

INFLAMMATORY BOWEL DISEASE, OSTEOPOROSIS, EXERCISE, AND BONE
MINERAL DENSITY

By

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To my parents who always stressed the value of education and the belief that anything is possible.

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Abstract of Dissertation Presented to the Graduate School
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Patients with inflammatory bowel disease (IBD) are at increased risk of developing osteopenia and osteoporosis. The purpose of this study was to examine the feasibility of a non-pharmacological nursing intervention designed to prevent bone loss, reduce the risk of fractures, and promote self-efficacy in adults with Inflammatory Bowel Disease (IBD), Crohn's disease and Ulcerative Colitis (UC). The intervention consisted of progressive load-bearing walking utilizing a weighted vest. Sixteen men, age 30 to 75 years, were recruited to participate in the study. Following baseline testing, subjects were randomly assigned to an exercise group (n=7), or to a sedentary control group (n=9). Subjects in the exercise group participated in 32 weeks (three, 50 minute sessions/week) of exercise training. Training consisted of a home based walking while wearing weighted vests. Measurements included (1) dual-energy x-ray absorptiometry (DEXA) scans of the hip and lumbar spine, (2) serum biochemical markers of bone formation, bone-specific alkaline phosphatase, marker of bone anabolism, and pyridinoline cross-links, an indicator of bone catabolism, or resorption, (3) Osteoporosis Self-Efficacy Scale and (4) change in systolic blood pressure. Results showed no significant differences between the groups.

CHAPTER 1 INTRODUCTION

Background of the Problem

Epidemiology of osteoporosis-related fractures. In the United States, one in two women and one in eight men older than 50 years will suffer an osteoporosis-related fracture in their lifetime (Cooper, 2000). Of the more than 1.5 million fractures that occur each year, over 300,000 are fractures of the hip, 250,000 are fractures of the distal forearm, 700,000 are vertebral fractures, and 250,000 are fractures at other sites (Riggs & Melton, 1995). A low bone mineral density (BMD) has been reported in 30-75% of patients with IBD in cross-sectional and prospective studies (Pollak et al., 1998). Compared to the general population, patients with IBD have up to 40% more fractures (Frei et al., 2006). Most hip fractures are attributed to falls at home while the majority of distal forearm (Colles') fractures are caused by extending the arm out to break a fall. Vertebral fractures have a multiplicity of causes, but rarely result from a single traumatic event. Of all fractures, those to the hip are the most devastating as they result in the highest rate of morbidity and mortality (Kelley, 1998).

It is estimated that up to 33% of all hip fractures occur in men. Although women typically experience hip fractures related to postmenopausal osteoporosis, men of all ages with IBD experience increases morbidity and mortality due to steroid-related osteoporosis (Lawson, 2001). The incidence of fracture among persons with IBD is 40% greater than that in the general population (Bernstein, Blanchard, Leslie, Wajda and Yu, 2000). Twenty-four percent of patients die in the year after a hip fracture, and more than 40% are discharged from a hospital to a nursing home (National Osteoporosis Foundation [NOF], 1997). By the end of one year, one-third of those hip fracture patients are still in the nursing home. In addition, approximately 50% of all people suffering a hip fracture will be unable to walk without assistance. Degenerative fractures

of the osteoporotic spine are subtle, but kyphosis due to vertebral collapse greatly diminishes quality of life for many older men. The health-care cost of osteoporosis-related fractures is nearly \$14 billion annually in this country (NOF, 1997), but the cost in pain, suffering, lost personal freedom and independence cannot be measured. Moreover, with the demographic shift occurring in our population, the problem of osteoporosis-related morbidity and mortality will likely increase.

Purpose of Study

The purpose of this study was to examine the feasibility of a home based non-pharmacological nursing intervention to prevent bone loss, reduce the risk of fractures, and promote self-efficacy in adults with Inflammatory Bowel Disease (IBD), Crohn's disease and Ulcerative Colitis. The goal was to reduce morbidity associated with falls and bone fractures in this population. The intervention consisted of progressive load-bearing walking and daily calcium and vitamin D supplementation.

Conceptual Framework

Self-efficacy and exercise. An active lifestyle is particularly important for adults given the broad constellation of physiological, behavioral, cognitive, and biochemical outcomes that are influenced by physical activity. However, the majority of adults do not exercise or participate in sports on a regular basis per a National Health Interview Survey (National Institute of Health, 1991). There are a number of theoretical explanations that provide an understanding of why individuals choose to participate or not participate in health-related behaviors. Recently, self-efficacy has received considerable support as a predictor of the initiation and maintenance of an exercise program for health and fitness. The construct of self-efficacy is derived from Bandura's social cognitive theory (1986). According to the theory, people are motivated to engage in a behavior based on the belief that: (a) the behavior will result in a favorable outcome (outcome

expectation), and (b) the individual is capable of executing the behavior (efficacy expectation). A meta-analysis of studies of health-related behaviors revealed consistent support for the importance of self-efficacy as a determinant of healthy lifestyles, including regular exercise (Gillis, 1993). Considerable literature further suggests that participation in exercise training has a positive influence on self-efficacy. McAuley, Bane, and Mihalko (1995) examined the effects of both long-term exercise participation and acute bouts of exercise on the physical self-efficacy of middle-aged men and women. In addition to demonstrating the utility of physical mastery experiences in influencing efficacy, McAuley Bane, and Mihalko (1995) reported some interesting patterns with respect to gender responses. Whereas men and women demonstrated significant gains in perceived capabilities in response to both acute and long-term exercise, men initially were significantly more efficacious than women. I hypothesize that subjects in the exercise group would gain both the psychomotor skills and the self-efficacy to continue exercising as part of a healthy lifestyle.

Significance of this Study

The evidence clearly demonstrates that exercise training can offer a nonpharmacological alternative for improving bone health in those who do not choose to take osteoporosis medications (e.g., Biphosphonates). Other benefits associated with regular exercise include a reduction in risk factors for many diseases, enhancement of overall functional fitness and well being, and improved self-efficacy. It has not been clearly determined, however, what type, magnitude, and duration of exercise would be the most efficacious for adults with IBD. The exercise-training program described in this proposal combines ground-reaction and joint-reaction forces to repeatedly place moderate, progressive strain on the whole skeleton, but more specifically on the spine, femoral neck and hip, of men with IBD. Subjects trained for 50 minutes/day, 3 days/week, for 32 weeks. The first exercise session was closely supervised for

the subject's safety, and included warm-up and flexibility exercises, followed by walking while wearing a weighted vest. Exercise with weighted vests improved dynamic balance, leg strength and muscle mass in older women (Shaw & Snow, 1998). By walking while wearing vests with a moderate weight (20% of body weight), adults with IBD were able to safely apply a load-bearing strain to the bones of the spine and hip without the risk of plyometric (jumping or bouncing) or high impact maneuvers. It is anticipated that the intervention would improve bone density, physiologic exercise induced changes in vital signs, biochemical markers for bone resorption and formation, and self-efficacy in adults with IBD.

Research Hypotheses

- **Hypothesis 1:** Thirty-two weeks of progressive load-bearing walking exercise by adults with IBD who are not taking osteoporosis medications would result in increased bone density of the lumbar spine, hip and femoral neck (measured by dual-energy X-ray absorptiometry) significantly greater than that of adults with IBD who do not exercise.
- **Hypothesis 2:** Thirty-two weeks of progressive load-bearing walking exercise by adults with IBD who are not taking osteoporosis medications would result in increased serum levels of BAP and increased ratios between BAP and DPD significantly greater than that of adults with IBD who do not exercise.
- **Hypothesis 3:** Completion of a weeks exercise program by adults with IBD who are not taking osteoporosis medications would result in improved self confidence in managing their own care (measured by the Osteoporosis Self-Efficacy Scale) that are significantly higher than those of adults with IBD who do not participate in exercise training.
- **Hypothesis 4:** Thirty-two weeks of progressive load-bearing walking exercise by adults with IBD would result in improved systolic blood pressure.

CHAPTER 2 LITERATURE REVIEW

Pathogenesis of Osteoporosis

Osteopenia is defined as failure of the rate of osteoid tissue synthesis to keep up with the rate of bone loss without respect to cause. It is characterized by abnormally low bone mass/density and a disruption in the microarchitecture of bone tissue, leading to a reduced effectiveness of trabecular cross bracing (Sheth, 1999). This loss of bone connectivity results in bone fragility and fatigue. Once bone fatigue occurs, osteoblastic apoptosis ensues, resulting in osteoporosis. If there is impact from a mechanical load, the bone may fracture. Osteoporosis is clinically defined as bone mineral density (BMD), measured by dual energy x-ray absorptiometry (DEXA) or computed tomography, of more than 2.5 standard deviations below the reference value for a normal, healthy adult (Black, Palermo, & Bauer, 2000). Osteoporotic fracture, however, is not a single disease with a single etiologic agent. It has multiple levels of pathogenesis that involve genetic and cellular factors, developmental processes of bone remodeling (bone growth in children and bone loss in aging), and environmental factors such as falls (Cooper, 2000). Although bone loss is a universal concomitant of advanced age affecting both men and women, it proceeds at a much faster rate in gastrointestinal disorders, hypogonadism, immobilization, organ transplants or with certain medications.

Inflammatory Bowel Disease and Osteoporosis

The pathogenesis of bone loss in IBD is multifactorial, consisting of general risk factors for osteoporosis and disease-specific factors including corticosteroid use, sex hormone deficiency, lack of physical activity, vitamin D and calcium malabsorption secondary to active disease and/or intestinal resection, and secondary to osteoclast activation by proinflammatory cytokines (Southerland & Valentine, 2001). According to a study on young males, mean age 26,

who were steroid naïve and a recent diagnosis of IBD, 28% had a decreased bone mineral density (Sakellariou et al., 2006). Low body mass index was an independent factor for low bone mineral density (Hela et al., 2005). Corticosteroid usage is the most common cause of secondary osteoporosis. Chronic or excess corticosteroid has multiple effects on bone metabolism. Corticosteroids not only decrease bone formation, they also increase bone resorption (Manolagas & Weinstein, 1999). It has been demonstrated that corticosteroids inhibit osteoblast activity, which stimulates osteoclast activity thus increasing bone resorption (Lawson, 2000). Due to the increased rate of bone resorption and inhibition of bone formation, their usage associated with rapid bone loss. Reid and Heap demonstrated that subjects starting corticosteroid therapy lost a mean of 27% of the lumbar spine BMD within the first year of therapy.

Risk Factors for Osteoporosis

Risk factor identification for osteoporosis-related fractures is complex and agreement between leading population-based studies is limited. It is clear that corticosteroid usage is a major etiologic component and risk factor in bone fragility (Figure 2-1). Regardless of gender, up to 50% of patients taking corticosteroids on a chronic basis sustain osteoporotic fractures (Lane & Lukert, 1998). Established risk factors for osteoporotic fractures in men include a family history of osteoporosis, Caucasian, physical inactivity, low calcium and vitamin D intake, previous history of fracture, mental depression, tobacco smoking, long-term use of steroids, benzodiazepines, and anticonvulsant medications, gastrointestinal disease and hyperparathyroidism (Cooper, 2000).

Treatment and Prevention of Osteoporosis

The treatment and prevention of osteoporosis includes both pharmacologic and nonpharmacologic interventions. There have been great advances in the pharmacologic treatment of osteoporosis in the past 15 years. The antiresorptive bisphosphonate agents, alendronate

(Fosamax®) and risedronate (Actonel ®) have been shown in clinical studies to reduce spine fractures by about 50% when used in combination with estrogen replacement therapy (ERT) in estrogenic women (Tonino, Meunier, & Emkey, 2000). The bisphosphonates have serious side effects, however, including esophageal ulceration, nausea, vomiting, diarrhea, hypocalcemia, and renal toxicity. Other drugs have been investigated for the treatment of osteoporosis. In the 1980s, sodium fluoride, an anabolic agent, was widely advocated as a treatment that reduced fractures by improving BMD. Although BMD in treated subjects increased, they had significantly more fractures of the lower extremities than the placebo control subjects (Gray, 2000). Unfortunately, there is low compliance with osteoporosis drug therapy primarily due to cost. For example, daily alendronate costs approximately \$50 monthly. For many patients this cost makes drug therapy an unrealistic option for the prevention and treatment of osteoporosis.

Nutritional Factors and Osteoporosis: The Role of Calcium and Vitamin D

Nutrition is a modifiable risk factor for osteoporosis. There is substantial evidence that adequate calcium and vitamin D intake influences all aspects of bone health throughout the life cycle, from the development of peak bone mass in adolescents, to the maintenance of bone mass in adults, to the reduction of bone loss and fracture in the elderly (Heaney, 2000). A meta-analysis of 15 randomized clinical trials found that Calcium supplementation improved BMD at all skeletal sites in postmenopausal women (O'Shea et al., 2000). Other researchers found that daily supplementation with 1000 mg calcium plus 400 IU vitamin D (ergocalciferol) for 12 months inhibited bone remodeling and significantly increased BMD in women who were 10 years postmenopause (Huang, Lu, Zhou, Liu, & Wang, 2000). Additionally, individuals with IBD are at increased risk for vitamin D and calcium malabsorption secondary to active disease and/or intestinal resections.

Effects of Exercise on Bone Health

Although there is substantial evidence that physical activity stimulates bone formation, research on the mechanisms by which bone is affected by mechanical stress is in its early stages. In 1892, Wolff (Smith, 1988, p. 81) hypothesized that weight bearing compresses and bends long bones, consequently strengthening them and making them less likely to fracture. Weight bearing (gravity) and muscle contraction are the major mechanical forces on bone. Bone mass increases with greater weight bearing, muscle contraction or both and decreases with immobilization or weightlessness. The degree of bone change is proportional to the difference in magnitude and frequency of the mechanical stimulus from normal. Bassett (1971) indicated that bone functions as a piezoelectric crystal, generating an electric charge in proportion to the forces applied to the bone. Bone matrix is removed from areas of positive charge and laid down in areas of negative charge. Carter (1984) hypothesized that mechanical forces produce microfractures, which stimulate osteoclastic remodeling coupled with osteoblastic activity. Lanyon (1981) demonstrated that both the rate and magnitude of strain influenced bone remodeling. He monitored bone mineral in the radii of sheep under artificial stimulation. No change occurred with strain magnitude less than that of the animal's normal walking load. With higher strain magnitude and normal strain rates, periosteal bone deposition increased slightly. When both magnitude and rate were higher than in normal walking, periosteal bone increased substantially. Thus bone, like muscle, requires a specific magnitude and rate of stimulus in order to stimulate hypertrophy. Although the specific level and magnitude of exercise to improve bone density in humans has not been clearly delineated, most studies indicate 20 to 30 minutes of weight-bearing exercise, 3 to 4 days per week will maintain skeletal health.

Exercise is considered to be an attractive alternative to pharmacologic interventions for preventing and treating osteoporosis. Numerous case-control and retrospective and prospective

cohort studies suggest that exercise improves balance, coordination, and bone strength and thus reduces the incidence and the severity of fall-related fractures (Kannus, 1999). Unfortunately, no clinical trials have examined the effects of exercise on osteopenia or osteoporosis in men with IBD. Numerous studies of the effects of exercise on osteoporosis in postmenopausal women have been conducted, however, but with conflicting results. For example, one study found no change in femoral neck BMD (Bloomfield, Williams, Lamb, & Jackson, 1993), while a second study reported no change in BMD at the femoral neck or Ward's triangle, but did find a significant increase in the trochanteric region (Kronhed & Moller, 1998). A third study reported significant increases in BMD at the femoral neck, Ward's triangle, and trochanteric region (Caplan & Ward, 1993), while a fourth study reported that exercise alone had no effect at any of the hip sites, but that exercise and calcium supplementation had a positive effect on the femoral neck (Lau, Woo, Leung, Swaminathan, & Leung, 1992). A more recent study from Jessup, Horne, Vishen, and Wheeler (2003) reported significant improvements in bone mineral density of the femoral neck and lumbar vertebra in postmenopausal women following 8 months of exercise training and calcium supplementation. The training consisted of 30-60 minutes of walking, three days/week while wearing weighted vests. Subjects also took 1000 mg calcium citrate and 400 IU vitamin D daily during the study period (Appendix F). Taken together these studies show 4 to 12 months of exercise can inhibit bone loss and improve BMD in adults.

Biochemical Markers of Bone Metabolism

Previous studies of the effects of resistance exercise training on BMD have utilized the analyses of serum chemical markers of bone metabolism. Serum levels of osteocalcin (OC) and bone-specific alkaline phosphatase (BAP), both markers of bone anabolism, have been shown to be sensitive to alterations in bone metabolism following disease, menopause, and hormone replacement therapy. Serum pyridinoline cross-links (PYD) are an indicator of bone catabolism,

or resorption. In theory, an increase in BMD would be reflected by an increase in OC and BAP as well as in increase in the ratios between OC and BAP and PYD. Vincent and Braith (2002) analyzed serum levels of OC, BAP, and PYD in a group of men and women before and after 6 months of low-intensity (LEX) or high-intensity (HEX) resistance exercise training. Although there were no differences in serum levels of the three biochemical markers between the LEX, HEX and control groups, nor between the male and female subjects at the beginning of the study, there were significant increases in OC in both the HEX and LEX groups after 6 months of training. BAP increased significantly for the HEX group but not for the LEX or control groups. They also found that the ratios of OC and BAP to PYD increased in the exercise groups but not in the controls after the 6-month period. They concluded that the increases in the biochemical markers of bone anabolism and the increased ratios of OC and BAP to PYD were consistent with increases in BMD measured by dual-energy x-ray absorptiometry observed in the exercise groups. These three biochemical markers may help explain the alterations that occur in bone turnover as a result of disease, menopause, hormone replacement and other therapies as well as exercise training. In a multifactorial analysis of risk factors for decreased bone mineral density in inflammatory bowel disease, the biochemical marker DPD were consistently elevated indicating an increase in bone resorption (Bartram et al., 2006).

Self-Efficacy and Exercise

An active lifestyle is particularly important for older adults given the broad constellation of physiological, behavioral, cognitive, and biochemical outcomes that are influenced by physical activity. The majority of adults, however, do not exercise or participate in sports on a regular basis according to the National Health Interview Survey (NIH, 1991). There are a number of theoretical explanations that provide an understanding of why individuals choose to participate or not participate in health-related behaviors. Recently, self-efficacy has received

considerable support as a predictor of the initiation and maintenance of an exercise program for health and fitness. The construct of self-efficacy is derived from Bandura's social cognitive theory (1986). According to the theory, people are motivated to engage in a behavior based on the belief that: (a) the behavior will result in a favorable outcome (outcome expectation), and (b) the individual is capable of executing the behavior (efficacy expectation). A meta-analysis of studies of health-related behaviors revealed consistent support for the importance of self-efficacy as a determinant of healthy lifestyles, including regular exercise (Gillis, 1993). A considerable literature further suggests that participation in exercise training has a positive influence on self-efficacy. McAuley, Bane, and Mihalko (1995) examined the effects of both long-term exercise participation and acute bouts of exercise on the physical self-efficacy of middle-aged men and women. In addition to demonstrating the utility of physical mastery experiences in influencing efficacy, McAuley, Bane and Mihalko (1995) reported some interesting patterns with respect to gender responses. Whereas men and women demonstrated significant gains in perceived capabilities in response to both acute and long-term exercise, men initially were significantly more efficacious than women. We hypothesize that subjects in the exercise group will gain both the psychomotor skills and the self-efficacy to continue exercising as part of a healthy lifestyle.

Literature Review Summary

The literature has demonstrated that osteoporosis is a significant healthcare concern. Osteoporosis is associated with a high morbidity and mortality rate and is a risk factor for fractures. Due to the long-term use of corticosteroid drugs and other factors, patients with inflammatory bowel disease (IBD) are at increased risk of developing osteopenia and osteoporosis compared to the general population. There have been multiple interventions that have demonstrated an improvement in BMD. The literature review has demonstrated exercise as an effective non-pharmacological intervention for BMD.

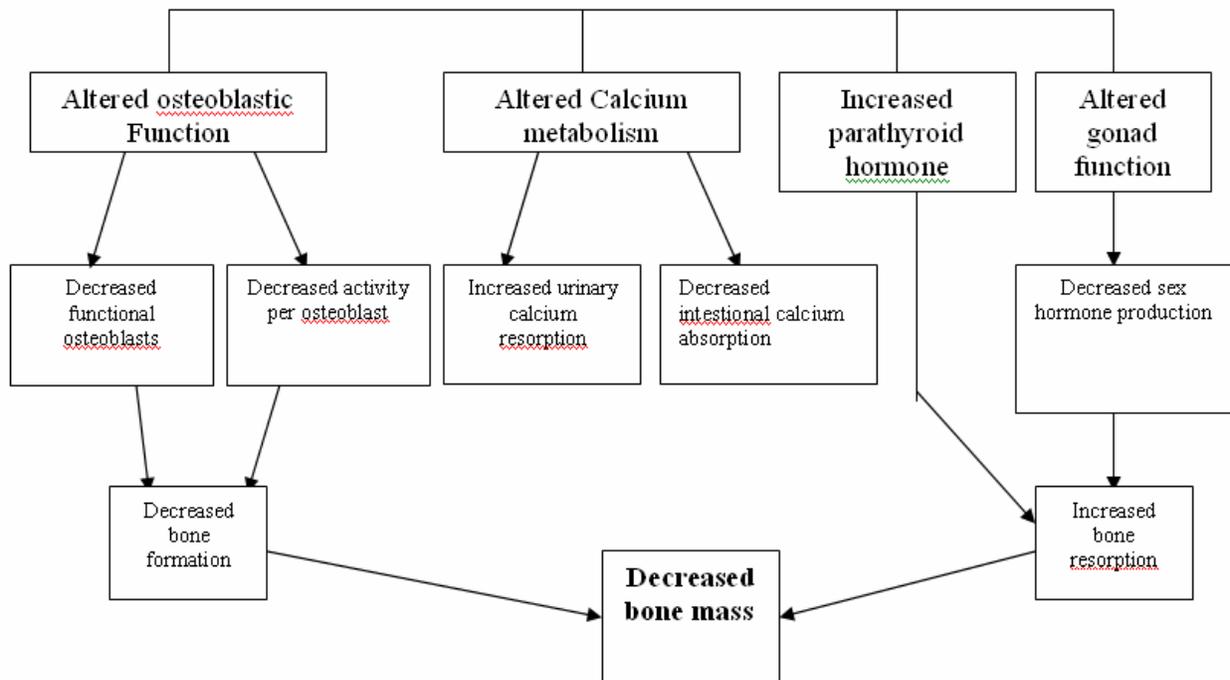


Figure 2-1. Corticosteroids and bone mineral density

CHAPTER 3 MATERIALS AND METHODS

Research Design

This study was a randomized parallel design to examine the effects of progressive load-bearing walking exercise in adults with IBD and a prior history of steroid usage but not within the last 12 months and who have chosen not to take osteoporosis medications. Following initial screening and testing procedures, subjects were randomly assigned to an exercise group or a sedentary control group. The principal investigator (PI) supervised the testing of all subjects and the initial exercise training session of subjects randomized to the exercise group. The co-investigator assisted with the testing and training. The control group did not participate in regular exercise during the study period. Sixteen adults, age 21 to 75 years, were recruited to participate in the study. Following baseline testing, subjects were randomly assigned to an exercise group (n=7), or to a sedentary control group (n=9). Subjects in the exercise group were issued a weighted vest, a pedometer/step counter, an exercise log-book, Calcium/Vitamin D log-book and instructed in their use. Training consisted of stretching and flexibility calisthenics and walking while wearing weighted vests. Subjects completed three, 50 minute exercise sessions/week for 32 weeks at home. Measurements for all subjects included: (1) dual-energy x-ray absorptiometry (DEXA) scans of the hip and lumbar spine, (2) biochemical markers of bone metabolism: serum bone specific alkaline phosphatase (BAP) and urinary deoxypridinoline (DPD), (3) Osteoporosis Self-Efficacy Scale (OSES) and (4) systolic blood pressure. All variables were measured at baseline and after 32 weeks. Statistical analyses compared changes in Systolic Blood Pressure, bone density of the femoral neck, hip and lumbar spine, serum levels of BAP and DPD and the ratios between the BAP and DPD, and scores on the OSES within and between the two groups.

This research project was approved by the University of Florida, Institutional Review Board and North Florida/South Georgia Veterans Health Care System Subcommittee for Investigation.

Sample and Setting

Eighteen men, aged 21 to 75 years, were recruited from the Gastroenterology clinics at the North Florida/South Georgia Veterans Health Care Center. Sample size calculations revealed that a sample size of 18 subjects (n=9 in each group) would give a statistical power of 0.80. However, due to recruitment difficulties that will be discussed later, the study was halted with a final sample size of 16 subjects, 9 in control and 7 in exercise groups. To estimate the effect size, the investigators assumed there would be no changes in variables in the control group, and a standard deviation for the changes from baseline scores in the experimental group. The standard deviation estimates are based on the results from previous studies conducted by the investigators and from the literature review (Jessup, Horne, Vishen, & Wheeler, 2003; Vincent & Braith, 2002).

Inclusion criteria. Subjects selected were adults with IBD, who were not currently taking hormones (e.g., testosterone), osteoporosis medications, or steroids, and have not done so for the prior 12 months. Subjects agreed to undergo two DEXA scans of their lumbar spine, femoral neck and dominant hip, to take 1200mg of calcium and 400 IU vitamin D daily, and to participate in either an exercise group or a non-exercise group for 32 weeks. In addition, all subjects selected were sedentary (i.e., not currently participating in regular exercises such as walking, jogging, cycling, dance aerobics, strength training, etc., and have not done so for the previous 12 months). There was no exclusion of subjects from the study based on race or ethnic origin. Subject attrition was minimized by weekly phone calls by the investigator to subjects in both groups. During these phone calls the investigator will answer questions and offer

encouragement to follow study protocols. Each subject was also paid a \$100.00 honorarium (prorated) for participating in the study.

Exclusion criteria. Subjects were excluded from the study if their medical history or physical examination demonstrates evidence of significant cardiovascular disease or other disorders that would prevent safe participation in the study. The following conditions were considered exclusionary:

Hospitalizations within the past 12 months for angina pectoris, myocardial infarction, coronary artery revascularization procedures (angioplasty and/or coronary artery bypass-graft surgery), or any other cardiac surgeries.

- Congestive heart failure, cardiac pacemakers, heart rate >100 or <50 at rest.
- Blood pressure (uncontrolled or controlled by medications): Resting systolic blood pressure >160 mmHg and/or resting diastolic blood pressure >100 mmHg.
- Dual-energy x-ray absorptiometry (DEXA) scan revealing bone mineral density of lumbar vertebra 2, 3, and 4 or femoral neck of the dominant hip greater than 3.5 standard deviations below that of a normal, healthy adult.
- Diabetes mellitus or other metabolic or endocrine disorders requiring hospitalization within the past 12 months.
- Neuromuscular or orthopedic limitations to normal, unassisted ambulation.
- Known or suspected sensitivity to calcium or vitamin D supplements.
- Any other medical, cognitive impairment, or psychiatric conditions, which, based on the clinical expertise of the investigators or the subject's personal health-care provider would make participation in the study not in the subject's best interest.

Random Assignment to Treatment Groups

Following the baseline screening and testing procedures, subjects were randomly assigned to either the exercise or control groups using a computerized random number generator. All subjects were asked to not change their usual daily eating habits during the study, and subjects assigned to the control group were asked to continue their usual activities of daily living but to

not begin an exercise program during the 32-week study period. To minimize individual variations in the dietary intake of calcium and vitamin D, subjects in both groups were asked to discontinue taking any over-the-counter calcium or vitamin D supplements or any multivitamin/mineral supplements containing calcium or vitamin D during the study period as it was provided by the study. Subjects in both groups were issued a 90-day supply (180 doses) of medication bottles containing 600-mg calcium citrate and 200 IU vitamin D as cholecalciferol. After contacting the subjects on their adherence to the medications the PI then refilled the subjects 90 day supply (180 doses) of medications. Subjects were instructed to take one capsule every morning and one capsule every evening at least 1 hour before or after eating a meal and record in a daily log book (total daily dose of 1200 mg calcium and 400 IU vitamin D). Subjects were instructed that if they should miss taking a scheduled capsule, to not "double-up" by taking 2 capsules, but rather to continue taking the capsules with the next scheduled dose. Subjects were also instructed to immediately notify the investigator(s) if they experience any type of adverse reaction that could be associated with the calcium or vitamin D such as nausea, vomiting, constipation, dry mouth, metallic taste, or skin rashes. Subjects were asked to bring their log usage of calcium/vitamin D and bring their medication bottles to the investigators at the Malcolm Randall Veteran's Medical Center, Gainesville Florida at the end of the study (Appendix E). They were also asked to notify the investigators if there are any changes in their health status or prescription medications during the study period.

Measures and Research Variables

Independent variable

The independent variables in this study is progressive load-bearing walking exercise. The exercise-training program described in this proposal combines ground-reaction and joint-reaction forces to repeatedly place moderate, progressive strain on the whole skeleton, but more

specifically on the spine, femoral neck and hip, of men with IBD. Subjects trained for 50 minutes a day, 3 days a week, for 32 weeks.

Dependent variables

The dependent or outcome variables measured in this study included bone density of the lumbar spine, hip and femoral neck of the dominant leg, Osteoporosis Self-Efficacy Scale, exercise measurements and biochemical variables.

Bone density of the lumbar spine (L-2, 3, and 4), hip and the femoral neck of the dominant leg measured by a Lunar Prodigy™ Bone Densitometer at the Nuclear Medicine Department, Malcolm Randall Veterans Medical Center, Gainesville, Florida. The Lunar instrument uses a technique known as dual-energy x-ray absorptiometry (DEXA) to perform non-invasive estimates of BMD in specific regions of the body (Lunar Prodigy™). DEXA utilizes a pencil-beam x-ray filtered to provide the two distinct energy peaks necessary to distinguish bone from soft tissue. Dual NaI scintillation crystals are used to separately detect the two x-ray energies. The technique for separating x-ray output into two distinct energy levels is known as K-edge filtration. In K-edge filtering, a rare earth element is placed in the beam path and x-rays are sharply attenuated at energy levels particular to that element. Lunar uses samarium as the filter material because it produces energy peaks at 46.8keV and 80keV, which have proven to be most effective at differentiating between soft tissue and bone tissue. The DEXA scans were conducted by a radiology technician especially trained to operate the Lunar DEXA equipment. The subjects were asked to lie on the table where padding and adjustable straps were placed to prevent movement. The scan took approximately 15 minutes for each subject. Once the scan was completed, the Lunar equipment produces a printout indicating the BMD in g/cm² and the BMD percentage compared with young healthy normal controls (the T score with standard deviations

above or below normal). The density in g/cm² and the T scores were used in the data analyses of this study. Subjects with bone mineral densities of the femoral neck or lumbar spine greater than 3.5 SD below young healthy normal controls were excluded from the study.

The osteoporosis self-efficacy scale (OSES)

The OSES instrument, developed and evaluated by Horan and colleagues (1998), is a self-administered instrument, worded at a sixth grade readability level that consists of 21 items in a visual analog format. The lower anchor of a 10-cm line is labeled “not at all confident” and the upper end is labeled “very confident”. The phrase “If it were recommended that you do any of the follow this week, how confident would you be that you could” is used as the stem for the items. Items include such statements as “begin a new or different exercise program”, “exercise for the appropriate length of time”, and “do exercises even if they are tiring”. Subjects were asked to indicate the degree of confidence they feel in their ability to do the activity by placing an X on the line that is calibrated from 0 to 100mm, on each of the 21 items. Horan and colleagues evaluated the criterion-related validity of the OSES by comparing responses on the instrument from 201 women, ages 35 to 95, with responses on the Atherosclerosis Risk in Communities (ARIC)/Baecke Habitual Physical Activity (ABHPAQ; Baecke, Burema, & Frijters, 1982) instrument. The ABHPAQ measures self-efficacy on a sport/leisure scale and on a general exercise scale. Controlling for biographic (age, height, and weight) variables and experiential (years of education, friends, family, or both with osteoporosis) variables, the OSES had a correlation of 0.52 ($p < 0.01$) with the sport/leisure scores and a correlation of 0.65 ($p < 0.01$) with the general exercise scores of the ABHPAQ instrument. The internal consistency estimates of the OSES were also strong (0.94) (Horan, Kim, Gendler, Froman, & Patel, 1998).

Exercise measurements

A pedometer was used to measure the time, distance and adherence to the exercise protocol. Each subject was provided a pedometer/step counter (Fitness Pedometer 360™, Sportline Inc., Campbell, CA) and instructed in its use. The pedometer will record up to 100,000 steps. The pedometer also measured time the subject has walked. After their walks, subjects were asked to log the time, mileage, and steps in a logbook provided.

Biochemical variables

Non-fasting blood and urine samples were collected from each subject at baseline and at 32 weeks. Bone-specific alkaline phosphatase (BAP) was measured in serum using an Alkphase-B® enzymatic immunoassay kit (EIA) (Metra Biosystems, Mountain View, CA). The assay is highly specific for BAP, cross-reacting $\leq 8\%$ with liver alkaline phosphatase and not significantly with other alkaline phosphatase isoenzymes. Urinary deoxypyridinoline (DPD) was measured from Quest Diagnostics Nichols Institute utilizing luminescent immunoassay. To explore the possible influence of load-bearing exercise on the state of bone metabolism, ratios of BAP (anabolic indicator) to DPD (catabolic indicator) were calculated.

Procedures

A timeline for individual subjects can be found in Appendix D Table 2. Below is a description of Visit 1 Part a, Visit 1 Part b, and Visit 2.

Visit 1 Part a. Potential subjects were invited to an orientation session at the Malcolm Randall Veteran's Medical Center, Gainesville Florida. The investigators explained the purposes, procedures, potential risks and benefits, and general conditions for the study. Questions were encouraged and time was allowed for subjects' inquiries prior to agreeing to participate in the study. Subjects who agreed to participate were asked to sign an informed

consent document and to complete demographic and health-history questionnaires. Subjects were then asked to complete the Osteoporosis Self-Efficacy Scale (OSES, Appendix C).

Visit 1 Part b. Subjects who have completed Visit 1(a) underwent a physical examination conducted by the PI, including resting heart rate and blood pressure measurements. Subjects who met the preliminary inclusion criteria were given an appointment to visit the Nuclear Medicine Department, Malcolm Randall Veterans Medical Center, Gainesville, Florida for DEXA scans of their spine, femoral neck and hip. Subjects were informed by telephone of the results of their DEXA scans and whether they met the inclusion criteria for the study. Subjects who met the inclusion criteria were scheduled to attend Visit 2. They were asked to wear comfortable, loose-fitting clothing and rubber soled walking shoes suitable for exercising when they attend Visit 2.

Visit 2. Blood drawing: Visit 2 was conducted at the Malcolm Randall Veteran's Medical Center, Gainesville Florida. The lab collected a 30-mL blood sample from each subject via venipuncture and obtained urine sample. During this visit, the subjects in the experimental group were instructed in proper stretching and warm up exercises prior to exercise. Subjects were instructed regarding proper footwear, clothing, and hydration for exercising. The control group was instructed to not engage in any new exercise programs.

Exercise Group Protocols

The investigators monitored all exercise training progress either by weekly telephone or email correspondence with each subject in the exercise group. All exercise training was conducted according to the guidelines published by the American College of Sports Medicine (ACSM, 2000). Subjects in the exercise group completed 32 weeks (three, 50 minute bouts/week) of walking at a normal pace while wearing weighted vests. Subjects were instructed regarding proper footwear, clothing, and hydration for exercising. Each exercise session will

begin with 10 minutes of stretching and warm-up calisthenics, and end with 10 minutes of cool down walking and stretching.

Load-bearing walking. Subjects were issued and fitted with an adjustable lightweight nylon vest (All Pro Weight Adjustable Exercise Vest™, Fit-1, Inc., Salisbury, Ma). The vest has foam cushioning for the shoulders, chest, and back, and has twenty pockets with Velcro™ closures on the front and back that will each accommodate a 0.48 kg (1 lb) weight. The pockets can accommodate a total of 18.2 kg (40 lbs). For the first week, the subjects walked wearing only the vest (without weights). Weights were added gradually for all subjects to increase load bearing up to max of 20 pounds of weight during weeks 9-12 (Appendix D Table 1: Load bearing walking schedule of progression). Each subject was provided a pedometer/step counter (Fitness Pedometer 360™, Sportline Inc., Campbell, CA) and instructed in its use. The pedometer will record up to 100,000 steps. The pedometer also measured time the subject has walked. After their walks, subjects were asked to log the time, mileage, and steps in a logbook provided. The PI either contacted by telephone or email each subject weekly to inquire about progress and to discuss any concerns or problems the subject may be experiencing. The exercise log-book information was collected every 7 days when the subjects were contacted by the investigator as described above.

End-point testing. End-point testing was conducted no longer than 5 days after the end of the training/control periods.

Visit 3. Visit 3 was conducted at the Malcolm Randall Veteran's Medical Center, Gainesville Florida at the end of the 32-week study period for the experimental and the control group. Repeat resting heart rate and blood pressure measurements were obtained. Urine sample and 30 mL of blood sample were collected in the laboratory at the Malcolm Randall Veteran's

Medical Center, Gainesville Florida. subjects were then be asked to complete the OSES instrument and DEXA scans of the lumbar spine, femoral neck and dominant hip were repeated exactly as in Visit 1, Part b.

Data Analysis

The data analysis for this study was conducted using the Statistical Package for the Social Sciences (SPSS) program, version 15.0 (SPSS Inc., Chicago, IL). Descriptive statistics were first obtained to provide summary measures for both exercise and control groups. Descriptive characteristics were compared between groups using analysis of variance (ANOVA). All statistical analyses were performed using the SPSS statistical software program. An alpha level of $p \leq 0.05$ was required for statistical significance.

As previously discussed, subjects were recruited from the North Florida/ South Georgia Veterans Healthcare System. Over 300 participants were initially assessed for the study, however only 18 actually began the program with 16 completing the study. The two participants did not complete the study, one control subject was not able to arrange travel for the post test evaluation and one experimental subject moved and was not able to make the trip for post test evaluation. Thus the data analysis was performed on the 9 participants who comprised the control group and 7 participants who comprised the treatment group.

Potential Health Risks

The risks associated with this study protocol include the risks associated with DEXA scans, venipuncture, exercise training, and the oral administration of calcium and vitamin D. There were no potential psychological, social, legal, or other risks to subjects participating in this project. Risks are discussed in the paragraphs below.

Dual-energy x-ray absorptiometry (DEXA) scans. The radiation exposure from a Lunar Prodigy™ bone density scan of the spine and hip ranges from 1–3 millirems (mREMs),

depending on the body size (thickness and density) of the individual subject. Compared with 70 mREMs from a typical two-view chest x-ray, or up to 100 mREMs from some dental x-rays, radiation exposure from the DEXA scan is minimal. In fact, the radiation dose is so low that no external shielding is required for either the subject or the technologist performing the test (Lunar Prodigy™, 2000). In this project, each subject had two DEXA scans approximately 8 months apart.

The risks of the exercise training, walking, was minimized in this project by the study design: (1) the rigid exclusion criteria eliminated subjects with unstable cardiovascular or other diseases, (2) all subjects underwent a physical examination prior to exercise testing, (3) the principal investigator, a registered nurse and an Advance Nurse Practitioner experienced in exercise testing and training of older adults, conducted all exercise tests, (4) subjects were instructed in proper stretching and warm-up techniques prior to testing, (5) subjects were instructed to stop and notify the investigator if they notice any type of pain or discomfort during the testing, and (6) following testing, subjects were instructed on proper stretching and “cool-down” calisthenics to minimize muscle/joint soreness. Walking for exercise is associated with very little cardiovascular risk. Only one fatal event has occurred over the past 15 years of exercise training at the Aerobics Activity Center in Dallas; an event rate of less than one in over one-million miles of walking and running (Pollock & Wilmore, 1995). A five-year follow-up study of the risks of strenuous exercise in 2,935 men women, 17 to 76 years of age, reported two fatal cardiovascular events in over 370,000 person-hours of exercise which represented over 1,600,000 miles of walking and running (Hagberg et al., 1989). The risks associated with training in this project also included the potential for minor musculoskeletal injuries from the weighted-vest walking exercises.

The risks of musculoskeletal injuries and falling during the weighted-vest walking were minimized in this project. Subjects were fitted with an adjustable lightweight nylon vest that has foam cushioning for the shoulders, chest, and back, and has ten pockets with Velcro™ closures on the front and back that will each accommodate a 0.48kg (1lb) weight. During the first week of training, subjects walked wearing the vest without weights; weight was added gradually to increase load bearing to 20% of the subject's body weight during the 40-week study period.

Nutritional supplementation with calcium and vitamin D: All subjects were supplied with and asked to take one capsule, twice per day containing 600 mg calcium citrate and 200 IU of vitamin D as cholecalciferol (total daily dose of 1200 mg calcium and 200 IU vitamin D per day). The RDA for adults of calcium is 1200 mg per day and for vitamin D is 400 IU per day (Dickinson, 2002). Adverse effects associated with oral calcium supplementation include constipation, nausea, vomiting and kidney stones. Adverse effects associated with vitamin D supplementation include nausea, vomiting, anorexia, dry mouth, metallic taste, and headache. To minimize risks to subjects in this project, subjects will be carefully advised to discontinue the study drugs and notify the investigators immediately if they experience any adverse effects or symptoms that could possibly be related to the calcium and vitamin D. During the initial screening period, subjects who reported having a history of intolerance, sensitivity, or any allergies to either calcium or vitamin D supplements were excluded from the study.

Venipuncture. There is minimal risk associated with the blood drawing techniques used in this study. Drawing blood from a vein causes discomfort, possible bruising, and is rarely associated with infection, and uncommonly, faintness. A certified phlebotomy staff member collected all blood in this study using proper sterile techniques to minimize these risks.

CHAPTER 4 ANALYSIS AND RESULTS

Descriptive Statistics

Participant demographics included in the analyses were the subjects age, IBD disease type, disease duration, bowel resection and education level. There was no significant difference in age, disease type or education level (Table 4-1). Participant baseline tests included in the analyses were body mass index, systolic blood pressure, diastolic blood pressure, heart rate, Osteoporosis Self-Efficacy Scale, lumbar spine bone mineral density, hip bone mineral density, femoral neck bone mineral density, bone alkaline phosphatase, and urinary deoxypridinoline. The systolic blood pressure, disease duration, and length of bowel resection were the only variables with a statistical significance between the groups at baseline (Table 4-1 and 4-2).

- Hypothesis 1: Thirty-two weeks of progressive load-bearing walking exercise by adults with IBD who are not taking osteoporosis medications will result in increased bone density of the lumbar spine, hip and femoral neck (measured by dual-energy X-ray absorptiometry) significantly greater than that of adults with IBD who do not exercise. There was no significant difference between the groups for lumbar spine bone mineral density (g/cm²) (F=1.493, p=0.241). There was a significant difference between the groups for hip bone mineral density (g/cm²) (F=6.403, p=0.023). There was a significant difference between the groups for the Femoral Neck bone mineral density (g/cm²) (F=13.279, p=0.002). Figure 4-1 demonstrates the pre-test and post-test bone density results.
- Hypothesis 2: Thirty-two weeks of progressive load-bearing walking exercise by adults with IBD who are not taking osteoporosis medications will result in increased serum levels of BAP and increased ratios between BAP and DPD significantly greater than that of adults with IBD who do not exercise. There was no significant difference between the groups for urine BAP (F=0.818, p=0.384). There was no significant difference between the groups for urine DPD (F=0.825, p=0.380).
- Hypothesis 3: Completion of a weeks exercise program by adults with IBD who are not taking osteoporosis medications will result in improved self confidence in managing their own care (measured by the Osteoporosis Self-Efficacy Scale) that are significantly higher than those of adults with IBD who do not participate in exercise training. There was no significant difference between the groups for Osteoporosis Self-Efficacy Scale scores (F=0.651, p=0.434).

- Hypothesis 4: Thirty-two weeks of progressive load-bearing walking exercise by adults with IBD will result in improved Systolic Blood Pressure. There was a no significant difference between the groups for systolic blood pressure (F=0.532, p=0.478).

Descriptive Variables

Descriptive analyses failed to demonstrate significance between the experimental and control group for body mass index (F=0.026, p=0.814), diastolic blood pressure (F=1.039, p=0.325), and heart rate (F=0.046, p=0.833). The Body Mass Index (BMI) did not show a significant difference between groups but met clinical significance for the exercise group. The BMI decreased for the exercise group. This decreased the BMI from >30 to <30 (Figure 4-3), resulting in a category change from obese to overweight. The reported compliance for calcium and vitamin D were similar in both groups. The exercise group reported 96% compliance, while the control group reported 95% compliance.

Table 4-1 Baseline data analysis: demographics

Variable	Total Sample (n=16)	Control Group (n=9)	Exercise Group (n=7)	F	P
Age (yrs)	54.7	58.2	49.6	4.167	ns
Education (yrs)	13.8	13.7	13.9	0.119	ns
Disease duration (yrs)	20	23.2	15.9	5.519	0.04
Crohns or Crohns Colitis	10	7	3	1.521	0.23
Ulcerative Colitis	6	2	4	1.640	0.22
Length of bowel resection (cm)	874.5	869.5	5	6.631	0.02

Table 4-2 Baseline data analysis: dependent variables

Variable	Total Sample (n=16)	Control Group (n=9)	Exercise Group (n=7)	F	P
Body mass index (kg/m ²)	30.04	29.11	30.67	0.39	ns
Systolic blood pressure (mmHg)	134.22	128.09	139.88	4.81	0.04
Diastolic blood pressure (mmHg)	79.11	79.51	78.63	0.04	ns
Heart rate (beats per minute)	76.11	77.62	74.25	0.96	ns
Osteoporosis self-efficacy scale (1-21)	15.04	13.41	16.24	0.65	ns
Lumbar spine bone mineral density (g/cm ²)	1.16	1.20	1.11	1.69	ns
Hip bone mineral density (g/cm ²)	0.98	1.05	0.88	2.11	ns
Femoral neck bone mineral density (g/cm ²)	0.93	0.98	0.92	0.05	ns
Bone alkaline phosphatase (IU/L)	26.41	25.22	27.75	0.14	ns
Urinary deoxypridinoline (nmol/mmol creatinine)	4.29	5.16	3.31	2.14	ns

ns: non significant

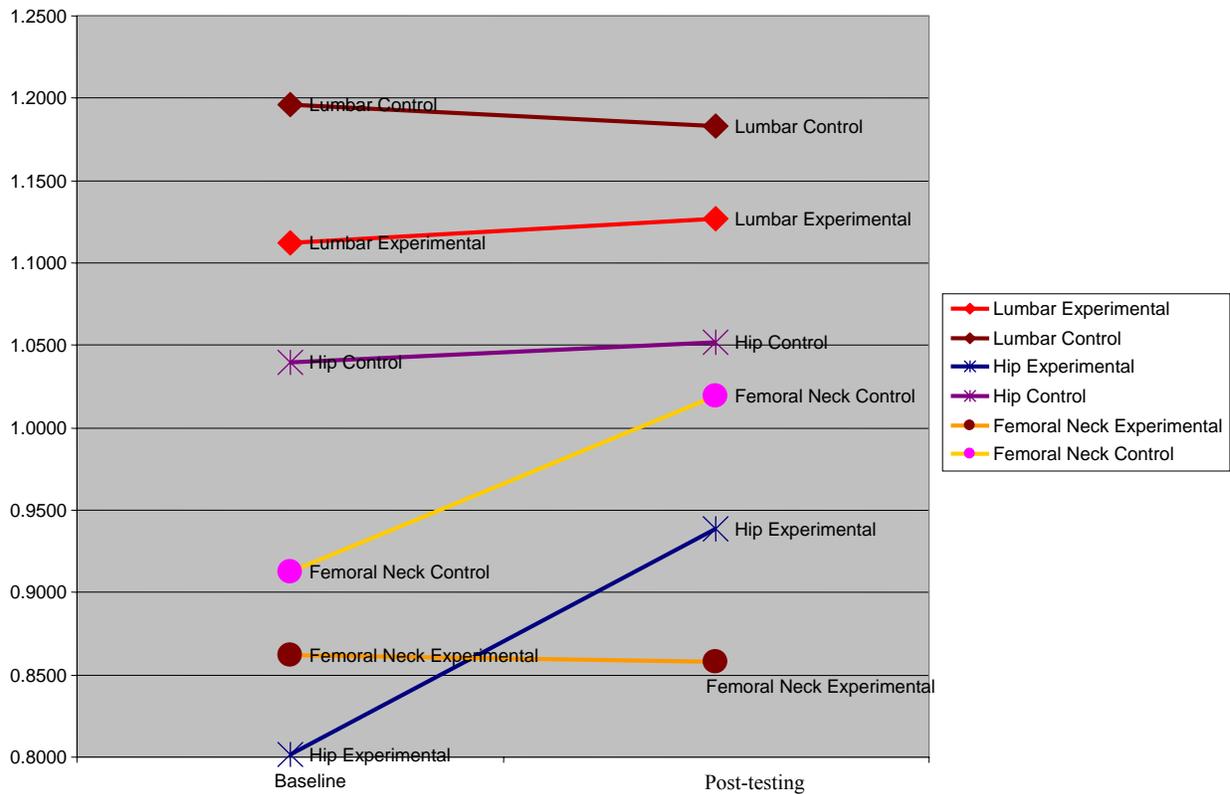


Figure 4-1. Pre and post DEXA scan results

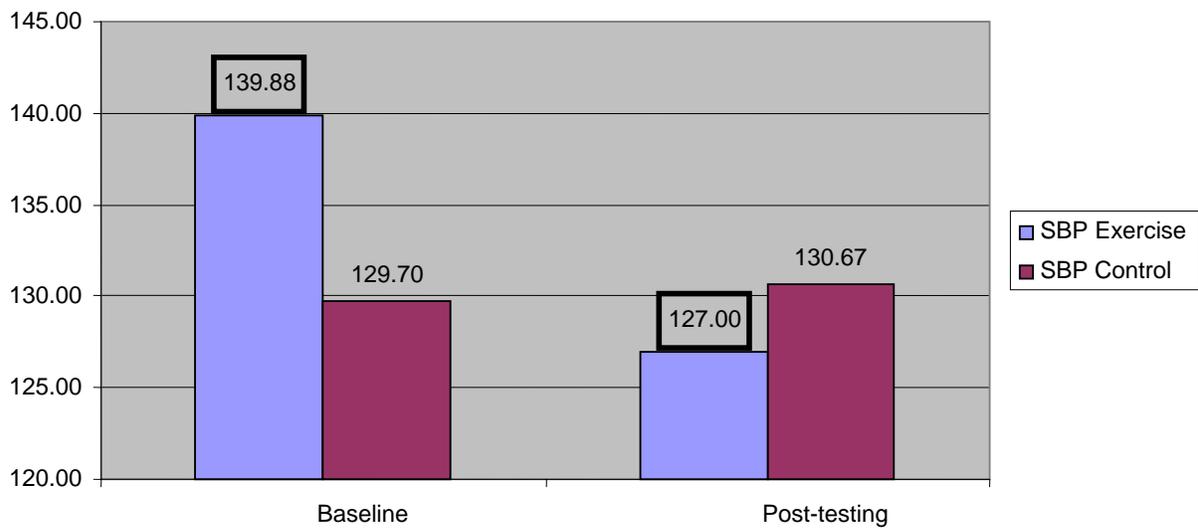


Figure 4-2. Effects of exercise on systolic blood pressure

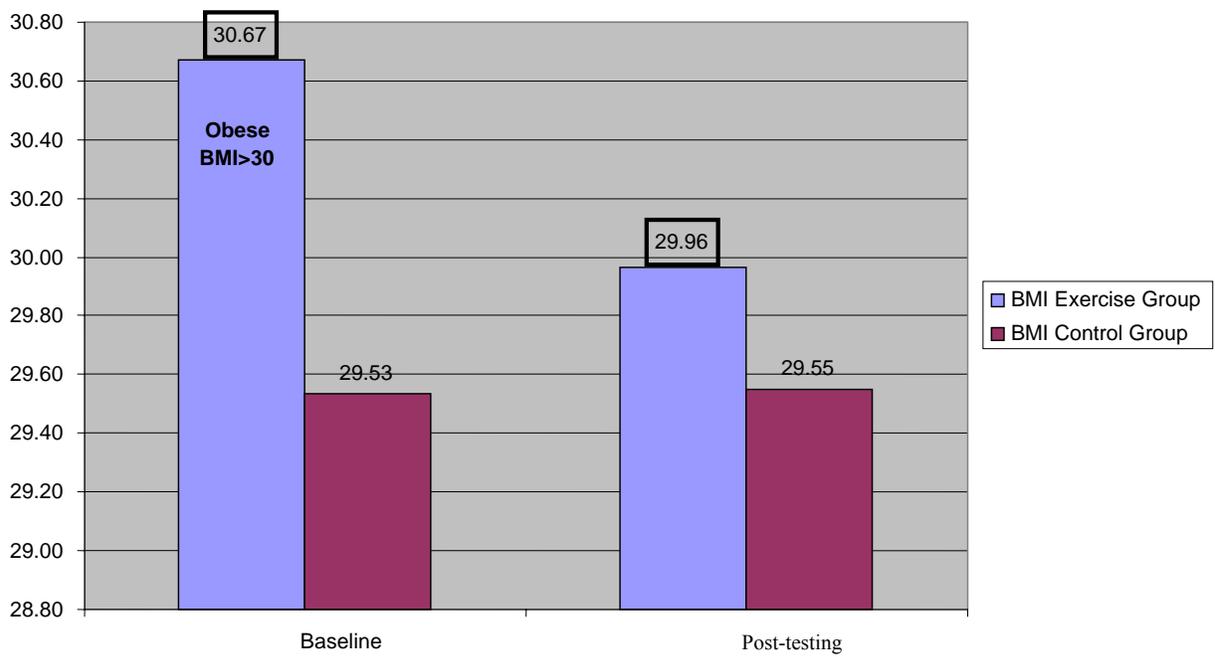


Figure 4-3. Effects of exercise on body mass index (BMI)

CHAPTER 5 DISCUSSION

Individuals with IBD have a up to 40% greater chance of having an osteoporosis-related fracture in their lifetime than the general population (Frei et al., 2006). Studies have demonstrated low bone mineral density in up to 75% for individuals with IBD. The pathogenesis of bone loss in IBD is multifactorial, consisting of general risk factors for osteoporosis and disease-specific factors. Studies are lacking for interventions, especially non-pharmacological, on improving bone mineral density in IBD. Therefore, this study looked at a non-pharmacological intervention to improve bone mineral density.

Discussion of Findings

The ANOVA statistics demonstrated systolic blood pressure had a statistical significance between the groups at baseline ($F=4.813$, $p=0.04$) with the exercise group having pre-hypertension. There is no obvious medical rationale to explain the difference in systolic blood pressure at baseline. The disease duration and length of small bowel removed had a statistical significance between the two groups. There were additional variables did reach clinical significance. The results along with some observations are further discussed in this chapter.

Hypotheses

- Hypothesis 1: Thirty-two weeks of progressive load-bearing walking exercise by adults with IBD who are not taking osteoporosis medications will result in increased bone density of the lumbar spine, hip and femoral neck (measured by dual-energy X-ray absorptiometry) significantly greater than that of adults with IBD who do not exercise. The hip measurement consists of 3 regions, (1) femoral neck, (2) trochanteric, and (3) intertrochanteric. This hypothesis had mixed results for bone density changes. Two of the 3 regions measured a difference in bone mineral density. There was a significant difference between groups in bone density for the hip and femoral neck, but the results for the femoral neck demonstrated a significant difference in the control group. The hip results demonstrated a significant difference in the exercise group. Although the lumbar spine experimental group increased over time while the control group decreased. The results of the femoral neck may be explained by several mechanisms; lack of sufficient weight vest, lack of time and distance walked and lack of further resistance training as demonstrated in previous studies. The hypothesis was not supported by the results of the study.

- Hypothesis 2: Thirty-two weeks of progressive load-bearing walking exercise by adults with IBD who are not taking osteoporosis medications will result in increased serum levels of BAP and increased ratios between BAP and DPD significantly greater than that of adults with IBD who do not exercise. There was no significant difference between groups for serum BAP and urine DPD. This hypothesis was not supported by the results of the study. This is possibly due to the low observed power leading to a Type II error.
- Hypothesis 3: Completion of a weeks exercise program by adults with IBD who are not taking osteoporosis medications will result in improved self confidence in managing their own care (measured by the Osteoporosis Self-Efficacy Scale) that are significantly higher than those of adults with IBD who do not participate in exercise training. There was no significant difference between groups for Osteoporosis Self-Efficacy Scale. This hypothesis was not supported by the results of the study. This is possibly due to the low observed power leading to a Type II error. In addition, this tool was designed and tested mainly on females while the study group was all males.
- Hypothesis 4: Thirty-two weeks of progressive load-bearing walking exercise by adults with IBD will result in improved systolic blood pressure (SBP). There was no significant difference between groups for SBP. This hypothesis was not support by the results of the study. Although a significant difference between groups was not met, the exercise group had a clinically significant change in systolic blood pressure. The 12.88 mmHg decrease in systolic blood pressure for the exercise group decreased the mean from pre-hypertensive to normotensive, while the control group had no change in baseline SBP. There was no addition medications started during the study that would contribute to the change in SBP. Also, the change in SBP is expected and consistent with a physiological change to exercise.

Descriptive Variables

The subjects baseline variables related to the disease state of IBD demonstrated significant difference in disease duration and length of bowel removed between experimental and control groups. The disease duration and length of bowel removed was significantly greater in the control group. These findings would suggest that the control group would have a increased factors for decreased BMD. These findings do not contribute to the results at post testing. There was no significant difference between groups for type of IBD (Crohn's disease or UC). The Body Mass Index (BMI) did not show a significant difference between groups but met clinical significance for the exercise group. The BMI decreased for the exercise group. This decreased the BMI from >30 to <30 (Figure 4-3), resulting in a category change from obese to overweight.

Increased BMI levels lead the other comorbidities such diabetes, renal disease, stroke and coronary artery disease. The reported compliance for calcium and vitamin D were similar in both groups. This similar intake of supplementary calcium and vitamin D would account for dietary differences between groups. The exercise group reported 96% compliance, while the control group reported 95% compliance. An observation was noted in the exercise group related to frequency of contact. During the study, two methods of contact were utilized to follow the exercise group, email and telephone. It was noted for subjects that contact took several attempts (n=4) and required them to call back, the average miles walked was markedly lower than group who had more frequent contact. The average weekly miles walked was 1.84. Among those four, three utilized email and excel spreadsheets I provided them, and one was able to set a time each week to call. The average miles walked was 6.27.

Limitations of Study

All studies have some degree of limitations. One limitation of this study included the marked distance subjects lived from the study site. Another limitation of this study included the home based protocol for exercise which does not allow for monitoring exercise participation. There is a limitation with home based self reported exercise programs, but with weekly calls or emails for log reports and measurement devices that record steps, subjects are more likely to continue the program protocol. The next limitation involved recruitment of subjects. The study was designed to minimize subjects to two trips to the Medical Center, many subjects did not want to make the extra trips due to time and gas prices. The PI tried to coordinate matching the study visits to other appointments at the medical center but still only had minimal effect with recruitment. Over 300 subjects were screened for the study with only 18 recruited and 16 completing the study. This leads to the limitation of small sample sizes. Given the small sample size, power was increased to minimize the chance of type II error. Even though there was a short

duration of treatment to the exercise group, exercise has been proven to cause changes in BMD in as little as 24 weeks. The short duration was also utilized due to difficulty maintaining enrollment to an extended exercise protocol.

Statistical Analysis Limitations

As discussed previously, power analysis for this study, based on the number of variables under consideration, recommended a sample of 9 experimental and 9 controls. The final was 9 controls and 7 experimental. It is possible that the significance in this study was not reached due to inadequate sample size. Type II errors occur when study findings fail to reject a false null hypothesis. Type II errors generally occur from not having enough subjects in the sample size to sufficiently test the hypothesis.

Strengths of Study

One of the strengths of this study included the consistency between groups with baseline characteristics. Although one of the limitations was a home based program, the protocol outlined weekly contact with the subjects who were exercising. This provided continue feedback and support to comply with the exercise protocol.

Conclusions

The demographics did not demonstrate a statistical significance for IBD disease type. The disease duration and length of bowel resection was statistically significant in the control group. These are risk factors related to decrease BMD and absorption of nutrients for bone maintenance. These was not clearly demonstrated in this study. The study demonstrated statistical significance for increase in femoral neck bone density but was in the control group. Also there was a significant increase in hip bone for the exercise group, which consists of 3 regions, (1) femoral neck, (2) trochanteric, and (3) intertrochanteric. The lumbar spine bone mineral density result were not statistically significant but the results show a decrease in the controls while the exercise

group showed a increase suggesting a trend of exercise benefit. Two of the findings, systolic blood pressure and body mass index, did not reach statistical significance but reach clinical significance thus demonstrating benefits to exercise. The observation of the average miles walked demonstrated a difference within the exercise group. Although there was an increased average miles walked in the subjects with frequent contact, the total average miles walked were possibly to low make an increase in BMD in the study's time frame.

Recommendations for Future Research

Unfortunately this study demonstrated some conflicting results for changes in bone mineral density. But, the bone mineral density increase suggests possible benefit from the exercise intervention. The clinical significance demonstrated with systolic blood pressure and body mass index are consistent with a physiological change related to exercise. The significance of low bone mineral density in IBD and the literature that supports exercise as an intervention for the improvement on bone mineral density support further study. Any future studies should focus on an adequate sample size, increase mechanical stress on the sites measure for BMD and increase frequency of contact during the study.

Implications for Clinical Practice

This study demonstrated a clinically significant improvement in systolic blood pressure and body mass index. This supports the importance of physical activity on multiple health factors. Additionally, support and frequent contact appear to increase exercise compliance for subject

APPENDIX B
MEDICAL HISTORY QUESTIONNAIRE

(All information will be kept confidential)

Please read the following health history questionnaire carefully and mark the most appropriate answer to each question. If you are unsure about a question, just circle it and go on to the next question.

General health history

Yes No

- 1. Has a doctor ever told you that you have heart disease?
- 2. Have you ever had a heart attack?
- 3. Has a doctor ever told you that you have high cholesterol?
- 4. Have you had heart surgery?
- 5. Do you have a cardiac pacemaker?
- 6. Do you have high blood pressure?
- 7. Have you ever had a stroke?
- 8. Do you have diabetes?
- 9. Do you take insulin for diabetes?
- 10. Have you had carotid artery surgery or an endarterectomy?
- 11. Do you have a heart valve problem?
- 12. Has a doctor ever told you that you have an aneurysm?
- 13. Have you ever had heart failure?
- 14. Has a doctor ever told you that you have an abnormal EKG?

Have you ever had, or do you now have, any of the following conditions?

Yes No

- 15. Rheumatic fever
- 16. Asthma
- 17. Chronic bronchitis
- 18. Emphysema
- 19. Varicose veins
- 20. Phlebitis
- 21. Arthritis
- 22. Rheumatism
- 23. Gout
- 24. Gastrointestinal problems
- 25. Epilepsy, or seizures
- 26. Dizziness or fainting spells
- 27. Loss of memory
- 28. Anemia

continued on next page

- 29. Chronic back pain
- 30. Kidney or bladder problems
- 31. Nervous systems problems
- 32. Visual or hearing problems
- 33. Hepatitis or other liver diseases
- 34. Gall bladder problems
- 35. Thyroid problems
- 36. Cancer or tumors
- 38. Do you sometimes lose urine when you cough, sneeze, or laugh?
- 39. Any other major illness or surgery? If yes, please explain:
- 40. Are you allergic to any medications? If yes, please list:
- 41. Are you now taking any prescription or non-prescription medications, including hormones, vitamins, and other supplements? If yes, please list:

Smoking

Yes No

- 42. Have you ever smoked? If no, skip to diet
- 43. Do you smoke now? If yes, how many cigarettes per day? ____. For how many years? ____.
- If no, when did you quit? _____.

Diet

- 44. What do you consider a good weight for yourself? ____ lbs.
- 45. What do you weigh now? ____ lbs.
- 46. What is the most you have ever weighed? ____ lbs.
- 47. Do you drink alcoholic beverages? ___yes ___no

Family health history

Have any of your blood relatives (your parents, brothers, sisters, uncles, aunts, cousins, or children) ever had:

Yes No

- 48. Heart attack
- 49. High blood pressure
- 50. Stroke
- 51. Diabetes
- 52. High cholesterol

Additional comments concerning your personal or family health history:

APPENDIX C
OSTEOPOROSIS SELF-EFFICACY SCALE*

Name: _____ Date: _____

Directions: Please read each of the following statements and indicate your feeling of confidence by marking an "X" on the line below the statement

"If it were recommended that you do any of the following this week, how confident would you be that you could?"

1. Begin a new or different exercise program

Not at all confident | _____ | Very confident

2. Change your exercise habits

Not at all confident | _____ | Very confident

3. Put forth the effort required to exercise

Not at all confident | _____ | Very confident

4. Do exercises even if they are difficult

Not at all confident | _____ | Very confident

5. Maintain a regular exercise program

Not at all confident | _____ | Very confident

6. Exercise for the appropriate length of time

Not at all confident | _____ | Very confident

7. Do exercises even if they are tiring

Not at all Confident | _____ | Very confident

8. Stick to your exercise program

Not at all confident _____ Very confident

9. Exercise at least three times a week

Not at all confident _____ Very confident

10. Do the type of exercises you are supposed to do

Not at all confident _____ Very confident

11. Begin to eat more calcium-rich foods

Not at all confident _____ Very confident

12. Increase your calcium intake

Not at all confident _____ Very confident

13. Consume adequate amounts of calcium-rich foods

Not at all confident _____ Very confident

14. Eat calcium-rich foods on a regular basis

Not at all confident _____ Very confident

15. Change your diet to include more calcium-rich foods

Not at all confident _____ Very confident

16. Eat calcium-rich foods as often as you are supposed to

Not at all confident _____ Very confident

17. Select appropriate foods to increase your calcium intake

Not at all confident _____ Very confident

18. Stick to a diet which gives an adequate amount of calcium

Not at all confident _____ Very confident

19. Obtain foods that give an adequate amount of calcium

Not at all confident _____ Very confident

20. Remember to eat calcium-rich foods

Not at all confident _____ Very confident

21. Take calcium supplements if you don't get enough calcium from your diet

Not at all confident _____ Very confident

* Horan, M.L., Kim, K.K., Gendler, P., Froman, R.D., & Patel, M.D. (1998). Development and evaluation of the Osteoporosis Self-Efficacy Scale. Research in Nursing and Health, 21, 395-403.

APPENDIX D
TIMELINE

Table D-1. Load bearing walking schedule of progression

Weeks	1	2-4	5-6	7-8	9-12	13-16	17-32
Walking duration (mins)	20	20	30	30	40	45	50
Vest weight % body wt	0	10	10	15	20	20	20

Table D-2. Timeline for individual subjects: Each subject will be required to participate in the study for approximately 45 weeks

Week 1	Visit 1 (a): Orientation, complete documents, sign informed consent, complete the OSES.
Week 2	Visit 1 (b): Physical exam, DEXA scan, Blood draw, Random assignment to exercise or control groups.
Week 3	Visit 2: Begin exercise training or control period, Issue calcium and vitamin D scripts
Week 35	Visit 3: DEXA scan, Blood draw, complete OSES, End of study

APPENDIX E
EXERCISE AND CALCIUM AND VITAMIN D SUPPLEMENTS LOG BOOKS

Exercise Log Book (subjects in exercise group only)

Front Cover

Exercise log book
Name _____
ID# _____

Please enter the date and time of your exercise session. Total distance walked (in miles), total number of steps taken during the walk, and total calories burned. Also, any comments you would like to make about that day's exercise. Session.

Important telephone numbers:

Principal Investigator
Charles J Zeilman
office (352)376-1611 ext 6261
pager 1-877-739-0639

In case of an emergency
telephone 911

Pages

Date: _____ Time _____
Miles walked: _____.
Total steps: _____
Calories burned: _____

Comments _____

Date: _____ Time _____
Miles walked: _____.
Total steps: _____
Calories burned: _____

Comments _____

Log Book to be constructed of heavy, brightly colored paper and "check book" in size.

Calcium and vitamin D supplement log book
(for subjects in the exercise and control groups)

Front Cover

Pages

Calcium and Vitamin D
Supplements Log Book

Name: _____
ID#: _____

Please take 1 capsule in the morning and 1 capsule in the evening. Take capsules 1 hour before or after meals

Please check the box after you have taken your calcium and vitamin supplements

Important telephone numbers:

Principal Investigator
Charles J. Zeilman
office (352)376-1611 ext 6261
pager 1-877-730-0639

In case of an emergency
telephone 911

	morning	evening
Date: _____	<input type="checkbox"/>	<input type="checkbox"/>
_____	<input type="checkbox"/>	<input type="checkbox"/>
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LIST OF REFERENCES

- American College of Sports Medicine. (2000). *ACSM's Guidelines for exercise testing and prescription* (6th ed.). Baltimore: Williams and Wilkins.
- Baecke, J. A. H., Burema, J., & Frijters, J. E. R. (1982). A short questionnaire for the measurement of habitual physical activity in epidemiological studies. *The American Journal of Clinical Nutrition*, *36*(5), 936-942.
- Bandura, A. (1986). *Social foundations of thought and action*. Englewood Cliffs: Prentice-Hall.
- Bassett, C. A. (1971). Biophysical principals affecting bone structure. In G.H. Bourne (Ed.), *The biochemistry and physiology of bone* (2nd ed.), p. 1, New York: Academic Press.
- Bernstein, C. N., Blanchard, J. F., Leslie, W., Wajda, A., & Yu, N. (2000). The Incidence of fracture among patients with inflammatory bowel disease: A population-based cohort study. *Annals of Internal Medicine*, *133*(10), 795-799.
- Black, D. M., Palermo, L., & Bauer, D. (2000). How well does bone mass predict long-term risk of hip fracture. *Osteoporosis International*, *11*(Suppl. 2), S121.
- Bloomfield, S., Williams, N., Lamb, D., & Jackson, R. (1993). Non-weight bearing exercise may increase lumbar spine bone mineral density in healthy postmenopausal women. *American Journal of Physical Medicine and Rehabilitation*, *72*, 204-209.
- Caplan, G. A., & Ward, J. A. (1993). The benefits of exercise in postmenopausal women. *Australian Journal of Public Health*, *17*, 23-26.
- Carter, D. R. (1984). Mechanical loading histories and cortical bone remodeling. *Calcification Tissue International*, *36*(Suppl. 1), S19-S24.
- Cooper, C. (2000). Global assessment of fracture risk. *Osteoporosis International*, *11* (suppl. 2), S44.
- Dickinson, A. (2002). Benefits of calcium and vitamin D: Building and maintaining healthy bones. Retrieved January 15, 2003, from http://www.crnusa.org/benpdfs/CRN003benefits_calciumandD.pdf
- Frei, P., Fried, M., Hungerbuhler, V., Rammert, C., Rousson, V., & Kullak-Ublick, G. A. (2006). Analysis of risk factors for low bone mineral density in inflammatory bowel disease. *Digestion*, *73*, 40-46.
- Gillis, A. J. (1993). Determinants of a health-promoting lifestyle: An integrative review. *Journal of Advanced Nursing*, *18*(3), 345-353.

- Gray, K. (2000). Bone-forming agents: New therapies for osteoporosis. Paper presented at the *World Congress on Osteoporosis 2000*. Retrieved February 21, 2002, from <http://search.medscape.com/all-search?queryText=Bone-forming%20agents:%20New%20therapies%20for%20osteoporosis>
- Hagberg, J. M., Graves, J. E., Limacher, M., Woods, D. R., Leggett, S. H., & Cononie, C. (1989). Cardiovascular responses of 70- to 79-year old men and women to exercise training. *Journal of Applied Physiology*, 66(6), 2589-2594.
- Heaney, R. P. (2000). There should be a dietary guideline for calcium. *American Journal of Clinical Nutrition*, 71(3), 658-670.
- Hela, S., Nihel, M., Faten, L., Monia, F., Jalel, B., Azza, F., et al. (2005). Osteoporosis and Crohn's disease. *Joint Bone Spine*, 72(5), 403-407.
- Horan, M. L., Kim, K. K., Gendler, P., Froman, R. D., & Patel, M. D. (1998). Development and evaluation of the Osteoporosis Self-Efficacy Scale. *Research in Nursing and Health*, 21(5), 395-403.
- Huang, O., Lu, J., Zhou, Q., Liu, Y., & Wang, Q. (2000). Effect of calcium and vitamin D supplementation on bone loss in postmenopausal Chinese women: A comparative study. *Osteoporosis International*, 11(Suppl. 2), S183.
- Jessup, J., Horne, C., Vishen, R. K., & Wheeler, D. (2003). Effects of exercise on bone density, balance and self-efficacy in older women. *Biological Research for Nursing* 1(4), 171-181. .
- Kannus, P. (1999). Preventing osteoporosis, fall and fractures among elderly people. *British Medical Journal*, 318(7178), 205-206.
- Kelley, G. A. (1998). Aerobic exercise and bone density at the hip in postmenopausal women: A meta-analysis. *Preventive Medicine*, 27(6), 798-807.
- Kronhed, A. C. & Moller, M. (1998). Effects of physical exercise on bone mass, balance skill and aerobic capacity in women and men with low bone mineral density, after one year of training--a prospective study. *Scandinavian Journal of Medicine and Science in Sports*, 5(1), 290-298.
- Lane, N. E., & Lukert, B. (1998). The science and theory of glucocorticoid-induced bone loss. *Endocrinol Metabolism Clinics of North America*, 27(2), 465-483.
- Lanyon, L. E. (1981). Bone remodeling mechanical stress and osteoporosis. In H.F. DeLuca, H.M. Frost, & W.S.S. Jee (Eds.). *Osteoporosis: Recent advances in pathogenesis and treatment* (p. 129). Baltimore: University Park Press.
- Lau, E. M. C., Woo, J., Leung, P. C., Swaminathan, R., & Leung, D. (1992). The effects of calcium supplementation and exercise on bone density in elderly Chinese women. *Osteoporosis International*, 2(4), 168-173.

- Lawson, M. T. (2001). Evaluating and managing osteoporosis in men. *The Nurse Practitioner*, 26(5), 2649.
- Manolagas, S. C., Weinstein, R. S. (1999). New developments in the pathogenesis and treatment of steroid-induced osteoporosis. *Journal of Bone and Mineral Research*, 14(7),1061-1066.
- McAuley, E., Bane, S. M., & Mihalko, S. L. (1995). Exercise in middle-aged adults: Self-efficacy and self-presentational outcomes. *Preventive Medicine*, 24(4), 319-338.
- National Institutes of Health. (1991). Osteoporosis research education and health promotion. (NIH Publication No. 91-3216). Bethesda, MD: Author.
- National Osteoporosis Foundation. (1997). *Stand up to osteoporosis: Your guide to staying healthy and independent through prevention and treatment*. Washington, D.C.: Author.
- O'Shea, B., Rosen, C. J., Guyatt, G., Cranney, A., Tugwell, P., & Black, D. (2000). A meta-analysis of calcium supplementation for the prevention of postmenopausal osteoporosis. *Osteoporosis International* 2000, 11(suppl. 2), S114.
- Pollak, R. D., Karmeli, F., Eliakim, R., Ackerman, Z., Tabb, K., & Rachmilewitz, D. (1998). Femoral neck osteopenia in patients with inflammatory bowel disease. *The American Journal of Gastroenterology*, 93(9), 1483-1490.
- Pollock, M.L. & Wilmore, J.H. (1995). *Exercise in health and disease: Evaluation and prescription for prevention and rehabilitation*. Philadelphia: W.B. Saunders.
- Reid, I. R, Heap, S. W. (1990). Determinants of vertebral mineral density in patients receiving long-term glucocorticoid therapy. *Archives of Internal Medicine*, 150(12), 2545-2548.
- Riggs, B. L. & Melton, L. J. (1995). The worldwide problem of osteoporosis: Insights afforded by epidemiology. *Bone*, 17(5), Supplement 1 505S-511S.
- Sakellariou, G. T., Moschos, J., Berberidis, C., Mpoumponaris, A., Kadis, S., Molyvas, E., et al. (2006). Bone density in young males with recently diagnosed inflammatory bowel disease. *Joint, Bone, Spine*, 73(6), 725-728.
- Shaw, J. M. & Snow, C. M. (1998). Weighted vest exercise improves indices of fall risk in older women. *Journal of Gerontology* 53A(1), M53-M58.
- Sheth, P. (1999). Osteoporosis and exercise: A review. *The Mount Sinai Journal of Medicine*, 66(3), 197-200.
- Smith, E. L. (1988). Bone concerns, in M.M. Shangold (Ed.) *Women and Exercise: Physiology and Sports Medicine* (pp. 79-87). Philadelphia: F.A. Davis.
- Southerland, J. C., & Valentine, J. F. (2001). Osteopenia and osteoporosis in gastrointestinal diseases: Diagnosis and treatment. *Current Gastroenterology Reports*, 3, 399-407.

Tonino, R. P., Meunier, P. J., & Emkey, R. D. (2000). Long-term efficacy and safety of alendronate in the treatment of osteoporosis in postmenopausal women. *Osteoporosis International*, *11*(supplement 2), S202.

Valentine, J. F. & Sninsky, C. A. (1999). Prevention and Treatment of Osteoporosis in Patients with Inflammatory Bowel Disease. *The American Journal of Gastroenterology*, *94*(4), 878-883.

Vincent, K. R. & Braith, R. W. (2002). Resistance exercise and bone turnover in elderly men and women. *Medicine and Science in Sports and Exercise*, *34*(1), 17-23.

BIOGRAPHICAL SKETCH

Charles Joseph Zeilman, III received his bachelor of science in nursing degree from the University of Florida in 1995. He began his career as a staff nurse in the general surgery and cardiac surgery unit at Shands Teaching Hospital in Gainesville, FL.

In 1998, Mr. Zeilman earned his master's degree in adult health from the University of Florida. After receiving his degree, he took a Advance Registered Nurse Practitioner position in the gastroenterology section at the North Florida/South Georgia Veteran's Healthcare System.

Mr. Zeilman is the 2006 recipient for the "Excellence in Nursing" annual award for Advance Registered Nurse Practitioner. He has several publications during his work as an ARNP. He is an affiliate faculty member for the College of Pharmacy at the University of Florida. He has served on the Dean's Advisory Committee , College of Nursing at University of Florida. He also is a guest lecturer for the College of Nursing at University of Florida.