extension (lb)	70±28	61±25	61±20	66±22
1 Year	% On HRT	27.8	52.4	57.5	42.9
	Weight change (1 year) (kg)	0.3±3.0	0.2±2.4	0.3±2.5	0.3±2.5
	Total Weight Moved (in 1000's of lbs)*	1086± .401	1236± .364	1243± .502*	973± .349
	Change in trochanter BMD (g/cm <sup>2</sup> )	0.014± 0.03	0.003± 0.02	0.015± 0.03	0.011± 0.02

\*p<.022 (ANOVA)

groups were similar in age, years since menopause, entry BMD, and BMI.

In contrast, the change in trochanter BMD of the women who exercised at Metro increased less than that of the women at the other facilities although differences were not statistically significant ( $p < .3$ ).

Mean total weight moved was lowest at UMC and highest at Metro and NW (Table 9). Women exercising at NW moved significantly more weight than women at UMC ( $p < .022$ ).

Table 9 also summarizes the mean weight moved for each of the individual exercises by fitness facility. The average weight moved in the seated leg press was significantly higher at Metro and NW than at FIT and UMC ( $p < .0001$ , Metro and NW compared to UMC;  $p < .027$ , Metro compared to FIT and NW). In the *Latissimus dorsi* pull, women at Metro moved more weight on average than at Naturally Women ( $p < .0001$ ) and UMC ( $p < .001$ ). The same pattern held for the seated row. Women exercising at UMC moved less weight than at other facilities in all individual exercises except in the weighted march and the back extension. No statistically significant differences

Table 9. Mean Weight Moved Overall and for Individual Exercises by Fitness Facility (n=140 Exercisers)

Fitness Center	FIT	Metro	Naturally Women	UMC
In 1000s lbs	Mean±SD	Mean±SD	Mean±SD	Mean±SD
<b>Total Weight*</b>	<b>1,086±401</b>	<b>1,236±364</b>	<b>1,243±502</b>	<b>973±349</b>
Seated Leg Press**	306±135	455±162	428±179	265±119
Lat. Dorsi Pull**	131±41	162±36	114±48	113±34
Weighted March (r.)	20±8	23±13	21±11	20±9
Seated Row**	106±31	136±33	97±45	91±26
Back Extension**	198±88	204±52	169±76	257±97
Military Press (r.)	21±8	19±6	19±9	18±6
Squats**	169±71	152±99	287±128	107±68
Rotary Torso***	115±41	67±32	90±45	84±40

\* p<.042 between NW and UMC (ANOVA)

\*\* p<.0001 overall (ANOVA)

\*\*\* p<.003 between FIT and Metro (ANOVA)

were found between centers in the military press exercise. A higher mean weight was moved in the squats at NW (Hack squats, primarily) than at the other three facilities (Smith squats, primarily) ( $p < .0001$ ). The mean weight moved in the rotary torso at the FIT center was significantly higher than the weight moved at the Metro center ( $p < .003$ ).

#### 4.5.3 HRT Status

Table 10 outlines selected characteristics of women using HRT and not using HRT. Seventy women reported taking HRT during the year of exercise, while 70 did not. There were no statistically significant differences between the two groups at baseline except in the number of years since menopause. Women using estrogen were 6.1 years past menopause versus 4.9 years for non-users ( $p < .009$ ).

Furthermore, there were no differences between estrogen users and non-users in body weight change, total exercise weight moved, and change in trochanter BMD.

#### 4.5.4 Weight Change

As a group, the women did not lose or gain significant amounts of body weight over the intervention year. The

Table 10. Selected Baseline and 1-Year Characteristics by HRT Status during the Exercise Period (n=140 exercisers)

Time Period	HRT Status	HRT - NO	HRT - YES
Baseline	N	70	70
		Mean SD	Mean SD
	Age (years)	55.7±4.7	54.8±4.0
	Years Post-menopausal*	6.1±2.9	4.9±2.3
	Body Mass Index (kg/m <sup>2</sup> )	26.8±3.4	25.4±4.1
	% Body Fat	39.3±6.0	38.0±6.2
	Trochanter BMD (g/cm <sup>2</sup> )	.737±.112	.752±.122
	LIDO hip extension (lbs)	64±24	62±21
1 Year	Body Weight change (kg)	0.4±2.5	0.1±2.6
	Total Weight Moved (in 1000's of lbs)	1141±44	1194±47
	Change in trochanter BMD (g/cm <sup>2</sup> )	0.009±.023	0.015±.025

\* p<.009 (T-test)

mean weight change was  $0.26 \pm 2.5$  kg, with the range from -13.9 to +12.2 kg.

Subjects were divided into three groups: weight loss of  $\geq 2.0$ kg (n=23), weight change of  $< 2.0$ kg (n=82), weight gain of  $\geq 2.0$ kg (n=35). Selected characteristics for these three groups are summarized in Table 11. The weight loss group tended to be older ( $p < .020$ ), and have more fat free mass ( $p < .034$ ) at baseline. The weight gain group had a higher baseline trochanter BMD than the other two groups, especially the group with little weight change ( $p < .007$ ).

While BMD change was somewhat greater among the women who gained two or more kilograms, the difference was not statistically significant. Weight moved by the three groups illustrated a reverse tendency with women who lost weight moving the most amount of weight, although the differences were not statistically significant.

#### 4.5.5 Regression Models Examining Potential Confounders

Regression models to explore the extent of confounding by cohort, facility, HRT use, and weight change were performed. Table 12 presents the results. Models were evaluated for total weight moved and then for specific

Table 11. Selected Baseline and 1-Year Characteristics by Body Weight Change Groups (n=140 Exercisers)

Time Period	N	Weight Change Group		
		Loss of $\geq 2.0$ kg	Change of $< 2.0$ kg	Gain of $\geq 2.0$ kg
Baseline		23	82	35
		Mean SD	Mean SD	Mean SD
	Age (years)*	56.5 $\pm$ 4.1	55.6 $\pm$ 4.2	53.5 $\pm$ 4.8
	Years Post-menopausal	5.9 $\pm$ 2.4	5.3 $\pm$ 2.6	5.5 $\pm$ 3.0
	Body Mass Index (kg/m <sup>2</sup> )	26.1 $\pm$ 3.5	25.3 $\pm$ 3.7	26.1 $\pm$ 4.0
	% Body Fat**	39.3 $\pm$ 5.5	38.0 $\pm$ 6.5	39.7 $\pm$ 5.6
	Trochanter BMD (g/cm <sup>2</sup> )***	.737 $\pm$ .125	.724 $\pm$ .101	.797 $\pm$ .135
	LIDO hip ext. (lb)	62 $\pm$ 22	60 $\pm$ 20	70 $\pm$ 27
1 Year	% On HRT at 1 year	52.2	48.8	51.4
	Total Weight Moved (in 1000's of lbs)	1331 $\pm$ 458	1167 $\pm$ 440	1064 $\pm$ 461
	Change in trochanter BMD (g/cm <sup>2</sup> )	0.011 $\pm$ .031	0.012 $\pm$ .023	0.014 $\pm$ .022

\* p<.020 (ANOVA)

\*\* p<.034 (ANOVA)

\*\*\* p<.007 (ANOVA)

Table 12. Coefficients and Statistical Test Results from Regression Analysis for Selected Exercises: Full Models and Models Minus Potential Confounding Variables

	Beta Coefficient	% Change from Full Model	T-score	P-value	Adj R <sup>2</sup>
<b>Seated Leg Press</b>					
full model	3.215E-14		1.865	0.064	0.109
minus wt change	2.867E-14	-10.8%	1.676	0.096	0.103
minus fit center*	2.036E-14	-36.7%	1.298	0.197	0.110
minus cohort*	4.447E-14	38.3%	2.717	0.007	0.069
minus HRT	3.171E-14	-1.4%	1.835	0.069	0.105
<b>Squats</b>					
full model	1.169E-13		3.294	0.001	0.157
minus wt change	1.135E-13	-2.9%	3.194	0.002	0.152
minus fit center*	8.377E-14	-28.3%	2.704	0.008	0.147
minus cohort	1.230E-13	5.2%	3.442	0.001	0.098
minus HRT	1.189E-13	1.7%	3.351	0.001	0.156
<b>Total weight</b>					
full model	5.232E-15		2.477	0.015	0.127
minus wt change	4.898E-15	-6.4%	2.326	0.022	0.121
minus fit center	4.499E-15	-14.0%	2.195	0.030	0.131
minus cohort*	6.329E-15	21.0%	3.073	0.003	0.083
minus HRT	5.311E-15	1.5%	2.512	0.013	0.124

\*designated confounder by 15% or greater change-in-predicted-value criterion

exercises. For two individual exercises and total weight, full models were adjusted by baseline age, baseline trochanter BMD, HRT status, one-year change in weight (squared), cohort, and fitness facility. Percent change between the full models and the models minus the control variable showed the effect of removing variables from the regression equation. If a change between the full model and the model with the potential confounding factor removed was  $\pm 15\%$  or more, the excluded variable was considered a significant confounder and controlled for in analysis. For the seated leg press, both fitness center (36.4% change in effect) and cohort (38.3%) confounded the relationship between weight moved and BMD change. The squats exercise was confounded by fitness center only (28.3%). The confounding effect of fitness center (14.0%) was weaker for total weight, while cohort remained a confounder (21.0%) (Table 12).

Table 13 shows the percent changes in beta coefficients for two exercises and total weight moved when cohort and fitness center are added first separately and then together to a regression model adjusting only for age and baseline trochanter BMD. In all three instances, the addition of cohort weakened, while fitness center

Table 13. Coefficients and Statistical Test Results from Regression Analysis for Total Weight: Base Model and Models Plus Potential Confounding Variables

	Beta Coefficient	% Change from Full Model	T-score	P-value	Adj R <sup>2</sup>
<b>Seated Leg Press</b>					
base model	3.169E-14		2.134	0.035	0.040
plus cohort	1.782E-14	43.8%	1.147	0.253	0.105
plus fit center	4.116E-14	-29.9%	2.517	0.013	0.056
plus cohort & fit center	2.865E-14	9.6%	1.673	0.097	0.102
<b>Squats</b>					
base model	1.036E-13		3.430	0.001	0.087
plus cohort	8.342E-14	19.5%	2.722	0.007	0.144
plus fit center	1.202E-13	-16.0%	3.358	0.001	0.088
plus cohort & fit center	1.155E-13	-11.5%	3.258	0.001	0.152
<b>Total weight</b>					
base model	5.732E-15		2.888	0.005	0.065
plus cohort	4.279E-15	25.3%	2.101	0.038	0.125
plus fit center	6.106E-15	-6.5%	2.962	0.004	0.072
plus cohort & fit center	4.997E-15	12.8%	2.375	0.019	0.121

base model adjusted for age, baseline trochanter

strengthened, the effect of weight moved on BMD change. For the seated leg press, for example, the change in beta coefficient for the addition of cohort was +43.8% and for fitness center, -29.9%. When entered into the model together, the cohort and fitness center variables appeared to moderate their respective effects on the relationship between weight and BMD change. For instance, the addition of both variables produced a change in coefficient of +9.6% in the seated leg press model.

#### 4.5.6 Summary of Potential Confounders

Cohort, fitness facility use, HRT use, and 1-year weight change were examined for potential confounding. Using a 15% change-in-effect criterion to define a confounder, regression models excluding cohort and fitness center showed substantial changes in the exercise effect on BMD and possible confounding by these variables. In contrast, the exclusion of the HRT use and weight change variables from models influenced regression coefficients only slightly. Since HRT use and weight change appeared to have little effect on regression models, eliminating these covariates in further analyses could conserve statistical power in regression analysis and should be considered.

#### 4.6 Does Strength Training Exercise Increase Trochanter BMD?

A significant increase in femur trochanter BMD was found in this group of 140 exercisers. The mean change was 0.012 ( $\pm 0.024$  g/cm<sup>2</sup>) ( $p < .0001$ ). This difference represented a 1.68 ( $\pm 3.39$ )% increase in BMD over baseline (Table 2).

#### 4.7 What is the Relationship between Amount of Weight Moved and Change in Trochanter BMD?

Regression coefficients and statistics from multiple linear regression modeling are found in Table 14. All regression beta-coefficients were very small due to the large number of pounds moved and the use of squared weight in the regression equation and difficult to interpret. Predicted BMD change, standardized to SD units of weight, and percent change from baseline are included. A one-unit SD for each exercise is also given. Models were adjusted for age, baseline trochanter BMD, HRT status, change in body weight (squared), cohort, and fitness facility. Independent variables accounted for 9.1% to 15.7% of the variation found in trochanter BMD change (adjusted  $r^2$ ).

Table 14. Regression Coefficients and Statistics for Change in Trochanter BMD by Weight Moved (weight squared) in Individual Exercises and Total Weight\* (n=140 Exercisers)

	Beta	T-score	P-value	Adj R <sup>2</sup>	Predicted Mean BMD Change (g/cm <sup>2</sup> ) per SD Weight (lbs)	Percent of Baseline BMD Mean	SD
<b>Total weight</b>	<b>5.232E-15</b>	<b>2.477</b>	<b>0.015</b>	<b>0.127</b>	<b>0.0011</b>	<b>0.14%</b>	<b>452,896</b>
Seated Leg Press	3.215E-14	1.865	0.064	0.109	0.00099	0.13%	175,632
<i>Latissimus dorsi</i> pull	4.779E-13	2.270	0.025	0.121	0.00100	0.13%	45,857
Weighted March	6.260E-12	1.557	0.122	0.102	0.00070	0.09%	10,542
Seated Row	5.666E-13	1.988	0.049	0.113	0.00094	0.13%	40,644
Back Extension	5.631E-14	0.925	0.357	0.091	0.00041	0.06%	85,486
Military press (right)	1.851E-11	2.627	0.010	0.132	0.00114	0.15%	7,851
Squats	1.169E-13	3.294	0.001	0.157	0.00202	0.27%	131,572
Rotary Torso	5.132E-13	1.872	0.064	0.110	0.00096	0.13%	43,214

\*adjusted for Baseline Trochanter BMD, Age, HRT Status, Body Weight Change (squared), Fitness Center, and Cohort

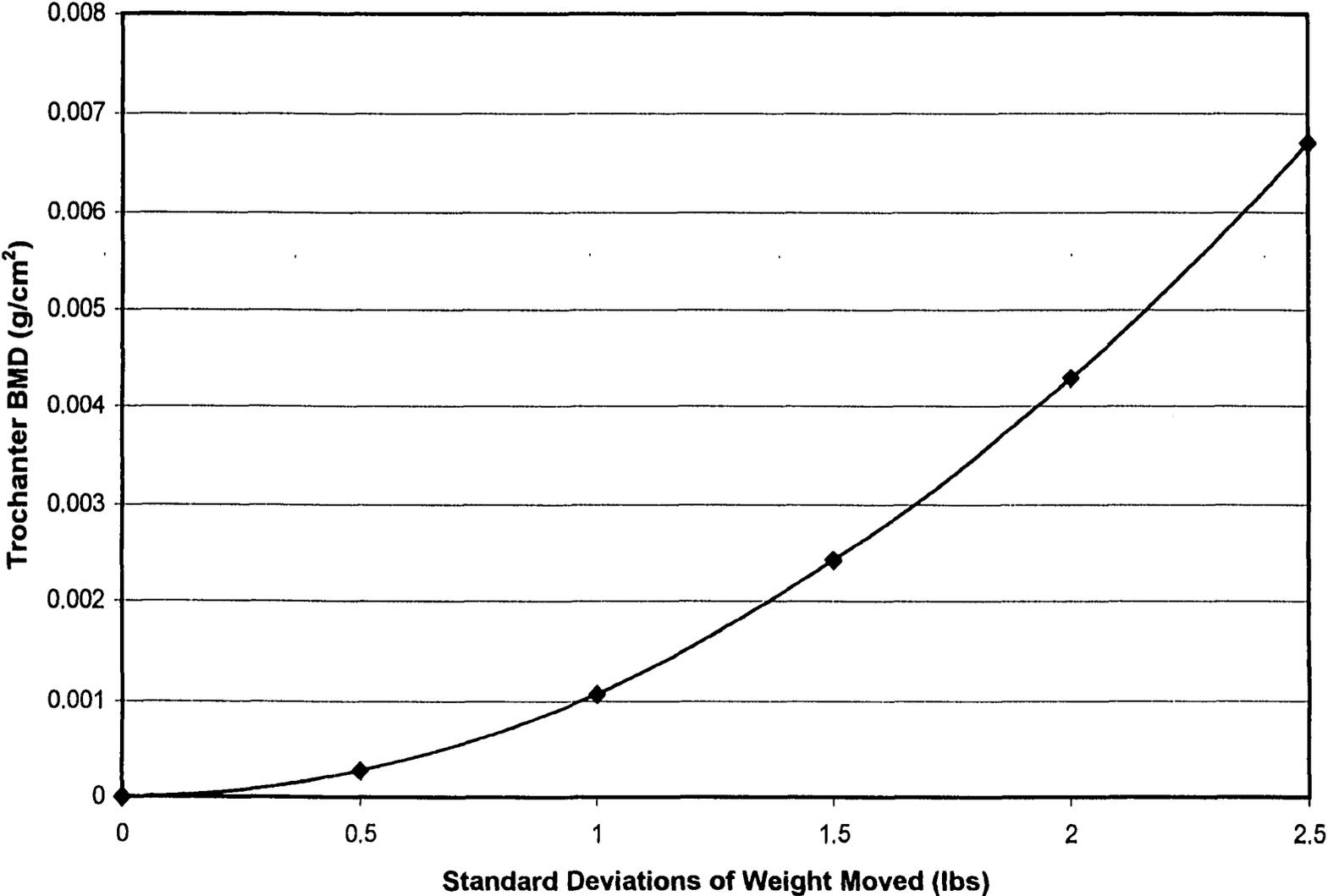
Total exercise weight moved during the one year was positively and significantly associated with change in trochanter BMD ( $p < .015$ ). For one standard deviation (SD) of weight moved, the mean BMD would increase  $0.001 \text{ g/cm}^2$  or  $0.14\%$ .

The trochanter bone responded somewhat differently to the individual exercises. Weight moved in the squats ( $SD=131,572$ ) had the largest association on trochanter BMD ( $p < .001$ ), and predicted a mean increase in BMD of  $0.002 \text{ g/cm}^2$  per SD or  $0.27\%$  of the baseline mean BMD. In contrast, the change in BMD with the amount of weight lifted in the weighted march ( $SD=10,542$ ) was predicted to be  $0.0007 \text{ g/cm}^2$  or  $0.09\%$  of baseline, and for the back extension ( $SD=85,486$ ),  $0.0004 \text{ g/cm}^2$  or  $0.06\%$  of baseline.

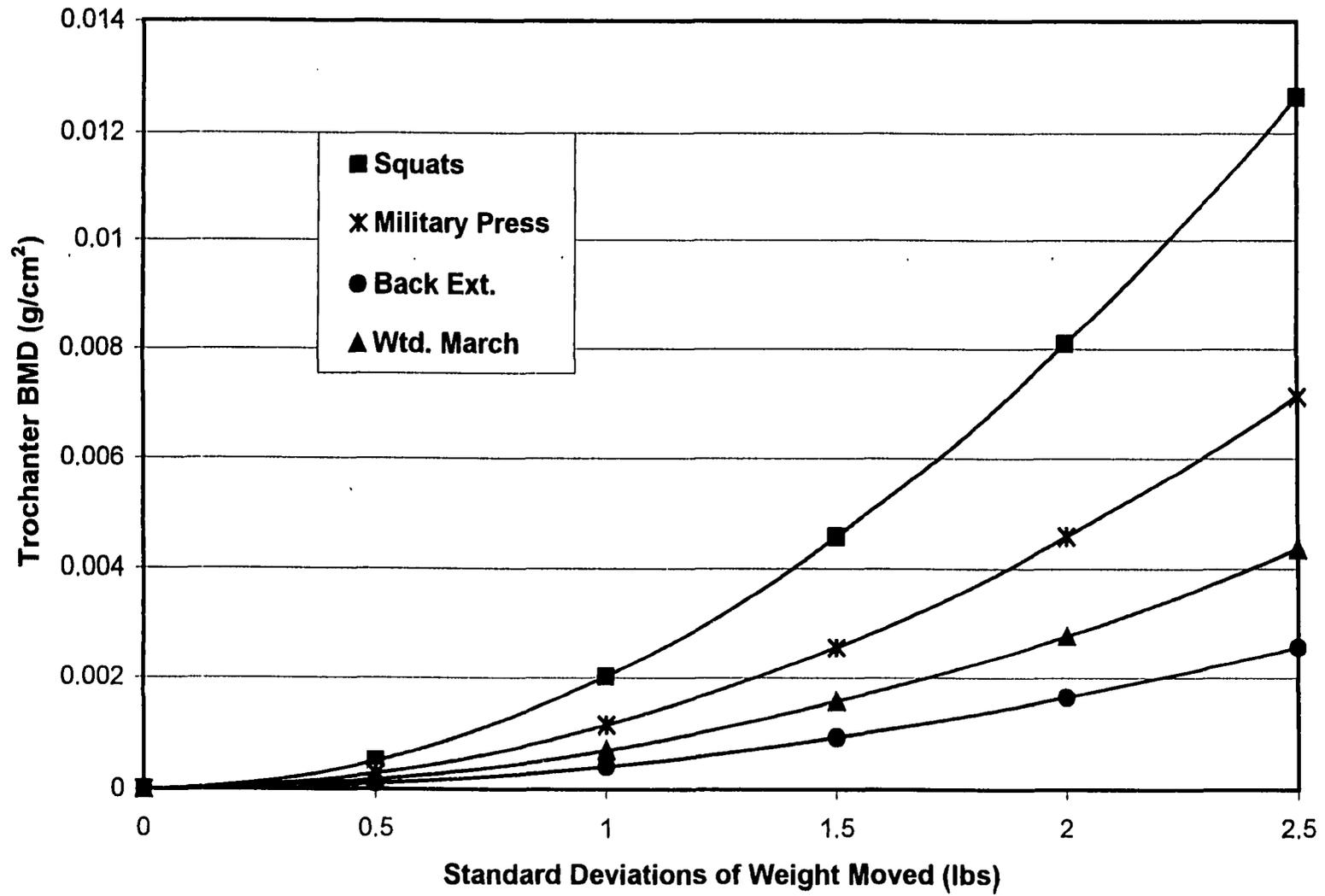
In Figure 4, the predicted change in trochanter BMD is graphed against SD units of total weight moved. At  $1.5 \text{ SD}$  of total weight lifted, the change in BMD was expected to be approximately  $0.0024 \text{ g/cm}^2$ . At  $2.5 \text{ SD}$ , the change was predicted to be about  $0.0067 \text{ g/cm}^2$ .

Figure 5 illustrates the predicted BMD change for weights of four selected exercises. The relative effects of the specific exercises are shown over three SD's of weight moved. The slopes of the regression curves are

**Figure 4. Predicted Mean Change in Trochanter BMD with Standard Deviations of Total Weight Moved**



**Figure 5. Predicted Mean Change in Trochanter BMD with Standard Deviations of Weight Moved in Selected Exercises**



visibly distinct. The curve for the squats exercise exhibits the steepest rise with SD of weight, while the back extension slope rises most slowly.

Table 15 shows the predicted mean percent change in trochanter BMD for each 1,000 pounds of weight moved in the individual exercises and combined total weight. While Table 14 compared SD's of weight moved, Table 15 compares the pound-for-pound effects of the specific exercises. Predicted percent change in BMD per 1,000 pounds of weight moved per week (%/1000lbs/wk) is highest for the military press (6.72%/1000lbs/wk) followed by the weighted march (2.27%/1000lbs/wk). The smallest percent increase was found in the seated leg press (.012%/1000lbs/week).

Table 15. Predicted Percent Change in Trochanter BMD for Each 1,000 lbs Moved per Week in Individual Exercises and for Total Weight Moved\* (n=140)

	Change as Percent of Baseline BMD Mean
<b>Total weight</b>	<b>0.002%</b>
Seated Leg Press	0.012%
<i>Latissimus dorsi</i> pull	0.173%
Weighted March	2.272%
Seated Row	0.206%
Back Extension	0.020%
Military press (right)	6.718%
Squats	0.042%
Rotary Torso	0.186%

\*adjusted for Baseline Trochanter BMD, Age, HRT Status, Body Weight Change (squared), Fitness Center, and Cohort

## CHAPTER 5 - DISCUSSION

Strength training has been proposed as an exercise intervention to maintain or increase bone mineral density in post-menopausal women. The results of this study confirm previous findings of the positive association between this type of exercise and change in BMD of the femur trochanter (27). The data clearly indicate that these post-menopausal women increased their bone density through a 1-year progressive strength training program and the effect appears to show a dose-response relationship.

### 5.1 Strength Training Exercise and BMD Change

A significant  $0.012 \pm 0.024$  g/cm<sup>2</sup> increase in femur trochanter BMD was found in this group of 140 exercisers completing one year of progressive strength training (different from 0;  $p < .0001$ ). The change represents an increase of  $1.68 \pm 3.39\%$  over the baseline mean BMD value of 0.745 g/cm<sup>2</sup>. This result concurs with previously reported increases of a 1-2% in BMD over a 1-year period of strength training intervention (25-27).

It is unknown how much bone these women would have lost had they not been exercising. Their menstrual status would have contributed substantially to BMD loss (77).

Evidence has shown that women in the early postmenopausal period may lose as much as 30% of their femur trochanter BMD (78). Thus, gain in bone could be more important when a positive change in BMD is compared to an expected decrease.

Since the BEST study exercisers and controls were randomized at baseline, these groups would be similar with respect to their risk of osteoporosis. A between-group comparison of changes in trochanter BMD might yield a more accurate estimate of bone retention or gain due to the exercise program. Because subjects were blocked by HRT status before randomization, the proportions of hormone use may have been different between the exercisers and controls. This difference would need to be taken into account. Similarly, 1-year changes in body weight and levels of physical activity among the controls would need to be assessed.

Forces exerted by surrounding muscles strengthened through exercise can stimulate bone formation (30). Many muscle attachments are found in the trochanter hip region. Given the location and muscles involved, specific exercises can be expected to impact specifically this area. The seated leg press, *latissimus dorsi* pull, weighted march,

squats, and the rotary torso exercises could strengthen one or more of these muscles. The intimacy of the trochanter region with so many of the muscles involved in the exercises may have accounted for the strong reaction of the trochanter to exercise.

A clear association between the amount of weight lifted in the military press and BMD increase was reported. For every SD of weight lifted in the military press exercise, the trochanter was predicted to gain  $.0011 \text{ g/cm}^2$  ( $p < .01$ ), an amount comparable to that found with a SD of total weight moved.

The barbell in the military press is lifted directly over the seated body. Such direct skeletal loading could stimulate osteogenesis (28,30). Furthermore, Skerry proposes that weight-lifting behavior other than, but associated with, loading might enhance the effect on bone formation (79). He postulates that an abrupt change in loading could trigger a reaction in the bones under strain. Releasing a barbell, he surmises, may produce an effect additional to raising the load. Thus, although muscles exercised in the military press are not adjacent to the trochanter site (see Appendix), the effect of that exercise may be produced more by the alternation of loading and

unloading. Changes in loading could stress the whole skeleton even when direct muscle forces on the bone are not involved.

It is not known whether muscle forces are more or less influential than loading in bone building. Possibly both mechanisms are at work in this dose-response relationship at the trochanter site. Table 15 showed the relative expected osteogenic effects of the individual exercises if 1,000 pounds/week were moved. A greater percent increase in trochanter BMD was predicted for the military press and weighted march than for the other exercises. These two exercises involved direct loading of the skeleton, while the other exercises targeted muscles in or near the hip region. Based on these findings, loading might, therefore, have contributed more to positive trochanter BMD change than muscle strengthening.

It is, however, essential to consider the non-independence of the specific exercise types when interpreting their effects. For example, the effectiveness of the military press might be dependent on the amount of muscle strengthening accomplished in the back extension and seated row. Interventions and analyses combining various

types of exercise could be a fruitful area for further research.

Exercise programs designed to load the skeleton need not involve elaborate weightlifting equipment. Inexpensive barbells and leg weights would be sufficient and could be kept and used at home. Nevertheless, a program designed solely to load the skeleton to levels of weight comparable to those moved in the squats, for example, may be inadvisable and impractical. In the BEST exercise program, a SD of weight lifted in the military press (free weights) represented only 6% of a SD of weight moved in the squats (attached weights) (Table 14).

In multiple linear regression, the 1-year change in BMD was significantly associated with total weight moved. Furthermore, regression analysis demonstrated positive, linear associations between specific exercise types and total weight moved and BMD change. Results were in the same direction, and many were statistically significant.

Most notably, the squats and the military press produced a strong reaction at the trochanter site and both exercises placed weight on the skeleton from above. Body weight in the squats and barbell weight in the military press added vertical load to the exercise movement. For

the squats, which elicited the strongest reaction in the trochanter, muscle strengthening occurred directly surrounding the trochanter region. Thus muscle forces could have provoked bone increase.

Both the rotary torso and the seated leg press utilized muscles in proximity to the trochanter site. Body weight did not contribute load to the seated leg press since exercisers were lifting from a semi-prone position (see Appendix). The rotary torso twisted trunk muscles attached to the hip region and the upper body also contributed weight to the trochanter area. Moderate responses were reported for these two exercises.

These analyses assumed a curvilinear relationship between the amount of weight moved and change in trochanter BMD. Further regression models categorizing the weight variable might uncover dose-response attributes not revealed in the present analysis. Threshold or leveling-off effects might be found at different levels of weight moved.

## 5.2 Confounding Effects

Bone density change and weight moved were analyzed by cohort, fitness facility, HRT status, and body weight change to examine the potential confounding effects.

Cohorts at time of entry to study exhibited unique traits. For example, Cohort 1, as a whole, was reported by staff to be highly enthusiastic and motivated and these attributes could have reflected greater physical strength. The weight moved in one year and BMD increase in Cohort 1 was higher than for most of the other Cohorts even though other baseline characteristics were similar. Furthermore, the variance of weight moved for several exercises was smaller for Cohort 1 (Table 7).

Cohort 6, in contrast to Cohort 1, experienced only a small increase in BMD. The lower baseline LIDO strength might indicate a weaker group (Table 5). Furthermore, last-cohort status might also have set Cohort 6 apart from the other cohorts and could have demonstrated what Sackett calls "late-comer" bias, a variation of "non-respondent" bias (80). The women recruited late in the study might have hesitated or been less willing to change their sedentary habits.

Characteristics unique to each fitness facility might also have affected both the amount of weight moved as well

as BMD change. Exercise equipment differed among the centers (see Appendix). The seated leg press was stiffer at UMC and FIT than at the other two facilities. The Hack squats at NW were easier to perform than the Smith Squats at the other 3 facilities. Equipment attributes may have accounted for significant differences in the amounts of weight moved at the facilities (Table 9).

An examination of HRT status was undertaken because of the possible benefit of estrogen therapy to post-menopausal bone density (50). While, bone cells respond to the mechanical loading of weight lifting and muscle forces, they react as well to their chemical surroundings. As part of this fluid environment, estrogen plays a positive role in the formation of bone (81). Hormone replacement therapy (HRT) protects against bone loss in post-menopausal women whose natural estrogen levels are decreasing. Many studies have supported the role of HRT in reducing or reversing bone loss in older women (82). In a study by Kohrt et al., an additive effect of estrogen and exercise was found in women age 60-72 at the femur hip and lumbar spine sites (83).

In the present study of exercisers, a statistically significant difference was not found in trochanter BMD

change by HRT status even though HRT users had experienced menopause more recently than non-users.

Only one fifth of Cohort 2 took HRT at baseline and this proportion did not change with subject attrition. The small percent of HRT use in Cohort 2 might have accounted for part of the non-response of BMD in that cohort. Cohort 2 averaged almost 7 years postmenopausal compared to around 5.5 for the other cohorts. Nevertheless, controlling for HRT status produced little effect on regression coefficients and did not alter the relationship between weight moved and trochanter BMD change (Table 14).

Women were asked to maintain their weight for the duration of the study year. However, more than 40% of the exercisers either gained or lost two or more kilograms of body weight. Cohort membership and fitness center use did not impact body weight change behavior (Tables 6 and 8). This finding refuted the possibility that friends or acquaintances within these groups planned to lose weight together.

As with HRT status, body weight change affected the weight moved/BMD relationship little. Regression coefficients did not change appreciably between the full models and those without adjustment for body weight change.

The issue of body weight loss as an intermediate factor in the weight moved/BMD relationship is of interest. Larger amounts of exercise could potentially produce more weight loss and lead to lower gains in BMD. The weight loss group in this study moved more weight than the maintenance and gain groups, but the difference was not statistically significant.

Weight lifting does not normally produce weight loss without concomitant restriction of food intake. However, the possibility of an intermediate role for weight loss is worth future consideration.

In addition to changes in calorie intake, changes in diet quality either with or without calorie adjustment may influence BMD. Food record data recorded during the intervention year may yield new insights into the broader role of diet in bone density changes.

HRT use and change in body weight exerted little effect on the relationships between the weight moved in the specific exercises and trochanter BMD change. Cohort and fitness center, on the other hand, were possible confounders. From the results in Table 13, it was shown that when entered together in regression, cohort and fitness center showed a weak confounding effect on the

relationship between weight moved and BMD change. However, the variables entered separately showed opposing effects and might be important confounding, if not independent, factors (Figure 3). Nevertheless, it is essential to view the effects of these two variables with caution. The subjects in Cohorts 1 and 2 did not exercise at Metro or UMC. Similarly, Cohort 5 and 6 exercisers did not train at FIT (Figure 3). Categories with no subjects were therefore compared in analysis and might have contributed to large fluctuations in confounding effects.

On the whole, confounding effects need to be taken into account when interpreting effects of exercise on BMD (23,30). Controlling for study entry time and exercise facility appeared to be particularly important because the study was large, involving extended recruitment and the need to engage several training centers.

### 5.3 Strengths of Study

#### 5.3.1 Introduction

The evidence for a statistically significant linear relationship between weight moved and trochanter BMD is consistent across several exercise types and total weight. These strong results derive in large part from the

strengths inherent to the study: large size, design features, and good retention and compliance rates. Additional support for these findings comes from consistency with other studies, biological plausibility and coherence, and the presence of a measurable dose-response relationship.

### 5.3.2 Size

A unique feature of the BEST Study was the number of participants retained over the first year of the study. Two hundred sixty-six completed the 11-year DXA scanning. To date, participant numbers retained in studies involving strength training and postmenopausal women have not exceeded 50 exercisers (2, 44, 46, 47, 84, 85). Large participant numbers increased the power of the analysis and permitted adjustment for confounding factors.

### 5.3.3 Study Design

#### 5.3.3.1 Subject Selection

Post-menopausal white women are at the highest risk for osteoporosis in healthy populations. Among white women, age and menopause combined can induce bone losses of between 20% and 30% depending in part on the skeletal

region measured (39,41). Approximately two-thirds (18%) of this loss is attributed to age, the other third (11%), to menopause (40).

Although other ethnic groups were not excluded from the study, 88% of the subjects at one year were white and were predominantly 3 to 10 years post-menopausal. Participants were considered eligible if they had sedentary lifestyles. Evidence from human trials suggests that those who are less physically active and have lower levels of baseline bone density may benefit more from increasing levels of exercise (31).

#### 5.3.3.2 Choice of Intervention

Strength training may enhance BMD more than aerobic exercise or walking (43). Frost has shown that the BMD of weight lifters can exceed that of runners (21). The larger muscles of the weight lifter exert larger forces on bone and induce greater bone mass. The leaner, small muscles of runners, despite their high endurance, do not put pressure on the bone beyond the simple strain of running.

Strength training exercises aimed at a target bone site have been shown to improve BMD at that site (27). The BEST study selected exercises to strengthen a range of

muscles. The hip and thigh muscles impacted surrounded the trochanter femur region, which was measured for density.

Progression in resistance training appears to promote bone building (45). Gradual increases in load permit ever-larger weights to stress the bone and initiate bone growth. Furthermore, progressive exercise may encourage compliance and reduce the incidence of injury (23).

Larger loads with smaller numbers of repetitions also appear to enhance bone formation (27,29,79). Lower numbers of repetitions seem to produce more change in BMD than do higher numbers of repetitions (86). Loads up to 80% of 1RM were encouraged and training protocol recommended a maximum of eight repetitions in all individual exercises.

Current research suggests that the initiation of bone response to exercise may require at least half a year (30). The BEST study's exercise intervention period was designed to provide adequate time to produce bone change.

The subjects recorded pounds and repetitions on exercise logging cards. In addition to providing number of repetitions as a variable for analysis, this procedure allowed the easy calculation of the quantity of weight moved. On-site trainers taught the women how to do the exercises and stayed with them throughout the sessions.

The training and additional monitoring assured the uniformity of the exercise and data quality.

The detail, completeness, and quality of the data could allow an analysis of exercise progression. Do women who increase the amount of weight moved more quickly or steadily show higher levels of trochanter BMD change than do women who progress more slowly or reach a weight plateau sooner? The answer to this question could help to identify more effective and feasible exercise programs for postmenopausal women.

#### 5.3.3.3 Retention and Compliance

More than 80% of the women in this study who completed baseline DXA testing returned for the same testing one year later (177 at baseline; 142 at one year) (Table 2). Furthermore, in this group, full compliance to the three sessions of intervention regimen per week averaged 71.5% (Table 3). This is comparable to the 75% retention rate reported by Kerr et al. (27) but much lower than that reported by Nelson et al. in 1994 (100% retention). The latter study, however, included only 20 exercisers.

#### 5.3.4 Adjustment for Covariates

The size of the BEST study necessitated staggered recruitment and the use of several training facilities. Cohort and fitness center differences could potentially have confounded the relationship between exercise and BMD change. Regression models included adjustment for these factors to remove confounding effects and describe the independent effect of the quantity of exercise on trochanter BMD change.

#### 5.3.5 Consistency

As discussed previously, recent studies have reported a positive response to trochanter BMD with progressive strength training (25,27). Although the evidence from other studies does not always support an exercise effect on BMD (63,64), meta-analyses (2,44-47,84,85) have uniformly supported role of exercise in increasing or at least maintaining hip BMD in postmenopausal women. Furthermore, site specificity was reported by Kerr et al (27). A significant positive association was reported between the trochanter hip site and the seated leg press.

#### 5.3.6 Biological Plausibility

Support for the plausibility of a bone response to exercise comes from cell culture and animal studies (12,23,28,48). Citing a natural experiment, Frost noted that well-nourished adults with congenital paraplegia exhibit substantial losses in bone strength and density (87). He proposed that dietary calcium deficiency and genetic factors could prove less important to bone strength than exercise.

#### 5.5.4 Specificity

As discussed previously, bone response to direct loading of bones has been established in animal research (28). The specificity of this response is reduced in human populations due to the diversity of genetic and lifestyle factors. Exercise and the covariates used in the current linear regression models explained only a small portion of the variation in BMD change (9%-16%). However, the models supported the presence of an independent effect of exercise on that change. Thus, despite the contribution of other factors to BMD, these exercises demonstrated a positive and measurable association with trochanter bone formation.

#### 5.3.7 Dose-Response

The presence of a dose-response relationship supports a causal relationship between the amount of strength training exercise and an increase in trochanter BMD. Several authors have reviewed this topic and provided theoretical support (12,28,30,79).

#### 5.5.5 Strength of Association

Criticism of exercise as a panacea for the prevention of osteoporosis centers on the small effects seen with rigorous exercise regimes. However, elevated risks of hip fracture have been seen with small amounts in BMD loss. Cummings reported an odds ratio of 2.7 associated with only a 10-15% decrease in BMD in postmenopausal, white women (13). Thus, the 1.68% increase seen in this group of women might produce a substantial reduction in hip fracture risk.

Concern has been expressed concerning the deleterious effect of strenuous exercise intervention programs that focus on increasing BMD by very small amounts while jeopardizing joint health (88,89). Progressive training provides one means of protecting joint integrity. Injury research can help to clarify the association of vigorous exercise with vulnerable areas of the skeleton, especially in older individuals.

## 5.4 Limitations of Study

### 5.4.1 Selection Bias

Women recruited into the study may have differed from those who did not respond to advertisement. If participants were healthier with respect to factors related to bone response to exercise, selection bias would have been likely. The healthy volunteer effect, as described by Sackett in 1979 (80), suggests that the group of women in this study might not have represented those with the highest risk for osteoporosis or hip fracture. Indeed, those who are attracted to a strenuous exercise intervention might be fitter than those who do not enroll.

The consequences of this selection bias are unpredictable. On the one hand, those healthier volunteers might add bone more readily due to factors other than exercise such as nutrition level or less bone-lowering drug (e.g., steroids) and alcohol use. On the other hand, the effect seen in these women might have been more substantial in a less healthy population. Since it has been proposed that women with lower baseline BMD might respond to exercise gain bone more readily than women with higher beginning levels of BMD (30), the latter possibility

receives support as well. Furthermore, this group of women did not have higher levels of trochanter BMD than did other populations of women of similar age. Mazess computed a mean trochanter BMD of  $0.745 \text{ g/cm}^2$  for several national samples of white women ages 50-59 (90). This mean matched that found among the BEST exercisers with a mean age of 55.5 years. The national sample did not exclude women with illness or drug use that might have lowered BMD levels.

A further bias described by Sackett that may have influenced factors related to the intervention and outcome is membership bias, which is often related to exercise. Similar to the healthy volunteers, those attracted to joining a fitness club may be healthier overall and respond differently to an exercise intervention than those who are less healthy.

In this study, loss to follow-up bias (91) could have reinforced selection bias. Trainers reported that the rigor of the strength training regimen led some women to leave the study. Injury, which could be associated with low initial BMD, also led some women to drop out of the study. If these women differed systematically from those who remained in the study, the survivors might not resemble the target population in ways related to bone change

capability. If, as mentioned before, low initial BMD elicited more bone response and those with lower BMD dropped out at higher rates, the effect of exercise on BMD would have been underestimated. However, the direction of the bias may be difficult to determine when unmeasured correlates of the outcome are different between participants and those lost to follow-up (92).

#### 5.4.2 Measurement and Information Bias

The women entered approximately 480,000 penciled entries onto exercise logging cards (see Appendix). Recording as well as data entry errors could have contributed imprecision to the measurement of the intervention. However, it is likely that this error was independent of the ability of the women to perform the exercises and of their change in BMD.

Many women did not record changes in physical activity performed away from the fitness centers. If those who moved higher amounts of weight at the facilities also increased other exercise more than those who moved smaller amounts of weight at the sessions, the effect of exercise on the trochanter might have been enhanced. For further analyses, physical activity recall information recorded at

six months and one year may be a valuable indicator of the presence of bias.

#### 5.4.3 Statistical Considerations

In any study considering multiple factors, chance statistical significance may impact the validity of the results. Multiple comparison tests, such as the ANOVA, increase the risk of chance findings. The women in six cohorts and four fitness facilities were compared with respect to baseline characteristics, change in BMD and weight, and weight moved in several exercises. The probability of finding statistically significant results increased with the number of comparisons made. However, Bonferroni post-hoc tests were performed to identify statistical significance between two levels.

A further concern arose in multiple linear regression with the addition of multi-level categories of cohort, fitness center, and HRT status. Several categories had fewer than the recommended minimum of five subjects per category (69). Since HRT status and weight change did not confound the relationship between amount of weight moved and trochanter BMD change, excluding these two variables in

future analyses could improve the power of regression models.

#### 5.4.4 Generalizability

The BEST exercisers were well educated. This group of 140 women had attended on average 15.3 years of schooling (Table 1) compared to 13.3 years for a national sample of non-Hispanic white women aged 55 (93). Evidence has shown that older adults with a greater level of education may also be more active (94). Thus, the level of baseline physical fitness of this group might not have been representative of US women of similar ethnicity and age.

Furthermore, the exercisers in this study had a lower mean BMI at baseline than women 50-59 years old surveyed in the National Health and Nutrition Examination Survey III (NHANES III) (95). The BMI of the NHANES III women averaged 28.4 kg/m<sup>2</sup>, while these exercisers averaged 25.6 kg/m<sup>2</sup> (Table 1). Thus, in this study, anthropometric measures influencing BMD may not represent national means.

In this group of postmenopausal women, 50% were on HRT. In a population-based sample of women 50-74 years old, 37.6% used hormones (96). Use was 3.7 times more likely among college graduates than among non-graduates.

Although the survey included women with diabetes who were less likely to be on HRT, the higher use of hormones among the BEST exercisers might be associated with different bone change amounts than lower use in the general population.

Finally, baseline BMD levels may differ from the US mean for postmenopausal non-Hispanic white women. Some reference data for trochanter BMD compares well with that of this group of women (90). However, a mean femur trochanter BMD of  $.635 \text{ g/cm}^2$  for non-Hispanic white women 50-59 years old was reported in the NHANES III survey (97). This average is approximately 15% lower than that measured in this study.

While results from this study show strong internal validity, they may not apply as well to the national population of postmenopausal women.

## CHAPTER 6: SUMMARY AND CONCLUSIONS

"That which is used develops. That which is not used wastes away."

- Hippocrates

## 6.1 Introduction

Each year there are approximately 300,000 hip fractures in the United States. Osteoporosis or very low bone mineral density has been reported to be a significant risk factor for hip fracture among older white women (13). The direct costs of osteoporosis are currently estimated to be between 10 and 15 billion dollars annually. Worldwide prevalence of the disease is expected to reach 6.26 million by 2050.

Evidence supports an osteogenic effect of strength training exercise in postmenopausal women (25,27). To date, there has been little research relating the type and amount of resistance training to positive change in BMD. Improvements in strength have been reported with strength training regimes (26,64). A positive change in trochanter BMD has been found with the leg press exercise (27); however, a quantification of this relationship has not been undertaken.

This thesis examined the dose-response relationship between the amount of weight moved in one year of strength training and change in femur trochanter BMD in a group of 140 exercising post-menopausal women. The impact on trochanter BMD of different types of strength training exercises was also explored.

In order to isolate the independent effect of strength training exercise on trochanter BMD change, this thesis further analyzed the possible confounding effects of time of study entry, fitness facility use, HRT status, and 1-year change in body weight.

## 6.2 Materials and Methods

A large intervention trial examining the impact of strength training on osteoporosis and cardiovascular disease risk factors in postmenopausal women, the BEST study provided data on 140 exercisers who had completed one year of progressive strength training.

At three weekly sessions, the women performed and logged eight individual exercises designed to strengthen a range of muscles. For each exercise, weight moved was calculated from the weight moved with each repetition and

the number of repetitions. Exercise weights were summed to produce total weight moved. Further, the women underwent DXA bone scans at baseline and one year to measure bone mineral density and change in various skeletal regions.

### 6.3 Results

A statistically significant 1-year increase in trochanter BMD (1.68%) was found for the exercise group. In multiple linear regression, a statistically significant, positive, curvilinear relationship was found between total weight moved and change in trochanter BMD ( $p < .015$ ). A change of  $.001 \text{ g/cm}^2$  in BMD was predicted for every standard deviation (SD) of total weight moved. The regression model was adjusted for age, baseline trochanter BMD, change in body weight, study entry time (cohort), and fitness facility.

A comparable model was produced for each individual exercise. The squats exhibited the strongest effect on trochanter BMD ( $.002 \text{ g/cm}^2$  per SD of weight moved;  $p < .001$ ) followed by the military press ( $.001 \text{ g/cm}^2$  per SD of weight moved;  $p < .01$ ), the latissimus dorsi pull ( $.001 \text{ g/cm}^2$  per SD;  $p < .025$ ), the seated leg press ( $.001 \text{ g/cm}^2$  per SD;  $p < .064$ ), the rotary torso ( $.001 \text{ g/cm}^2$  per SD;  $p < .064$ ), and the seated

row (.001 g/cm<sup>2</sup> per SD; p<.049). The weakest associations were found in the weighted march (.0007 g/cm<sup>2</sup> per SD; p<.122) and the back extension (.0004 g/cm<sup>2</sup> per SD; p<.357).

In linear regression models excluding each confounding variable separately, confounding effects of study entry time (cohort) were found for total weight moved. Confounding by fitness center was also noted for the seated leg press and squats. There was no evidence of confounding by HRT status and body weight change. A change-in-coefficient criterion of 15% was used to define confounding.

#### 6.4 Discussion

Two mechanisms may account for these exercise-related changes in trochanter BMD: forces exerted by muscle in close proximity to the trochanter and mechanical loading. Loading and unloading strain may have exerted the most influential effect in the military press. In addition to loading the bone, the squats exercise may have improved the strength of muscles in direct proximity to the trochanter site.

Substantial confounding was reported for time of study entry and fitness center. Recruiting and training large

numbers of subjects may interject confounding by factors related to these study-design variables.

## 6.5 Conclusions

In this group of 140 post-menopausal women, the quantity of weight moved in strength training exercises over a 1-year period was positively and significantly associated with the amount of BMD change in the femur trochanter. Furthermore, the relationship of individual exercises to change in trochanter varied in a quantitative way. The squats and military press exercises were associated most strongly with BMD change. The extent of the response may reflect the mechanisms responsible for osteogenesis: skeletal loading and muscle forces.

Confounding by cohort and fitness center was evident in this study. Control of confounding factors related to study design is necessary to establish better the independent effect of exercise on BMD change.

## APPENDIX

5/14

facility: NW

Month/yr: 4/99

4/99

Name: \_\_\_\_\_

PP/DD

Cohort 6

	4-2	4-5	4-7	4-9	4-12	4-14	4-17	4-19	4-21	4-23	4-26	4-28	4-30														
	S1	S2	S1	S2	S1	S2	S1	S2	S1	S2	S1	S2	S1	S2	S1	S2	S1	S2	S1	S2	S1	S2	PB	70/80			
100 Leg Press	100	100	100	100	110	110	110	110	110	110	R	R	120	120	120	120	120	120	130	130	130	130	135	135			
	8	8	8	8	8	8	8	8	8	8			8	8	8	8	8	8	8	8	8	8	8	8			
35 Lat Pull (handle _)	35	35	40	40	40	40	40	40	40	40	45	45	45	45	45	45	45	45	45	45	45	45	45	45	45	45	45
	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8
9 Weighted March (R)	9	9	9	9	9	9	9	9	9	9	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8
Weighted March (L)	9	9	9	9	9	9	9	9	9	9	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8
45 Row (machine _)	25	25	25	25	25	25	25	25	25	25	30	30	30	30	30	30	30	30	30	30	30	30	30	30	30	30	30
	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8
50 Back Extension	75	75	80	80	80	80	80	80	80	80	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85	85
	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8
12 Military Press (R)	10	10	10	10	10	10	10	10	10	10	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
	8	8	8	8	8	8	8	8	8	8	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6
12 Military Press (L)	10	10	10	10	10	10	10	10	10	10	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
	8	8	8	8	8	8	8	8	8	8	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6
56 Squats/Hack Squat	50	50	50	50	60	60	60	60	60	60	65	65	65	65	65	65	65	65	65	65	65	65	65	65	65	65	65
	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8
35 Rotary Torso	35	35	35	35	35	35	35	35	35	35	35	35	35	35	35	35	35	35	35	35	35	35	35	35	35	35	35
	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8
Perceived Exertion																											

Personal Best

## Leg Press

### Targeted muscles:

Quadriceps, gluteus (buttocks), hamstrings. Putting your feet higher on the foot plate activates more gluteus muscles.

### Function:

Basic leg strength for walking, climbing, running, bounding.

Aesthetics: Adds a shapely sweep to the thighs. It also helps raise and round the buttocks.

### Movement:

**Setting up:** Place your feet parallel to each other on the foot plate about hip width apart. Your toes are pointed upward or slightly outward. Place a ball between the knees to stabilize.

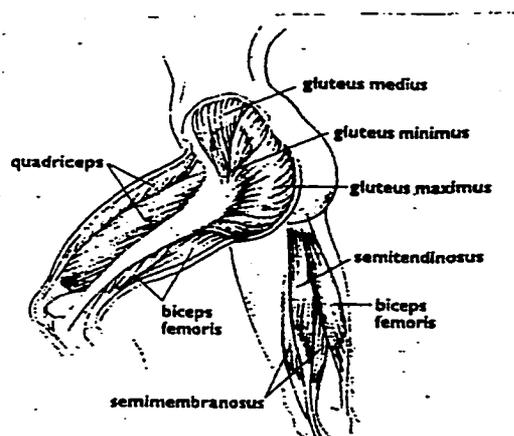
**Execution:** Lower the sled *slowly* until your knee angle reaches 90 degrees. Make sure your knee angle doesn't drop below 90 degrees and your heels stay on the plate through the full range of motion. Next, straighten your legs, pressing through your heels. Do not lock your knees at full leg extension. Your thighs, lower legs, and feet should stay parallel to each other throughout the exercise. Exhale as you push up.

### Safety tips:

1. Keep your lower back in neutral (Pink Panthers use a lumbar roll).
2. Aim for a full range of motion but avoid dropping your knee angle below 90 degrees.
3. Always use a weight you can handle so you can achieve the full range of motion.
4. Press through your heels, not the balls of your feet.
5. Don't lock out your knees.
6. Make sure the small of your back stays pressed against the back pad and the buttocks remains stays in the seat.

### Reminders:

1. Keeps legs and feet parallel.
2. Aim for a 90 degree knee angle.
3. Press with heels.



## Lat Pull Down

### Targeted muscles:

Lats, biceps brachii, brachialis, forearm flexors, posterior deltoid.

### Function:

Strengthens postural muscles in the upper back.

Aesthetics: Develops lats, helps give the torso a flattering V shape, creating the illusion of a narrow waist.

### Movement:

**Setting up:** Take an underhanded grip on the bar at approximately shoulder distance apart. Sit up tall in the seat, sternum up with feet flat on the floor and your knees at a 90 degree angle to better ground yourself. Press heels into the floor and tuck your thighs snugly under the knee pads for better stabilization.

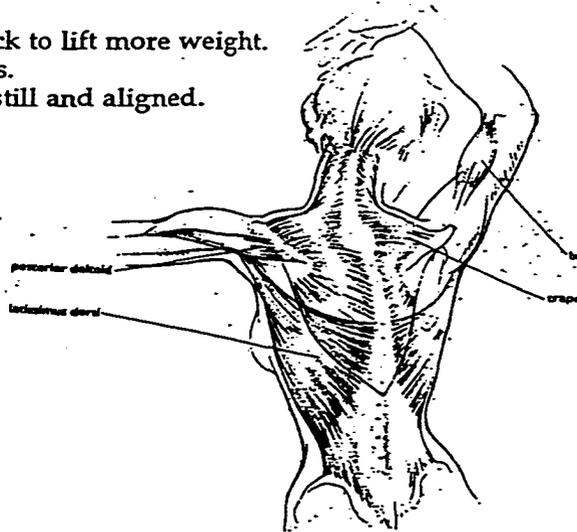
**Execution:** Depress your scapula first before you pull with your arms. Focus on not rounding your shoulders. Elbows should finish at your sides and not surpass the plane of your body. Straighten your arms and slowly return the weight to the starting position. Be careful not to overstretch your shoulders or lock your elbows when your arms are fully extended.

### Safety tips:

1. Beware of adding a swing into the lower back to lift more weight.
2. Don't let the weights jerk up your shoulders.
3. Use abdominal strength to keep your torso still and aligned.
4. Don't lock out your elbows.

### Reminders:

1. Depress your shoulders first, then add arms.
2. Lift chest to meet the bar (sternum up).
3. Don't arch lower spine.
4. Exhale as you pull down.



### Weighted March

*Target muscle:*  
Iliopsoas (hip flexors).

*Function:*  
Postural realignment in the pelvic region. Highest correlation to increases in bone density.

*Movement:*

**Setting up:** Strap the appropriate weight around your ankles. Stand with the pelvis in neutral, holding one pole in each hand in front of you (like ski poles) for balance.

**Execution:** With sternum up, raise one knee until your thigh is parallel to the floor, forming a 90 degree angle at both the knee and hip joints. Lower your leg until your toe barely touches the floor and repeat. Alternate sets with the other leg.

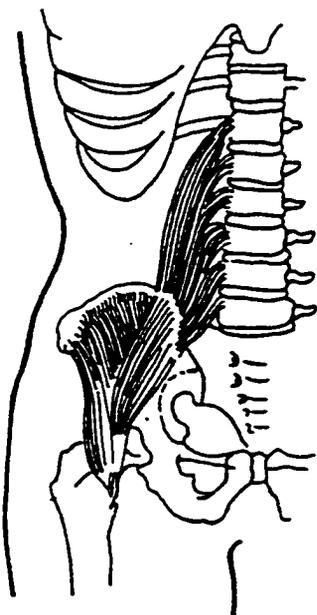
*Safety tips:*

In order to protect the lower back, make sure to keep the pelvis in neutral throughout the entire range of motion. Do not allow it to rock forward or backward.

Helpful hint: squeeze your buttocks, keep your abdominals long, and keep your sternum up while raising and lowering your leg.

*Reminders:*

1. Keep your pelvis in neutral.
2. Keep your sternum up.
3. Aim for a 90 degree angle at the hip and knee joints.
4. Exhale as you raise your knee.



Anterior

## Seated Row

### Targeted muscles:

Lats, middle trapezius, rhomboids, biceps, brachialis, posterior deltoid, forearm flexors

### Function:

Strong back muscles assist in all pulling actions, general torso stability and in most sports.

Aesthetics: Contribute to v-tapered torso, and strong posture.

### Movement:

**Setting up:** On a seated, cable row machine sit with your torso upright, knees bent. While remaining in the upright position, grasp the handle with both hands and extend your legs until you are seated comfortably with your knees slightly bent.

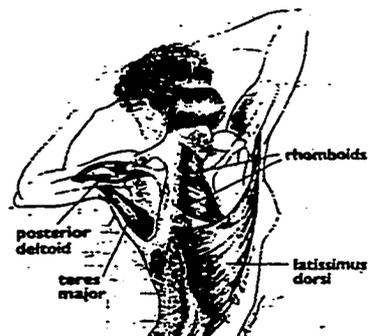
**Execution:** With the sternum up, and back flat, retract the shoulders by squeezing your shoulder blades together. Next, follow with the arms, pulling the weight into your lower rib cage (abdomen/belly button area). Keep your elbows close to your sides, continuing to contract your lats throughout the entire range of motion. Your elbows should finish just slightly to the back of your rib cage. Return to the starting position by releasing your arms and the lats. Do not round the lower back or all your shoulders to come forward.

### Safety tips:

1. Rounding forward for a stretch between reps not only compromises the lower back but also puts a strain on your rotator cuffs.
2. In order to avoid straining the lower back, it is necessary to use your legs rather than your lower back to situate yourself in the extended leg position during the set up phase.

### Reminders:

1. Sit upright, sternum up.
2. Retract the shoulders first using the back muscles. Then, add the arms.
3. Bring the handle into the abdomen/belly button area.
4. Keep the shoulders down to avoid tension in the upper trapezius muscles.
5. Make sure knees are at least slightly bent to protect the low back.
6. Exhale as you pull the weight in.



## Back Extension

### Target Muscles:

The erector spinae the major muscles working. Gluts (buttocks) and upper hamstring are also involved..

### Function:

Provides back stability. Whenever you lift your torso to straighten your body from a bent position, your erector spinae muscles do most of the work. These muscles run from the hip to the neck on either side of your spine and branch off to attach at the ribs and spine.

### Movement:

**Setting up:** Sit on a back-extension machine with your upper back against the back roller, knees bent, and feet flat on the foot plate. The back roller should touch your back at your shoulder blades. Buckle yourself in the seat belt, if desired. Align your head, neck and spine in the neutral position. Position your pelvis in a neutral position, and contract your abs in order to maintain pelvis stability and protect your lower back. Squeeze your shoulder blades together in order to maintain the sternum up position during the full range of motion. You may cross your arms over your chest or relax them at your side.

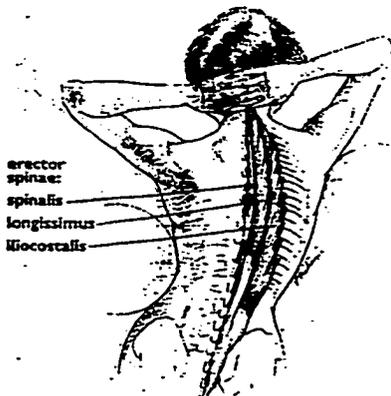
**Execution:** Leading with your shoulders, extend your back to press the roller back to approximately 45 degrees beyond the upright position. Keep your head, neck and spine aligned and in the neutral position. Return to the starting position and repeat.

### Safety tips:

1. Do not thrust or jerk your back, press in a controlled motion.
2. Do not arch your back.
3. Use your abdominal muscles to provide pelvis stability and support for your lower back muscles as they contract.
4. Keep your sternum up throughout the full range of motion to prevent rounding of the shoulders and strain on the lower back.

### Reminders:

1. Do not jerk or thrust your back backwards.
2. Do not arch your back.
3. Keep your head, neck and spine aligned.
4. Slow is better.
5. Exhale as you push back.



### One Arm Military Dumbbell Press

**Target muscles:**

Front and middle deltoid, triceps, erector spinae.

**Function:**

Lifting items overhead. This exercise adds shoulder shape and size.

**Movement:**

**Setting up:** Each press should initiate from a spot where your thumb would point at your neck if you weren't holding a weight. If you hold it too high you'll have a shortened range of motion; too low causes your shoulders to drop, which could lead to pain in the joint. Bring the weight to the starting position by your shoulder, palm facing forward.

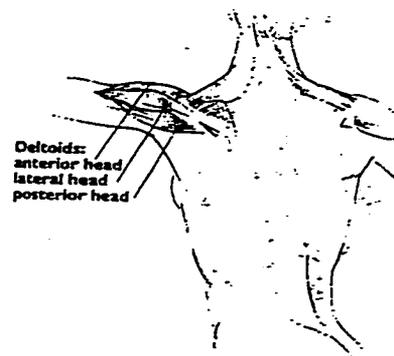
**Execution:** Press the weight over your head until your arm is fully extended, keeping the weight directly over your shoulder within the plane of your body. Be sure to press the weight straight up along the line of gravity, not forward or out to the side. Do not lock your elbow when your arm is fully extended. As you lower the weight, keep your forearm perpendicular to the floor. Return to the starting position. If you feel your back beginning to arch or that you are leaning off to the side while pushing the weight up, finish the set with a lighter weight. Once you have completed a set with one arm, alternate to the opposite arm and repeat.

**Safety tips:**

1. Do not lock your elbows.
2. Do not arch your back (Donald Ducks pelvic tilt) or lean off to the side.
3. If your shoulder is "popping", or any pain is experienced, lift with your palm facing your ear.

**Reminders:**

1. As you press up, think "down" with your shoulders.  
No shrugging.
2. Imagine the weight travelling up and down on a track.
3. Exhale as you push up.



## Wall Squats

### Targeted muscles:

Quadriceps, hamstrings, and gluts (buttocks).

### Function:

Strengthens and defines lower body, strong gluts take pressure off the lower back. This exercise can be used as an introduction to squats before performing the hack squat or smith squats.

### Movement:

**Setting up:** With your back to the wall, place a rubber ball between the small of your back and the wall. Place another rubber ball between your knees. Let your hands hang down at your sides, holding the appropriate dumbbell weight in each hand. Feet are positioned out in front of your body so the knees do not come forward of the ankles when squatting down to a 90 degree angle.

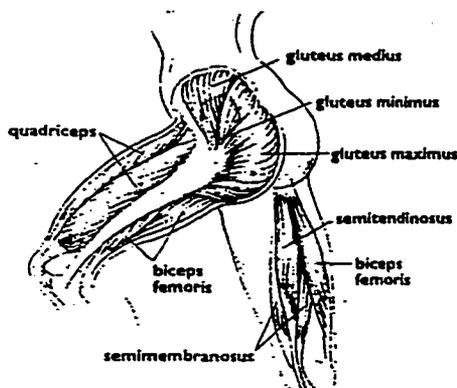
**Execution:** Squat down until there is a 90 degree angle in the knees and thighs are parallel to the floor. Straighten legs to the starting position, pressing through the heels. Do not lock the knees. Keep the back straight, sternum up, and abdominals tight going in both the up and down directions.

### Safety tips:

1. Through the full range of motion, make sure to keep the sternum up and back straight to prevent strain on the lower back.
2. Do not squat below 90 degrees.
3. Make sure that the knees do not lock at the top of the up motion.

### Reminders:

1. Keep sternum up and back straight through the full range of motion.
2. Squat down as if you were going to sit down in a chair.
3. Do not lock your knees.
4. Do not squat below 90 degrees at the knee.
5. Do not allow your knees to come forward of the ankles.
6. Contract your abdominals for stabilization.
7. Focus on contracting your buttock as well as your legs.



## Hack Squat

### Targeted Muscles:

Quadriceps, gluts (buttocks), and hamstrings.

### Function:

Basic leg strength. A good power move for all sorts of athletics and activities.

Aesthetics: Develops a shapely sweep to the thigh.

### Movement:

**Setting up:** Place your feet on the foot plate hip-width apart. They should be high enough to prevent your knees from going forward of your ankles as you squat down. Place a ball between your knees and your hands on the hand rests.

Align your head, spine, and hips. Your low back should be in neutral (Pink Panthers use a lumbar roll). Contract the abdominals to stabilize the pelvis.

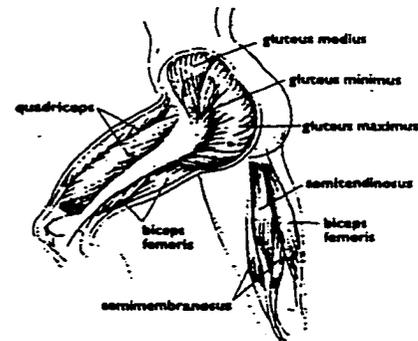
**Execution:** Squat down slowly until your knees reach a 90 degree angle. Do not bounce at the bottom of the range of motion. Pause at the bottom, then press through your heels to return to the starting position without locking your knees.

### Safety tips:

Make sure your spine stays in neutral, your heels stay on the foot plate, and your knees stay over you ankles.

### Reminders:

1. Knees and hips form 90 degree angles as you squat down.
2. Press through the heels.
3. Don't bounce at the bottom or the top of the range of motion.
4. Exhale as you push up.



## **Smith Squats**

### *Targeted muscles:*

Quadriceps, hamstrings, gluts (buttocks), low back

### *Function:*

Basic leg strength. A good power move for athletics and activities.

Aesthetics: Develops a shapely sweep to the thigh.

### *Movement:*

**Setting up:** Position yourself with hips and feet directly underneath the bar. Feet are parallel and hip width apart. The bar is resting on the upper trapezius below the cervical spine. Hands are shoulder width apart or slightly wider. Sternum is up. Release the bar from the locks by straightening your legs, then step your feet forward so that your knees do not come forward of your toes when the 90 degree knee angle is reached during your squat.

**Execution:** Keeping your sternum up and eyes focused just above eye level, squat down until your knees create a 90 degree angle. You will be simulating the motion of sitting down in a chair. Make sure your thighs remain parallel, sternum stays up, heels stay on the floor, and hips remain under the bar through the full range of motion. Allow your lumbar spine to arch slightly in its normal position in order to maintain your balance without dropping your chest. Do not allow your knees to buckle inward or outward. Your weight should remain over your heels and not your toes. Do not bounce at the bottom of the motion.

Return to the starting position by straightening your legs, using your thighs and your buttocks. Do not lock your knees at full leg extension.

### *Safety Tips:*

1. In order to prevent strain on the lower back, it is necessary to keep your hips underneath the bar and sternum up through the full range of motion.
2. In order to prevent strain on the knees, it is necessary to position your feet far enough forward. It is also important to prevent your knees from buckling inward or outward.

### *Reminders:*

1. Keep your sternum up and eyes focused above eye level.
2. Keep your hips under the bar.
3. Keep your heels on the floor.
4. Do not bounce at the bottom of the motion.
5. Do not lock your knees.
6. Push through your heels.
7. Exhale as you push up.

## Rotary Torso

*Target Muscles:*  
Obliques

*Function:*  
Develops definition and shape to the torso.

*Movement:*

*Setting Up:*

- FIT** Straddle the seat and cross your ankles securely. Keeping your torso erect, turn to the side without leaning and position your forearms on the arm pads with one hand holding each of the metal bars extending up the middle of the movement arm.
- NW** Straddle the seat and cross your ankles securely. Hook your arms securely around the arm pads on the movement arm.
- UMC** Adjust the seat height so that the chest pads rest on the upper chest. Straddle the seat with one knee on the outside of each knee pad. Plant your feet firmly on the foot rests. Press your upper chest against the chest pads while maintaining an erect torso (i.e. do not lean forward to do this). Grasp the handles underneath the chest pads.
- Metro** Adjust the back rest so that when your arms are hooked around the arm pads they may rest comfortably at your sides. Hook your arms around the arm pads. Straddle the seat with one knee on the outside of each knee pad. Plant your feet firmly on the ground.

*Execution:*

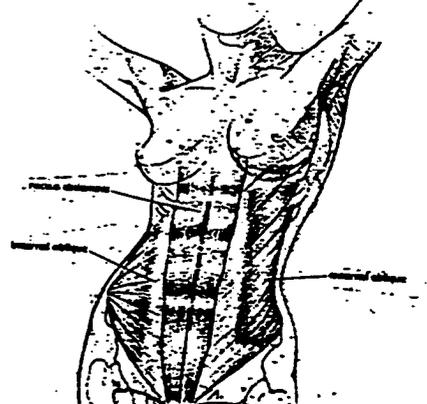
- FIT/NW** Moving the head, arms, and torso as a single unit, rotate the torso from the right to the left. Keep the sternum up through the entire range of motion. Do not allow the arms or the head to move ahead of the torso. Do not use the triceps or biceps to push or pull the movement arm. Keep the torso erect, and do not lean into the motion. Do not allow the hips and the legs to move with the torso. Pause in the contracted position. Return slowly to the starting position and repeat. Adjust the machine and repeat the exercise on the opposite side.
- UMC** Keeping your chest pressed against the chest pads and the upper body immobile, rotate your lower body from the right to the left. Keep the sternum up and do not allow your chest to leave the pads throughout the entire range of motion. Keep the torso erect, and do not lean into the motion. Adjust the machine and repeat the exercise on the opposite side.

*Safety tips:*

Do not push the weight or jerk it around. Control the movement throughout.

*Reminders:*

1. Sternum up.
2. Use slow, controlled movements.
3. Do not push or pull with your biceps or triceps.
4. Maintain an erect torso. Do not lean into the motion.
5. Exhale as you rotate.



## REFERENCES

1. National Institutes of Health. National Institutes of Health Consensus Development Conference Statement. Washington, DC: National Institutes of Health; 2000.
2. Kelley G. Exercise and regional bone mineral density in postmenopausal women : a meta-analytic review of randomized trials. *American Journal of Physical Medicine & Rehabilitation*. 1998;77:76-87.
3. Foundation NO. 1996 and 2015 Osteoporosis Prevalence Figures : State by State Report. Washington, DC: National Osteoporosis Foundation; 1997.
4. National Institutes of Health. Fast facts on osteoporosis. Washington, DC: Osteoporosis and Related Bone Diseases National Resource Center of the National Institutes of Health; 2000.
5. Riggs B, LJ M. The worldwide problem of osteoporosis: insights afforded by epidemiology. *Bone*. 1995;17:505-511S.
6. Chrischilles E, Shireman T, Wallace R. Costs and health effects of osteoporotic fractures. *Bone*. 1994;15:377-386.
7. Kannus P, Parkkari J, Sievanen H, Heinonen A, Vuori I, Jarvinen M. Epidemiology of hip fractures. *Bone*. 1996;18:57-63S.
8. Kanis J, McCloskey E. Evaluation of the risk of hip fracture. *Bone*. 1996;18:127-132S.
9. Obrant K, Bengner U, Johnell O, Nilsson B, Sernbo I. Increasing age-adjusted risk of fragility fractures : a sign of increasing osteoporosis in successive generations. *Calcified Tissue International*. 1989;44:157-167.
10. Kannus P, Parkkari J, Niemi S. Age-adjusted incidence of hip fractures. *The Lancet*. 1995;346:50-51.

11. Drinkwater B. Osteoporosis. In: Rippe J, ed. *Lifestyle Medicine*. Malden: Balckwell Science; 1999.
12. Smith E, Gilligan C. Dose-response relationship between physical loading and mechanical competence of bone. *Bone*. 1996;18:45S-50S.
13. Cummings SR, Black DM, Nevitt MC, et al. Bone density at various sites for prediction of hip fractures. *The Lancet*. 1993;341:72-75.
14. Marshall D, Johnell O, Wedel H. Meta-analysis of how well measures of bone mineral density predict occurrence of osteoporotic fracture. *British Medical Journal*. 1996;312:1254-59.
15. Nguyen T, Kelly P, Sambrook P, Gilbert C, Pocock N, Eisman J. Lifestyle factors and bone density in the elderly : implications for osteoporosis prevention. *Journal of Bone & Mineral Research*. 1994;9:1339-1346.
16. Cummings S, Nevitt M, Browner W, et al. Risk factors for hip fracture in white women. *New England Journal of Medicine*. 1995;332:767-73.
17. Cheng S, Suominen H, Heikkinen E. Bone mineral density in relation to anthropometric properties, physical activity and smoking in 75-year-old men and women. *Aging (Milano)*. 1993;5:55-62.
18. Prince R, Devine A, Dick I, et al. The effect of calcium supplementation (milk, powder or tablets) and exercise on bone density in postmenopausal women. *Journal of Bone & Mineral Research*. 1995;10:1068-75.
19. Anderson R, Wadden T, Herzog R. Changes in bone mineral content in obese dieting women. *Metabolism : Clinical & Experimental*. 1997;46:857-61.
20. Mosekilde L. Osteoporosis and exercise. *Bone*. 1995;17:193-195.
21. Dargeant P, Favier F, Grandjean H, et al. Fall-related factors and risk of hip fracture : the EPIDOS prospective study. *Lancet*. 1996;348:145-9.

22. Faulkner K, Cummings S, Black D, Palermo L, Gluer C, Genant H. Simple measurement of femoral geometry predicts hip fracture. *Journal of Bone & Mineral Research*. 1993;8:1211-7.
23. Bouxsein M, Marcus R. Overview of exercise and bone mass. *Rheumatic Disease Clinics of North America*. 1994;20:787-801.
24. Kushi L, Fee R, Folsom A, Mink P, Anderson K, Sellers T. Physical activity and mortality in postmenopausal women. *JAMA*. 1997;277:1287-1292.
25. Nelson M, Fiatorone M, Morganti C, Trice I, Greenberg R, Evans W. Effects of high-intensity strength training on multiple risk factors for osteoporotic fractures: a randomized controlled trial. *Journal of the American Medical Association*. 1994:1909-14.
26. Kohrt W, Ehsani A, Birge S. Effects of exercise involving predominantly either joint-reaction or ground-reaction forces on bone mineral density in older women. *Journal of Bone & Mineral Research*. 1997;12:1253-1261.
27. Kerr D, Morton A, Dick I, Prince R. Exercise effects on bone size in postmenopausal women are site-specific and load-dependent. *Journal of Bone & Mineral Research*. 1996;11:18-25.
28. Lanyon L. Using functional loading to influence bone mass and architecture : objectives, mechanisms, and relationship with estrogen of the mechanically adaptive process in bone. *Bone*. 1996;18:37-43S.
29. American College of Sports Medicine. ACSM position stand on osteoporosis and exercise. *Medicine and Science in Sports and Exercise*. 1995.
30. Chilibeck P, Digby G, Webber C. Exercise and bone mineral density. *Sports Medicine*. 1995;19:103-122.

31. Forwood M, Burr D. Physical activity and bone mass : exercises in futility? *Bone and Mineral*. 1993;21:89-112.
32. Coupland C, Cliffe S, Basse E, Grainge M, Hoskin D, Chilvers C. Habitual physical activity and bone mineral density in postmenopausal women in England. *International Journal of Epidemiology*. 1999;28:241-46.
33. Lord S, Ward J, Williams P, Zivanovic E. The effects of a community exercise program on fracture risk factors in older women. *Osteoporosis International*. 1996;6:361-7.
34. Kano K. Relationship between exercise and bone mineral density among over 5,000 women aged 40 years and above. *Journal of Epidemiology*. 1998;8:28-32.
35. Parra-Cabrera S, Hernandez-Avila M, Tamayo-Orozco J, Lopez-Carrillo L, Meneses-Gonzalez F. Exercise and reproductive factors as predictors of bone density among osteoporotic women in Mexico City. *Calcified Tissue International*. 1996;59:89-94.
36. Ulrich C, Georgiou C, Gilles CS-HD. Bone mineral density in mother-daughter pairs: relations to lifetime exercise, lifetime milk consumption, and calcium supplements. *American Journal of Clinical Nutrition*. 1996;63:72-9.
37. Brahm H, Mallmin H, Michaelsson K, Strom H, Ljunghall S. Relationships between bone mass measurements and lifetime physical activity in a Swedish population. *Calcified Tissue International*. 1998;62:400-12.
38. Greendale G, Barrett-Connor E, Edelstein S, Ingles S, Haile R. Lifetime leisure exercise and osteoporosis : the Rancho Bernardo study. *American Journal of Epidemiology*. 1995;141:51-59.
39. Conroy B, Kraemer W, Maresh C. Bone mineral density in elite junior Olympic weightlifters. *Medicine & Science in Sports & Exercise*. 1993;25:1103-9.

40. Nelson M, Fisher E, Dilmanian F, Dallal G, Evans W. A 1-y walking program and increased dietary calcium in postmenopausal women : effects on bone. *American Journal of Clinical Nutrition*. 1991;53:1304-11.
41. Bidoli E, Schinella D, Franceschi S. Physical activity and bone mineral density in Italian middle-aged women. *European Journal of Epidemiology*. 1998;14:153-7.
42. Cummings S. Epidemiologic studies of osteoporotic fractures : methodologic issues. *Calcified Tissue International*. 1991;49:S15-S20.
43. Michel B, Lane N, Bloch D, Jones H, Fries J. Effect of changes in weight-bearing exercise on lumbar bone mass after age fifty. *Annals of Medicine*. 1991;23:397-401.
44. Kelley G. Aerobic exercise and bone density at the hip in postmenopausal women : a meta-analysis. *Preventive Medicine*. 1998;27:798-807.
45. Layne J, Nelson M. The effects of progressive resistance training on bone density : a review. *Medicine & Science in Sports & Medicine*. 1999;31:25-30.
46. Ernst E. Exercise for female osteoporosis : a systematic review of randomized clinical trials. *Sports Medicine*. 1998;25:359-368.
47. Berard A, Bravo G, Gauthier P. Meta-analysis of the effectiveness of physical activity for the prevention of bone loss in postmenopausal women. *Osteoporosis International*. 1997;7:331-7.
48. Lohman T, Going S, Pamentier R, Hall M, Boyden T, Houtkooper L, Ritenbaugh C, Bare L, Hill A, Aickin M. Effects of resistance training on regional and total bone mineral density in premenopausal women : a randomized prospective study. *Journal of Bone and Mineral Research*. 1995;10(7):1015-1024.
49. Braith R, Mills R, Welsch M, Keller J, Pollock M. Resistance exercise training restores bone mineral

- density in heart transplant recipients. *Journal of the American College of Cardiology*. 1996;28:1471-1477.
50. Kohrt W, Ehsani A, Jr. SB. HRT preserves increases in bone mineral density and reductions in body fat after a supervised exercise program. *Journal of Applied Physiology*. 1998;84:1506-12.
  51. Bloomfield S, Williams N, Lamb D, Jackson R. Non-weightbearing exercise may increase lumbar spine bone density in healthy postmenopausal women. *American Journal of Physical Medicine & Rehabilitation*. 1993;72:204-9.
  52. Heinonen A, Sievanen OH, Pasanen M, Vuori I. Effect of two training regiments on bone mineral density in healthy perimenopausal women: a randomized controlled trial. *Journal of Bone and Mineral Research*. 1998;13:483-90.
  53. Basse E, Ramsdale S. Weight-bearing exercise and ground reaction forces: a 12-month randomized controlled trial of effects on bone mineral density in healthy postmenopausal women. *Bone*. 1995;16:469-76.
  54. Smidt G, Lin S, O'Dwyer K, Blanpied P. The effect of high-intensity trunk exercise on bone mineral density in postmenopausal women. *Spine*. 1992;17:280-5.
  55. Lau E, Woo J, Leung P, Swaminathan R, Leung D. The effect of calcium supplementation and exercise on bone density in elderly Chinese women. *Osteoporosis International*. 1992;168-73.
  56. McCartney N, Hicks A, Martin J, Webber C. Long-term resistance training in the elderly : effects on dynamic strength, exercise capacity, muscle, and bone. *Journal of Gerontology*. 1995;50A:B97-B104.
  57. Danz AM, Zittermann A, Schiedermaier U, Klein K, Hotzel K, Schonau E. The effect of a specific strength-development exercise on bone mineral density in perimenopausal and postmenopausal women. *Journal of Womens Health*. 1998;7:701-9.

58. Adami A, Gatti D, Braga V, Bianchini D, Rossini M. Site-specific effects of strength training on bone structure and geometry of ultradistal radius in postmenopausal women. *Journal of Bone & Mineral Research*. 1999;14:1634-5.
59. Prince R, Smith M, Dick I, et al. Prevention of postmenopausal osteoporosis. A comparative study of exercise, calcium supplementation, and hormone-replacement therapy. *New England Journal of Medicine*. 1991;325:1189-95.
60. Ryan A, Treuth M, Hunter G, Elahi D. Resistive training maintains bone mineral density in postmenopausal women. *Calcified Tissue International*. 1998;62:295-9.
61. Hartard M, Haber P, Ilieva D, Preisinger E, Seidl G, Huber J. Systematic strength training as a model of therapeutic intervention. *American Journal of Physical Medicine & Rehabilitation*. 1996;75:21-28.
62. Heikkinen J, Kurttila-Matero E, Kyllonen E, Vuori J, Takala T, Vaananen H. Moderate exercise does not enhance the positive effect of estrogen on bone mineral density in postmenopausal women. *Calcified Tissue International*. 1991;49:S83-S84.
63. Pruitt L, Taaffe D, Marcus R. Effects of a one-year high-intensity versus low-intensity resistance training program on bone mineral density in older women. *Journal of Bone & Mineral Research*. 1995:1788-95.
64. Rhodes E, Martin A, Donnelly JTM, Warren J, Elliot J. Effects of one year of resistance training on the relation between muscular strength and bone density in elderly women. *British Journal of Sports Medicine*. 2000;34:18-22.
65. Sinaki M, Wahner H, Bergstralh E, et al. Three-year controlled, randomized trial of the effect of dose-specified loading and strengthening exercises on bone mineral density of spine and femur in nonathletic, physically active women. *Bone*. 1996;19:233-244.

66. Preisinger E, Alacamlioglu Y, Pils K, Saradeth T, Schneider B. Therapeutic exercise in the prevention of bone loss. *Journal of Physical Medicine & Rehabilitation*. 1995;74:120-123.
67. Lohman T. Grant Proposal for the Bone Estrogen Strength Training Study. Tucson, AZ; 1993.
68. SPSS Incorporated. Statistic Program for the Social Sciences. Chicago: SPSS Incorporated; 2000.
69. Afifi A, Clark V. Computer-Aided Multivariate Analysis. 3 ed. New York: Chapman & Hall; 1996.
70. Rothman K, Greenland S. Modern Epidemiology. 2 ed. New York: Lippincott Williams & Wilkins; 1998.
71. Greenland S. Modeling and variable selection in epidemiologic analysis. *American Journal of Public Health*. 1989;79:340-349.
72. Lohman T. Personal communication. August, 2000.
73. Bortz WT 4th, Bortz WT 3rd. How fast do we age? Exercise performance over time as a biomarker. *Journals of Gerontology. Series A, Biological Sciences & Medical Sciences*. 1996;51:M223-5.
74. Frost H. On our age-related bone loss : insights from a new paradigm. *Journal of Bone & Mineral Research*. 1997;12:1539-1546.
75. Microsoft Incorporated. Excel. Seattle: Microsoft Incorporated; 1997.
76. Sonis J. A closer look at confounding. *Family Medicine*. 1998;30:584-8.
77. Mazess R, Barden H. Bone density of the spine and femur in adult white females. *Calcified Tissue International*. 1999;65:91-99.
78. Hedlund L, Gallagher J. The effect of age and menopause on bone mineral density of the proximal

- femur. *Journal of Bone & Mineral Research*. 1989;4:639-42.
79. Skerry T. Mechanical loading and bone : what sort of exercise is beneficial to the skeleton. *Bone*. 1997;20:179-181.
  80. Sackett D. Bias in analytical research. *Journal of Chronic Disease*. 1979;32:51-63.
  81. Watts N. Postmenopausal osteoporosis. *Obstetrical & Gynecological Survey*. 1999;54:532-8.
  82. Notelovitz M, Martin D, Tesar R. Estrogen therapy and variable-resistance weight training increase bone mineral in surgically menopausal women. *Journal of Bone & Mineral Research*. 1991:583-90.
  83. Kohrt W, Snead D, Slatopolsky E, SJ Birge J. Additive effects of weight-bearing exercise and estrogen on bone mineral density in older women. *Journal of Bone & Mineral Research*. 1995;10:1303-1311.
  84. Wolff I, Croonenborg JV, Kemper H, Kostense P, Twisk J. The effect of exercise training programs on bone mass : a meta-analysis of published controlled trials in pre- and postmenopausal women. *Osteoporosis International*. 1999;9:1-12.
  85. Specker B. Evidence for an interaction between calcium intake and physical activity on changes in bone mineral density. *Journal of Bone & Mineral Research*. 1996;11:1539-1344.
  86. Van der Weil HE, Lips P, Graafmans W. Additional weight-bearing during exercise is more important than duration of exercise for anabolic stimulus of bone : a study of running exercise in female rats. *Bone*. 1995;16:73-80.
  87. Frost H. Muscle, bone, and the Utah paradigm : a 1999 overview. *Medicine & Science in Sports & Exercise*. 2000;32:911-917.

88. Turner C. Exercise as a therapy for osteoporosis : the drunk and the street lamp, revisited. *Bone*. 1998;23:83-85.
89. Basse E. Mechanical loading and skeletal integrity : much needed debate. *Journal of Bone & Mineral Research*. 1999;14:1014-1015.
90. Mazess R, Barden H. Bone density of the spine and femur in adult white females. *Calcified Tissue International*. 1999;65:91-99.
91. Davies H, Crombie K. Bias in cohort studies. *Hospital Medicine*. 1999;61:133-5.
92. Greenland S. Response and follow-up bias in cohort studies. *American Journal of Epidemiology*. 1977;106:184-7.
93. Bureau UC. Educational Attainment in the United States. . Washington, DC: US Census Bureau; 1999.
94. Clark D, Patrick D, Grembowski D, Durham M. Socioeconomic status and exercise self-efficacy in later life. *Journal of Behavioral Medicine*. 1995;18:355-76.
95. Kuczmarski M, Kuczmarski R, Najjar M. Descriptive anthropometric reference data for older Americans. *Journal of the American Dietetic Association*. 2000;100:59-66.
96. Keating N, Cleary P, Rossi A, Zaslavsky A, Ayanian J. Use of hormone replacement therapy by postmenopausal women in the United States. *Annals of Internal Medicine*. 1999;130:545-553.
97. Looker A, Wahner H, Dunn W, et al. Proximal femur bone mineral levels of US adults. *Osteoporosis International*. 1995;5:389-409.