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UMI
A CROSS-SECTIONAL STUDY OF THE EFFICACY OF A SUPERVISED EXERCISE PROGRAM IN THE PREVENTION AND TREATMENT OF OSTEOPOROSIS

By

Mike Bruce Walker

A thesis in conformity with the requirements for the degree of Master of Science
Graduate Department of Community Health
University of Toronto

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ABSTRACT

A Cross-Sectional Study of the Efficacy of a Supervised Exercise Program in the Prevention and Treatment of Osteoporosis
Master of Science 1998, Mike Bruce Walker, Graduate Department of Community Health, University of Toronto

The Prevention and Rehabilitation of Osteoporosis Program (PRO) was introduced at The Rehabilitation Institute of Toronto (RIT) in 1983. The present study consisted of an evaluation of the RIT program based on a 5-year follow-up of 89 patients that were enrolled in the program. Potential differences in clinical outcomes were examined in a group of patients who attended a supervised (n=42) program compared to a group who chose to exercise on their own (n=49).

Both groups were similar at study entry, in BMD measurements of the lumbar spine and femoral neck (Hosp. 73.6 ± 11.8, 74.0 ± 12, Home 74.7 ± 10.4, 74.0 ± 8.4). Both groups were able to stabilize BMD in the lumbar spine and femoral neck over the course of the five-year follow-up. Both groups had a reduction in the incidence of fracture.

This study adds weight to the call for post-menopausal women to engage in exercise.
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A Cross-Sectional Study of the Efficacy of a Supervised Exercise Program in the Prevention and Treatment of Osteoporosis

INTRODUCTION

Osteoporosis is a condition that affects 1 in 4 women over the age of 50, and the number of women living beyond this age will increase in the next several decades. While the effect of exercise on osteoporosis has received increased attention in the last few decades, it has only recently become axiomatic that physical activity benefits the skeleton. Based on recent research, structured physical activity has considerable appeal as a primary, secondary, and tertiary prevention strategy. In principle, a number of structured exercise programs have been shown to be beneficial in the prevention and management of osteoporosis (1). There remain, however, many unanswered questions regarding the specificity, intensity, and duration of the exercise, which might be optimal for the prevention of bone loss.

Claims in the lay press that exercise, independent of other factors, can prevent osteoporosis are, at present, unfounded. The value of exercise, in and of itself, in preventing and treating osteoporosis remains unclear and controversial (2). The response of bone to exercise has many confounding variables, including nutrition, hormonal status, age, activity history, as well as the specific training protocol and initial bone density (3).

Any examination of the effect of exercise on osteoporosis must include an evaluation of many direct and indirect influences. Most researchers have found it difficult to demonstrate that the human skeleton engaging in exercise training programs experience significant increases in bone
mineral density (BMD).

It is not known what minimum threshold of physical activity is required to positively affect bone mass, and no data exists regarding suggested weekly caloric expenditure levels for the maintenance of bone density.

The pain, fear of fractures, inactivity, and loneliness associated with the condition often contribute to depression, and in turn, a reduced amount of physical activity. This inactivity will cause further bone loss and bone fragility, increasing the risk of future fracture. In an attempt to minimize this sequelae, a program for the prevention and rehabilitation of osteoporosis (PRO) was introduced at The Queen Elizabeth Hospital in 1983. The objective of the program was to develop an exercise program that improved fitness, was acceptable to patients, and that did not increase the risk of fracture. In 1997, the Queen Elizabeth Hospital was renamed the Rehabilitation Institute of Toronto (RIT). Currently, there are approximately 800 participants enrolled in the RIT Osteoporosis program. The present study will consist of an evaluation of the RIT program based on a five year follow-up of one hundred patients who have been enrolled in the program for a minimum duration of five years. As part of this evaluation, potential differences in clinical outcomes, including 1) bone density measurements, 2) incidence of fracture, and 3) loss of height, will be examined in a group of patients who attend a supervised exercise program and compared to group who chose to exercise on their own.
Review of the Literature

I. OSTEOPOROSIS

The World Health Organization (WHO) has defined osteoporosis as a bone density measurement (T score) of more than 2.5 standard deviations below the mean for young adults (4). Clinicians consider a bone to be osteoporotic if it has a sufficiently decreased density that it would be susceptible to fracture, or if the bone has already experienced a spontaneous fracture (5). As many as 2.5 million Canadians and 25 million Americans have sufficiently low bone mass to be at high risk for fracture (6). This reduction in BMD compromises the integrity of bone microstructure, enhances fragility, and increases the risk of fracture (6). Failure to reach an adequate bone mass by the fourth decade of life and/or an imbalance in the coupled process of bone formation and resorption are predisposing factors to osteoporosis (7). Starting around the fourth or fifth decade of life, both women and men lose bone at a rate of 0.3 to 0.5 percent per year. After menopause, the rate of bone loss increases as much as 10-fold (8).

II. PATHOPHYSIOLOGY

II.A. BONE TURNOVER AND OSTEOPOROSIS

The skeleton is composed of cortical and cancellous (trabecular) bone. Cortical bone is located in the diaphyses of long bones and provides structural support (11). Trabecular bone is located in the flat bones, vertebrae, and metaphyses of long bone (11). Although trabecular bone comprises only 20% of the skeleton, it has a high surface to volume ratio (12). Due to this, osteoporosis commonly affects trabecular sites early and floridly in the disease process.

Many factors, both systemic and local, influence bone metabolism and its remodelling
processes. Changes in skeletal metabolism and architecture largely determine the manner in which osteoporosis develops. Bone is constantly being remodelled in localized areas called bone remodelling units. Bone remodelling is a physiologic process occurring at the endosteal surface, located at the interface with bone marrow and Haversian canals in cortical bone (6). The sequence of bone remodelling lasts approximately 200 days (6). There is clinical and histologic evidence indicating that osteoporosis results from alterations in bone remodelling such that bone resorption is excessive and/or bone formation is inhibited (9). Postmenopausal bone loss is associated with excessive osteoclast activity leading to increased bone resorption. In contrast to postmenopausal (type 1) osteoporosis, the bone loss that accompanies aging (type 2 osteoporosis) is associated with a progressive decline in the supply of osteoblasts in proportion to the demand for them (10). Also, type 2 osteoporosis results in bone loss occurring primarily in cortical bone, whereas postmenopausal bone loss occurs primarily in trabecular bone.

Activation of bone remodelling units, as well as the resorption and formation phases, are controlled by a number of interrelated mechanical, hormonal, nutritional and genetic factors. As with all biological process, bone remodeling is not 100% efficient, and resorbed bone is not completely replaced as people age. Therefore, minimizing the rate of bone turnover through dietary, hormonal and exercise interventions offers a strategy for maintaining skeletal integrity.

II.B. The Cells Responsible For Skeletal Remodelling

The metabolic activities of the skeleton are responsible for the growth, shaping or sculpting, repair of microdamage, and repair of fracture. All bone-forming cells originate
from the marrow stromal cell lineage and are called osteoblasts (13). Osteoclasts, which are bone resorption cells, originate from the mononuclear line of hematopoietic stem cells (13). Lining cells remain on trabecular surfaces after bone formation has stopped at a bone-forming site. Their function is unclear; however, on exposure to parathyroid hormone (PTH) they secrete an acid collagenase which seems to prepare the bone surface for resorption by osteoclasts (14). Although the precise role of osteocytes requires further work, it is known that their location is ideal for sensing strain resulting from mechanical force (15). Therefore, osteocytes may play a role in initiating the adaptive response to mechanical usage.

New insights into bone pathophysiology have emphasized the role of osteoblasts in the regulation of bone formation (16). This includes the synthesis of type 1 collagen, the expression of alkaline phosphatase, the secretion of osteocalcin, and the production of mineralized matrix (17). Many growth factors and hormones, including Vitamin D, PTH, and growth hormone influence bone formation by direct action on osteoblasts. Osteoblasts control the bone resorption process at the level of proliferation, differentiation, and recruitment of osteoclast progenitors (18).

II.C. Aspects of Bone Quality in Osteoporosis

The various types of qualitative abnormality that have been described in osteoporosis are listed in Table 1.

**Table 1 Aspects of bone quality in osteoporosis**

1. Undermineralized matrix
2. Trabecular thinning, perforation, and disruption
3. Cortical porosity
4. Cement line accumulation
5. Fatigue accumulation
1. **Undermineralized matrix**: mineralization, which contributes to bone structural strength, is diminished in the aging skeleton.

2. **Trabecular thinning, perforation, and disruption**: loss of trabecular connectivity contributes significantly to skeletal fragility in osteoporosis. In particular, a loss of horizontal trabeculae decreases strength, as a single horizontal connecting element may confer a 4-fold increase in load bearing capacity (13). Approximately 20% of the skeleton is trabecular bone; however, in certain areas, there is a higher proportion of trabecular bone, for example, the vertebral bodies are approximately 42% trabecular bone (19). Reduced trabecular bone, as analyzed histomorphometrically, is a major factor related to skeletal fragility (20).

3. **Increased cortical porosity**: cortical bone, which occupies 80% of the skeleton, encases both the marrow and the latticework of trabecular bone (21). Haversian canals, osteocyte lacunae, and cutting cones represent holes within the bony cortex that have been produced by an increased bone resorption relative to bone formation (13). Cortical porosity in aging reflects an expansion of the remodeling space resulting from an increased remodeling activation rate (21). Remodeling is activated in situations of disuse, microdamage, estrogen withdrawal, dietary calcium restriction, and excess PTH and vitamin D hormone (22). Likewise, remodeling is suppressed by stimuli opposite to these. The pattern of bone loss in osteoporosis consists of the enlargement of the medullary canal, and results in the enlargement of the endocortical surface (23). The net effect of remodeling in this zone is bone loss.

4. **Cement line accumulation**: After many years of bone remodeling, both cortical and trabecular bone have a large number of cement lines which represent loci of least structural resistance (13). Cement lines are less mineralized than lamellar bone, and have been
postulated to serve as potential sites for crack initiation (24).

5. **Matrix microdamage**: Imbalances in the normal relationship between those factors causing microdamage and those involving repair processes result in the development of stress fractures and osteoarthritis (25). This also plays a role in the increased bone fragility associated with aging and osteoporosis (26). Using histomorphometric methods to examine the incidence and localization of microcracks in human femoral compact bone, it has been reported that the amount of microdamage present increases exponentially with age, and at a significantly higher rate in females than in males (27).

In cortical bone, microdamage appears as small cracks within the matrix. In trabecular bone, both matrix microcracking and complete fracture of individual trabeculae are observed (25). This has been reported in vertebral bodies, which contain a large proportion of trabecular bone (28). With aging, local mineralization in the unremodelled areas of interstitial bone is increased, causing a decrease in the local resistance of the bone to fracture at the microscopic level (29). The accumulation of microdamage is also likely related to alterations in the aging skeleton's ability to react to injury at the level of the bone matrix. If osteocytes are necessary to detect damage to the bone matrix, then regions in which osteocyte death has occurred would be unable to detect microdamage and initiate repair (30). An increased microdamage and deranged microstructure, as measured by ultrasound transmission, is observed in osteoporotics, suggesting both a decreased quantity and quality of bone (31). The accumulation of bone matrix microdamage, resulting from a slower remodeling rate, delays repair, and working in concert with a defective mechanism of detecting microdamage, results in an increased fragility of the aging skeleton (29).
II.D. Skeletal Transients

It has been hypothesized that when an intervention (exercise or estrogen replacement) suppresses the frequency of activation of remodeling sites, there will be a period of 6 to 12 months of bone gain until the majority of the resorption cavities brought into existence before the intervention are filled (32). This phenomenon, known as skeletal transients, still requires scientific clarification. The increase in bone mass resulting from a transient (from 2 to 12%) is limited and not necessarily permanent (13). The presence of skeletal transients can confound the interpretation of human treatment experiments, and thus, any experiment designed to evaluate an intervention must take them into account.

Osteoporosis can be the result of failure to maintain skeletal adaptation to the mechanical forces encountered in one's daily activities (33). The failure occurs in one or more of three areas of adaptation 1) a failure to maintain skeletal muscle mass, 2) a failure to maintain a mechanically favorable microarchitecture, and 3) a failure to repair skeletal microdamage at a rate sufficient to prevent it's accumulation (21). Osteoporosis is generally considered to be the result of multiple genetic, physical, hormonal, and nutritional factors acting in concert (13).

III. MEASUREMENT OF BONE DENSITY

Measurements must be made in order to characterize the mechanical properties of bone. Quantification of bone density aids in establishing the severity of bone loss and serves as a baseline for establishing the success of therapy. Most non-invasive measurements provide sitespecific information about the quantity of bone at the time of examination (34). However, these measurements do not provide information regarding the current or past rate of bone remodelling.
In order to determine the rate of bone loss in a patient, sequential measurements of bone density are necessary.

Although plain radiography is useful in the initial evaluation of osteoporosis and fractures, it is not sensitive enough for assessing bone density (34). Currently, the two most commonly used methods to evaluate bone density are dual energy x-ray absorptiometry (DEXA) and quantitative computed tomography (QCT). Two other methods, single photon absorptiometry (SPA) and dual photon absorptiometry (DPA), have been used in many of the studies reviewed here. The following section describes the various methods of clinically studying bone in humans.

**IIIA. Dual-energy X-ray Absorptiometry (DEXA)**

Dual-energy X-ray, DEXA allows measurement of integral bone mineral (cortical and trabecular) in the spine and the hip. The spine is commonly scanned between the 1st and 4th lumbar vertebrae (L1-L4).

This technique is highly acceptable to the patient (procedure time, 10-15 min), the radiation dose is low, and it yields highly accurate results. However, because DEXA measures all of the mineral within the path of its x-ray beam, aortic calcification and degenerative osteophytes may result in a false high reading (35). Currently, DEXA is the most reliable technique for the quantitative assessment of axial osteopenia. This technique promises to be an important diagnostic tool in the initial screening and long term follow up of patients with osteoporosis.

**IIIB. Quantitative Computed Tomography (QCT)**

QCT evaluates bone mineral in the vertebrae, allowing measurement of trabecular bone density. As the rate of turnover in trabecular bone is nearly eight times that in cortical bone, it is
a sensitive indicator of early metabolic changes. Since QCT measures trabecular bone only, this technique avoids osteophytes and areas of aortic calcification.

While the accuracy of this method is generally excellent, it may be reduced in patients who have severe osteopenia and kyphosis. In these patients, technical difficulties arise in positioning and locating the exact sites of previous measurements. QCT measures true bone density (mg/km³), whereas DEXA measurements are reported as area densities (g/km²). The use of dual-energy QCT reduces the small error in accuracy incurred as a result of the measurement of marrow fat; however, the radiation dose is increased with QCT.

III. Single Photon Absorptiometry (SPA)

SPA is based on the principles that x-rays and gamma rays are attenuated at the atomic level: in proportion to the density of the material, and that the photoelectric effect varies with the cube of the atomic number (36). Water, soft tissue, and muscle collectively, have an atomic number of 7, whereas calcium and phosphorus have average atomic numbers of 20 and 15 respectively. A low photon energy leads to a greater ratio of soft tissue attenuation; however, since a source of I-125 emits only 27 KEV of energy, it can only be used to assess appendicular sites with minimal soft tissue (36).

The radius, ulna or os calcis are the sites routinely assessed. Different proportions of trabecular and cortical bone are located along the forearm. Midshaft sites reflect a greater proportion of cortical bone, whereas distal sites are predominantly trabecular bone (37). This technique is not as accurate as the other methods mentioned above, and therefore often results in a higher percentage of false negatives and fewer true positives. Also, SPA measures of peripheral sites are only moderately correlated with axial and femoral bone density values (R²
III. Dual Photon Absorptiometry (DPA)

DPA exhibits a high level of reliability, requires little patient preparation, and involves a low radiation dose. The serious complications of fractures in the hip and spine make it important that this method be used to measure these areas. The usual sites of measurement include the L2-L4 lumbar vertebrae and the femoral neck, Ward’s triangle and the trochanter. The effects of variable amounts of soft tissue on absorption are eliminated by the dual energy emitter. As DPA does not represent a volume of bone, it is not actually a density measurement (39). Deformities, such as scoliosis, and severe spinal degeneration reduce the accuracy of DPA measurements.

IV. PHYSICAL ACTIVITY AND BONE MASS: GENERAL CONSIDERATIONS

Few studies utilizing exercise as the primary intervention have applied the same degree of scientific rigor in the design and protocol found in clinical trials using other interventional variables (40). The extent to which the various exercise program design principles affect the response of other physiologic systems to exercise training need to be considered (41). These include:

1. **Principle of specificity.** Outcome measurements of BMD should be at the site(s) that are known to have received the training stimulus since the response to loading appears to be a localized effect.

2. **Principle of overload.** The loading of the bone resulting from the training protocol must exceed, or be different, than that of habitual loading if bone mass is to be positively influenced.

3. **Principle of reversibility.** The observed improvement in bone mass will return to
baseline when the added loading is reversed, i.e., if the program is stopped.

4. **Principle of initial values.** Those with the lowest BMD will have the greatest capacity for improvement.

5. **Principle of diminishing returns.** Each person's peak bone density is genetically influenced, as is the extent of any possible training effect.

Additionally, some of the prospective investigations have included serious methodological flaws; some have failed to employ a randomized design, utilized a small sample size, and employed an exercise program of a short duration (42). In reviewing the literature, a series of methodological criteria similar to those employed by Block et al (42) were applied to the assessment of each study.

The following is a description of these criteria:

1. **Subject Selection:** Demographic profile of study population.

2. **Description of Exercise Program:** Mode, duration, frequency, and intensity of exercise.

3. **Reporting of Outcomes:** Statistical power was considered based on the sample size used.

4. **Methods of Observation:** Studies were grouped by study design, i.e., cross-sectional or longitudinal. Prospective studies were further subdivided into studies that utilized strength training or aerobic exercise in the treatment group.

5. **Measurement of Bone Density:** The techniques used to assess bone density were also noted.

**V. Exercise and Biomechanical Mechanisms Interacting with Bone**

When force is applied to bone, the bone bends or is temporarily deformed. The extent of the deformation is measured as a strain. The strain depends on the magnitude and direction of
the force, the distance from the point of application of the force to the axis of bending, and the moment of inertia of the bone (43). Mechanical strain is the key intermediate variable between mechanical loading of the skeleton and bone mass. Frost (44) has suggested that there exists a minimum effective strain for both modelling and remodelling, and that strains falling between these threshold values will generally result in no net change in bone mass. Bone strains in the form of weight bearing exercise exceeding the minimum effective strain for modelling may result in a net increase in bone mass. This theory, however, still requires experimental verification.

The response of bone to mechanical loading is immediate, site specific, and involves both cellular and tissue reactions. Mechanical loads stimulate bone cells within the loaded region to deform, and to increase their synthesis of prostacyclin, prostaglandin E₂, glucose-6-phosphate dehydrogenase and RNA (45). Thus, an adaptation to the imposed loading environment occurs within the osteoblasts and osteocytes.

Recently, advances in the understanding of the biochemical basis of bone metabolism has led to the development of radioimmunoassay techniques for the measurement of markers of bone turnover. It has also recently been demonstrated that acute, moderate exercise affects bone turnover as indicated by an increase in the markers of bone resorption, but not those indicative of bone formation. The results suggest a triggering of bone remodelling, which appears to be greatest the day following exercise (46).

The external shape of bone, and its internal organization, are well adapted to the forces placed on bone. In the proximal femur, for example, the trabeculae orient themselves in form and mass to best resist extrinsic forces. Muscle contraction creates an internal force, while gravitational pull (static) and weight bearing exercise (dynamic) create external forces. The intersecting
network of trabeculae is biologically suited to respond to these forces.

Immobilization or disuse leads to a progressive thinning and eventual loss of trabeculae. The loss of trabeculae is most dramatic in the axial skeleton, particularly in the weight bearing vertebral bodies. A young adult confined to bed rest for one week may have a one percent decrease in spinal density, whereas it may take full year of increased activity to gain the same amount (47). Therefore, it is much easier to lose bone through inactivity than to gain bone through changes in functional loading.

The skeletal response to exercise is greatest at the site of maximum stress. An example illustrating this effect can be seen in professional tennis players, whose playing arm can be up to 30% denser than the non-playing arm (48). The characteristic of the strain is also important in that osteogenesis is caused by dynamic, but not static, strain (49). It is imperative, however, that the loading be expressed in relative, and not absolute, terms when prescribing exercise for both the elderly and those with osteoporosis.

VI. Other Factors Affecting Bone

VI.A. Estrogen

Estrogens are female sex hormones produced by pre-menopausal women. They are produced primarily in the ovaries, in the form of 17-B estradiol. After menopause, estradiol production falls off, and a less potent form, estrone becomes the predominant source of estrogen (50). Therefore, many physiological processes will be disrupted, and numerous changes will occur in post-menopausal women who are estrogen deficient. The effects on bone are most relevant to this discussion.
Since individual medical histories vary, it is important to consider the risk of no hormone replacement therapy with the risk of side effects from the therapy. Estrogen is the only prophylactic agent with a well-established ability to inhibit post-menopausal osteoporosis, and to reduce the rate of fracture in both trabecular and cortical bone (51). Since 1948, estrogen deficiency has been implicated in the rapid rate of bone loss following menopause, yet the mechanism(s) are largely unknown (52). In the late 1980’s, Cawley and co-workers (53) demonstrated that endogenous estrone levels were related positively to radial BMD.

The mechanism(s) responsible for the increased bone resorption relative to bone formation were believed to be indirect, because repeated attempts to find estrogen receptors in osteoblasts had failed. However, Ernst and colleagues later discovered that estrogen could act directly on bone (54). They demonstrated that 17-B estradiol acted at a pre-translational level to augment the synthesis of bone collagen and enhanced osteoblast-like cell proliferation in vitro. Following this discovery, other researchers demonstrated that the administration of estradiol to specific estrogen receptor sites enhanced transforming growth factor B messenger RNA levels and pro-collagen (55). Therefore, a direct influence of estrogen on bone had been demonstrated.

During the past few years, there have been important advances in our understanding of the interplay between osteoclasts and osteoblasts, and the systemic and local factors that regulate their development. Specifically, a dramatic increase in the various cytokines involved in bone remodelling appears in the absence of estrogen. This results in a net increase in bone resorption leading to osteoporosis. Estrogen has an inhibitory effect on interleukin-6 production, which prevents excessive osteoclast development. In accordance with this, a loss of gonadal function in mice stimulates osteoclastogenesis in vivo through an increased production of interleukin-6 (56).
In addition, administration of 17β-estradiol prevents these cellular changes in ovariectomized mice. In a state of estrogen deficiency, the production of osteoclast precursors, and their responsiveness to interleukin-6 and interleukin-11, is enhanced.

In an estrogen-replete state, the production of interleukin-6 has been found to be below a critical threshold of sensitivity of osteoclastogenesis (57). The role of interleukin-6 in the stimulation of osteoclast formation, and the loss that follows, does not explain the increase in osteoblast activity that follows menopause (58). Presently, there is no mechanistic explanation for the simultaneous increase in the formation of osteoclasts and osteoblast progenitors in the marrow following menopause. The cellular and molecular mechanism(s) of the action of estrogen on bone cells are unclear. It has been postulated that interleukin-6 is the principle mediator of the action of estrogen on bone cells; however, the reported studies in humans were mostly based on short term cultures of peripheral blood monocultures (59). In a recent well controlled study by Kassem and colleagues, neither IL-1 nor IL-6 were found to be the major physiological mediator for the increased bone loss due to estrogen deficiency in the early post-menopausal period (60). It seems possible that there are multiple mechanisms of estrogen modulation of bone metabolism that require further study (61).

The disruption of the normal balance between bone resorption and bone formation results in the loss of bone. In post-menopausal osteoporosis, this mismatch between the formation and resorption is related to excessive osteoclastogenesis and inadequate osteoblastogenesis. There is a change in the number of bone cells, rather than changes in the activity of the individual cells (61). This finding forms the pathogenetic basis for osteoporosis, which represents a major advance in our understanding of the mechanism(s) involved in this disease.
VIB. Calcium

The serum calcium level is strictly regulated to maintain a range within 3% of normal (62). A low serum calcium triggers the release of parathyroid hormone, which leads to an increase in the fractional calcium absorption via a decreased kidney excretion of calcium and the formation of active vitamin D (30). The opposite occurs in the case of high serum calcium, along with the production of an increased level of calcitonin. A deficiency of calcium is believed to result in a net bone resorption to maintain adequate serum calcium levels, even though intestinal and kidney absorption of calcium are elevated (64).

In spite of the conflicting evidence regarding the effects of dietary calcium on bone, there is a general consensus that adequate calcium intake is required to achieve peak bone mass. Prince et al. (65) demonstrated a relationship between the effectiveness of calcium supplementation and the number of years since menopause. Dawson-Hughes et al. also reported that calcium supplementation prevented bone loss in women more than 6 years post-menopausal who had a low initial dietary calcium intake (66). Women in the early post-menopausal period, however, exhibited bone loss that was unaffected by calcium supplementation (66). Older persons may need more calcium to maintain a neutral balance because the absorption of calcium from the gastrointestinal tract becomes less efficient with age.

Generally, it may be appropriate to advise women with intermediate bone density values to adopt a routine of calcium supplementation and exercise. Because of the need for medical supervision with hormone replacement therapy, and the increased side effects, it may be appropriate to reserve estrogen therapy for women with low bone density (67).
VIC. **Other Hormonal and Nutritional Factors**

Growth hormone and testosterone have a stimulatory effect on bone. Since growth hormone is enhanced by estrogen, estrogen withdrawal may indirectly affect bone by lowering the level of growth hormone as well (68). Although it is known that testosterone production in women does not decline following menopause, no conclusive evidence exists with regard to testosterone and osteoporosis (68).

Glucocorticoid production and thyroid hormone are known to impair calcium absorption. The glucocorticoids can inhibit bone formation, while thyroid hormone stimulates bone resorption (69).

Prolactin has been associated with a decreased skeletal mass, although the mechanism(s) involved are unknown (70).

The active vitamin D metabolite, 1,25(OH)₂D₅, helps to maintain normal levels of serum calcium and phosphate (71). This is accomplished by increasing the absorption of calcium and phosphate from the intestine, and their resorption from bone.

Other important nutritional aspects of osteoporosis are the preservation of a healthy body mass, and the provision of an adequate nutritional intake. It is important to avoid an excessive loss of body mass at the onset of an exercise program, and to maintain an adequate nutritional intake to prevent an impaired immune function.

VID. **Genetic and Environmental Factors**

Various genetic and environmental factors have been studied in addressing the determinants of peak bone mass. The fact that serum osteocalcin levels are genetically influenced suggests a
genetic regulation of bone turnover (72). Genetic studies indicate that inherited familial and ethnic factors may determine achievable peak bone mineral density (73). While longitudinal studies have not conclusively demonstrated genetic effects (74), it is possible that genetic factors also influence the sensitivity of bone to environmental factors. Eisman and co-workers (74) concluded from their twin studies that bone density of the lumber spine is strongly influenced by genetic factors, while the bone density of the femoral neck is sensitive to environmental factors, such as physical loading.

VII. PHYSICAL ACTIVITY AND BONE

VIIA. Cross Sectional Studies

Currently, a bone mineral density of 2.5 standard deviations below that of normal premenopausal women is the standard criterion used by physicians to diagnose osteoporosis (5). Prospective studies show that a one standard deviation reduction in BMD confers a 2 to 3 fold increase in the risk of fracture (75). However, if the results of all prospective trials of exercise and BMD are averaged, the net increase has been found to be 1 % per year (1). These facts demonstrate that exercise can be considered beneficial in the treatment of osteoporosis, but does not represent a cure.

Cross sectional studies generally demonstrate a positive correlation between habitual physical activity and bone mass (Table 2). Participation in athletics is associated with a higher BMD at various skeletal sites depending on the activity and the site measured. For example, young swimmers have been found to have a lower femoral neck BMD than those involved in weight bearing activity, while no differences were found in the spine BMD (76). Orwoll et al. found
Table 2. Physical Activity and Bone in Women: Cross Sectional Studies

<table>
<thead>
<tr>
<th>Author</th>
<th>Type of Subjects</th>
<th>Age (yrs)</th>
<th>Methods/Bone Measurement</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Michel (1989)</td>
<td>78 healthy subjects, 28 women, 50 men</td>
<td>men, 60</td>
<td>QCT L₁</td>
<td>positive ( r ) between BMD and ( pa ) up to 300 min/week</td>
</tr>
<tr>
<td>Cheng (1991)</td>
<td>108 healthy p.a. women</td>
<td>50-60</td>
<td>3 groups, 0-3 h/week,</td>
<td>BMD ( r ) with h/week p.a.</td>
</tr>
<tr>
<td>Cheng (1993)</td>
<td>388 healthy finnish women</td>
<td>50-60, 75</td>
<td>SPA calcaneus</td>
<td>moderate ( r ) between p.a. and BMD</td>
</tr>
<tr>
<td>Conroy (1993)</td>
<td>elite junior weight lifters</td>
<td>17.4</td>
<td>DXA L₂-4, proximal femur,</td>
<td>weightlifters &gt; BMD than controls</td>
</tr>
<tr>
<td>Jonsson (1992)</td>
<td>30 runners, 30 controls</td>
<td>38-64</td>
<td>SPA radius and ulna, QCT L₁</td>
<td>Active &gt; trabecular bone mass in distal radius</td>
</tr>
<tr>
<td>Kannus (1994)</td>
<td>20 tennis players, 20 controls</td>
<td>19-34</td>
<td>DXA arm</td>
<td>tennis positive effect on BMD &amp; BMC of playing arm</td>
</tr>
<tr>
<td>Krall (1994)</td>
<td>239 postmeno women</td>
<td>62 ± 5</td>
<td>Matched on miles/week, DXA L₂-4</td>
<td>Positive ( r ) in miles walked/week BMD</td>
</tr>
<tr>
<td>Orwell (1989)</td>
<td>41 swimmers, 41 controls</td>
<td>55 ± 10</td>
<td>SPA Proximal radius QCT T₁₂-L₁</td>
<td>no association between swimming and BMD in women</td>
</tr>
<tr>
<td>Rutherford (1992)</td>
<td>216 women</td>
<td>21-82</td>
<td>QCT midshaft and distal femur</td>
<td>positive ( r ) between quadriceps strength and bone mass</td>
</tr>
<tr>
<td>Shimegi (1994)</td>
<td>11 volleyball players, 5 joggers, 9 controls</td>
<td>49-61</td>
<td>DXA L₂-4, proximal femur SPA radius</td>
<td>lumbar BMD greater in volleyball players and joggers</td>
</tr>
</tbody>
</table>
that male masters swimmers who swam at least 3 hours per week for 3 years had a significantly greater bone mineral density at both vertebral and radial sites than did the non-exercisers (77). Interestingly, however, no relationship could be found between swimming and BMD in women. The reason for this is unclear, although it is possible that the forces generated on the skeleton are less in women, and that this resulted in a diminished effect on bone remodelling. While considerable mechanical stress can be placed on the skeleton by swimming exercise, the resistance encountered is less than that developed in a weight bearing exercise. Nevertheless, in view of the popularity and safety of swimming in the elderly with musculoskeletal problems, it could represent a worthwhile addition to an exercise program in the prevention of bone loss.

In addition to the evidence obtained by studying younger athletes, an increasing interest in veteran sports worldwide provides researchers with active groups enabling an economical insight into the effects of long term physical activity in the elderly. Many of the earlier studies in elderly women found non-significant differences between athletes and non-athletes. However, it has been hypothesized by Kriska et al. that women who have been physically active throughout their lives (assessed by a retrospective survey) would be expected to have a greater bone area and bone density than sedentary controls (78). This was recently confirmed by Cheng et al., who examined the physical activity patterns in healthy women aged 50-60 (79). They concluded that women who participated in vigorous exercise two or more times per week, or those whose total physical activity amounted to 4 hours per week, had significantly higher BMD values than those who were less active.

In the study by Cheng et al., the measurement of BMD was performed in the right calcaneus applying the single photon absorption method (SPA). As mentioned earlier, this technique is not
as accurate as other methods. However, Vogel et al. concluded in their review that the BMC of the calcaneus reflects the degree of spinal osteoporosis as well as the measurement of the BMC of the spine (80). This re-emphasizes the importance of critically examining the reporting of outcome measures when interpreting studies.

Michel et al. also found that a strong correlation exists between bone density and weight bearing exercise in men and women over aged 50 (81). Michel et al. were also the first to report a potential harmful effect of intensive vigorous exercise on bone density in women after natural menopause. In this study, subjects who exercised up to 300 minutes per week exhibited an improved bone density, while 5 of the 28 women who exercised for more than 300 minutes per week had a surprisingly low bone density, which could not be explained by other factors. The authors hypothesized that the "overexercise" response might be reflected as a phenomenon of selective optimization of one organ system (needed to accomplish the physical performance) at the expense of others (the BMC of the lumbar spine).

Shimeg and co-workers also concluded that physical exercise increases the BMD in postmenopausal women (82). They examined the BMD of post-menopausal Japanese women who were either volleyball players, joggers, or control subjects. Their results indicated that the protective effect of exercise on the maintenance of BMD is localized to the skeletal sites used predominantly in the sport. There was no significant difference among groups in the BMD of the radius, whereas the volleyball players and joggers had a greater lumbar and femoral BMD.

Another recent cross-sectional study has reported that middle-aged women who have participated in impact loading physical activity for 20 years or more have a significantly higher BMD than women who have participated in non-impact loading sports or women who have been
sedentary (84). Sixty women, average age 46 years, selected from participants in the Australian Masters Games, were equally divided into three groups according to sports participation: a high impact group (basketball and netball players), a medium-impact group (runners), and a non-impact group (swimmers).

DEXA measurements revealed a significantly greater whole-body BMD in the high-impact group than in the non-impact and control groups. The high and medium impact groups were found to have a significantly higher leg BMD than both the non-impact and control groups. The leg extensor strength of the high-impact group was markedly greater than that of the control group, but no other significant between group differences were noted.

Most studies in post-menopausal female runners have shown higher bone densities in the spine and weight bearing bones when compared to sedentary controls (85). It is tempting to conclude from these studies that physical activity itself improves bone mass, but the cross sectional nature of these studies leaves open the possibility of ascertainment bias. For example, athletes who have been active for a sufficient time to be classified as a runner or a weight lifter may succeed by virtue of some baseline characteristics, for example, a higher bone mass before initiating the training program (86). Even if other factors contribute to the positive outcome, the differences in BMD observed between those who have devoted themselves to life-long training and those who have been sedentary should not be under-estimated (87).

In conclusion, evidence from basic bone biology (88), various exercise studies (89), and large epidemiological studies (90) all indicate that physical activity is an important factor concerning the maintenance of bone mass and the prevention of osteoporotic fractures.
VIIB. Intervention Studies

Clinical trials have used a variety of exercise regimes to show that an increase in physical activity can increase BMD. Studies that employ aerobic and endurance activities (Table 3) will be reviewed separately from the studies that have employed strength training in an effort to determine the most effective training studies for increasing bone mass.

VIIB.1 Aerobic Exercise and Bone Mass

Recent technological advances have made measurement of the proximal femur possible, and both this site and the lumbar site (L2-L4) are the most commonly tested sites in recent studies. Most previous studies have examined changes in the lumbar spine, radius, or os calcis. Drinkwater has calculated that the changes in the lumbar and radial BMD following training ranged from -12% to +8% and -3.7% to +3.0%, respectively (1).

Walking is the most commonly prescribed activity for older women because it is a relatively safe exercise due to the low risk of musculoskeletal injury. However, the results of studies examining the effects of walking on bone mass are conflicting. A study by Krall and Dawson-Hughes demonstrated that women who walk approximately one mile each day had a higher mean bone density for the whole body and legs than women who walked less than one mile per week (91). The number of miles walked per week was also correlated with longitudinal rates of change in bone density at the legs. Walking had no significant effect on the spine, which is consistent with a local effect of walking on the bone density of the lower extremities.

Comparisons among studies evaluating walking on bone density are limited by differences in the methods used to measure BMD, in the measures of walking activity, and in the confounding
<table>
<thead>
<tr>
<th>Author</th>
<th># of Subjects</th>
<th>Age</th>
<th>Design/Methods</th>
<th>Type of Exercise</th>
<th>Frequency/Duration</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bossey (1994)</td>
<td>14</td>
<td>13</td>
<td>32</td>
<td>random assignment DXA L1-4, rad., femur</td>
<td>High impact aerobics (test) low impact (control)</td>
<td>1x/week supervised daily at home, 1 yr. High impact &gt; increase trochanteric BMD</td>
</tr>
<tr>
<td>Michel (1992)</td>
<td>14</td>
<td>14</td>
<td>55-77</td>
<td>non-random, matched pairs QCT L1</td>
<td>running</td>
<td>5 years lumbar bone loss r with decrease in running time</td>
</tr>
<tr>
<td>Michel (1991)</td>
<td>12</td>
<td>5</td>
<td>58.5</td>
<td>non-random, matched QCT L1</td>
<td>running and aerobic dance</td>
<td>2 years exercise &gt;300 min/week decreased BMD.</td>
</tr>
<tr>
<td>Bloomfield</td>
<td>7</td>
<td>7</td>
<td>postmenopausal</td>
<td>DPA L2-4, femur</td>
<td>Bicycle ergometers</td>
<td>8 months Increase in lumbar BMD</td>
</tr>
<tr>
<td>Caplan (1993)</td>
<td>19</td>
<td>11</td>
<td>Ex.66.4 c.65.4</td>
<td>non-random DPA L2-4, femur</td>
<td>supervised low impact aerobics</td>
<td>2x/week 1 hr. 1x/week own, 40 weeks lumbar and trochanteric BMD &gt; in exercise</td>
</tr>
<tr>
<td>Grove (1992)</td>
<td>10</td>
<td>5</td>
<td>1-8 yrs postmenopausal</td>
<td>random, matched DPA L2-4</td>
<td>high, low impact aerobics</td>
<td>3x/week, 1 hr, 1 yr. both exercise groups increased BMD</td>
</tr>
<tr>
<td>Heikkinen (1991)</td>
<td>39</td>
<td>39</td>
<td>52.6</td>
<td>random, 3 groups DXA L2-L4, femur</td>
<td>wt.lifting, brisk walking</td>
<td>1x/week, 40 mins., 2h/week, 1 yr. Ex. with ERT did not increase BMD greater than ERT alone</td>
</tr>
<tr>
<td>Martin (1993)</td>
<td>20</td>
<td>19</td>
<td>50-60</td>
<td>random, DPA L2-4, SPA forearm</td>
<td>treadmill walking 2.5-4.0 mph, 3-7% grade</td>
<td>3x/week, 30 or 45 mins., 1 yr. ex. attenuated decrease in BMD £6 yrs.postmeno</td>
</tr>
<tr>
<td>Prince (1991)</td>
<td>41E</td>
<td>39E&amp;C, 40E&amp;H RT, 42 controls</td>
<td>56</td>
<td>random, double blind, forearm bone densitometer</td>
<td>low impact aerobics, brisk walking</td>
<td>1x/week, 2x/week, 2 yrs E+HRT &gt; E+Ca &gt; E for distal and median BMD</td>
</tr>
</tbody>
</table>
variables of nutritional and hormonal status. The annual rate of change in trabecular bone density showed a small increase (0.5%) in 18 post-menopausal women who walked more than 3 hours per week when compared to the change in 18 sedentary women in whom spine bone density decreased by 7% (92). In contrast, an earlier study revealed no differences in annual trabecular bone loss in 8 walkers and 9 sedentary women in the early years of menopause (93). This study however, involved only 2 hours of walking per week. It appears that a lower intensity, duration and frequency of walking, and a smaller sample size, may have contributed to the conflicting results.

A recent study examined the effects of two durations (30 or 45 minutes) of treadmill walking in post-menopausal women. The subjects exercised 3 times per week for 1 year, and the BMD of the lumbar spine and radius were measured before and after training (94). No statistical improvement in the BMD of either site was observed, but the training did attenuate the lumbar BMD loss in those women who were less than 6 years from the onset of menopause. The subjects in this study did not have osteoporosis, and none were taking estrogen replacement therapy. Therefore, walking may not be the best exercise mode to improve lumbar BMD in healthy post-menopausal women. However, the 45 minute exercise group exhibited a 0.8% increase in lumbar BMD, which was maintained over several years, compared to the 0.5% decline in the control group, a difference which may be clinically significant. Longer training studies are needed to determine if walking can sustain the 0.8% increase in lumbar BMD for more than one year.

Aerobic dance is another form of weight bearing exercise that may be more enjoyable for elderly women, and one which may promote an increased compliance to an exercise program.
Caplan and co-workers recently assessed the effects of a twice weekly aerobic exercise program on the lumbar and femoral bone density in post-menopausal women (95). The exercise program of low impact aerobics was conducted for forty weeks, and the subjects did not use any medication known to alter bone homeostasis. This was the first study to use DPA to demonstrate a change in the proximal femoral region following exercise. The mean change in the trochanteric bone mineral concentration was +9.6% in the exercisers vs. -4.4% in the controls. Both groups showed a decrease in bone density in the lumbar spine, though this was significantly greater in the control group (-0.8% vs. -3.8%). The authors commented that for many of the exercisees, it was a significant social outlet, and that this aspect of the program should not be under emphasized.

Grove and Londeree examined the effect of high and low impact aerobics on the BMD of the lumbar vertebrae in healthy, early post-menopausal women (96). Any exercise that produced a peak force greater than, or equal, to two times the body mass was considered a high impact activity. The low impact group performed exercises that imparted forces equal to, or less than, 1.5 times the body mass. The results showed that both the low and high intensity activities prevented the decline in BMD that occurred in the control group. The difference in BMD between the low and high impact exercise groups was not significant. These results suggest that the impact threshold for the maintenance of BMD may be less than 1.5 times body mass, whereas the high impact exercise in this study was not of sufficient stimulus to further increase in BMD any further. Studies in post-menopausal women have demonstrated that high impact exercise has a significant effect on BMD. Bossey and Ramsdale demonstrated a 3.4% increase in trochanteric bone density in a test group of high impact exercisers (97). This increase was
significantly different from that of the control group, which performed low impact exercise. In the second 6 months of the study, the control group began high impact exercise, and showed a significant increase of 4.1% in trochanteric bone density.

The specific effect at the femur may be the result of two sources of locally increased functional strain (44), namely, compressive forces to the weight bearing skeleton and tensile forces produced by the attachments to the trochanter (97). The tensile force will be developed rapidly during the muscle contractions to provide sufficient momentum for takeoff, and will rise again during the eccentric contractions which occur during landing. The femur would receive more of an overload in this type of exercise than the spine. This is important to note in that there is evidence to suggest that the trochanteric density is the most sensitive indicator of the overall vulnerability to fracture in the proximal femur (98). By contrast, in jogging, which has been associated with spinal improvements (but not femoral), the heel strike may give rise to a higher compressive force with a different tensile pattern.

Michel and co-workers examined the relationship between long-term running (5 years) and changes in lumbar bone mineralization (99). Their results demonstrated that over a 5 year period, runners and control subjects lost comparable amounts of bone, although the runners maintained a significantly greater absolute BMD of L₁ after 5 years. The subjects who substantially decreased their running time (by 20%) had the most significant bone loss. Thus, a higher level of regular loading appears to prevent bone loss compared to lower levels of activity. Michel et al. concluded that weight-bearing exercise is mandatory to prevent excessive bone loss.

Post-menopausal women who have participated in an exercise program that have typically shown improvements in bone measurements lose this accrued benefit after the program is
discontinued (99). The obvious conclusion is that the stress on the skeleton is beneficial as long as it is continued on a regular basis.

An area of recent interest has been the relationship between muscle strength, muscle mass, and BMD. A resistance training program aimed at increasing muscular strength satisfies the training principles discussed in the earlier section on general considerations. The intensity can be increased slowly, but consistently, following the principle of progressive resistance. Also, the external loading can be designed to stress specific skeletal sites satisfying the principle of specificity.

Calmels recently reported a significant correlation between femoral bone density and muscle strength of the legs, and between vertebral bone density and muscle strength of the upper limbs (100). The muscle strength of the arms decreases markedly between the ages of 50-60, whereas the muscle strength in the lower limbs shows a more significant decline among 60-69 year olds (100). Also, muscle atrophy caused by disuse is less pronounced in the lower limbs which are used more in routine daily activities than the upper limbs (101). It can be concluded from the above that the optimal exercise prescription for post-menopausal women should not necessarily be uniform for everyone from age 50-70. Rather, exercises targeting upper body strength and vertebral bone density should be prescribed for women in the 50-60 age range, and exercises to increase lower limb strength and balance should be prescribed for the older age groups. Also, there is a need for further studies to confirm the step-wise, age-related decrease of muscle strength and bone mineral density during the post-menopausal period. Prospective investigations that have utilized strength training in the exercise program will be discussed next (Table 4).
Table 4. Prospective Training Studies Utilizing Resistance Training

<table>
<thead>
<tr>
<th>Author</th>
<th>Design/Methods</th>
<th>Type of Exercise</th>
<th>Frequency/Duration/Intensity/Length of Program</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fiatarone (1994)</td>
<td>random, resistance training</td>
<td>hip and knee extensors</td>
<td>3x/week, 45 min, 3 sets of 8 80% 1 RM, 10 weeks</td>
<td>muscle strength increased by 113±8%</td>
</tr>
<tr>
<td>Meaks (1993)</td>
<td>random DXA lumor &amp; femur</td>
<td>strength training</td>
<td>3x/week, 1 set of 15, 2 sets lower body, 16 weeks</td>
<td>2.0±, 9% increase in lumbar BMD and 3.8%±1 increase in femoral neck</td>
</tr>
<tr>
<td>Nelson (1994)</td>
<td>random, total body BMC DPA L2-4, Femur</td>
<td>hip, back, knee extension, lat pulldown, ab flexion</td>
<td>2x/week 45mm, 80% IRM 52 weeks</td>
<td>increase in BMD, BMC maintained in wt. trained group</td>
</tr>
<tr>
<td>Kerr (1996)</td>
<td>random, DEXA femur, radius</td>
<td>muscle endurance muscle strength</td>
<td>3x/week 3 sets 20, 3 sets 8-10, 70%RM</td>
<td>BMD increased in strength group only</td>
</tr>
<tr>
<td>Pruitt (1992)</td>
<td>non-random, BMC radius + ulna, DPA L2-4, femur</td>
<td>universal gym, free weights, upper &amp; lower body</td>
<td>3x/week, 1 h., 1 set of 10-15 60% 1 RM, 9 months</td>
<td>Significant improvement in lumbar BMD in wt.trained</td>
</tr>
<tr>
<td>Rikli (1990)</td>
<td>non-random SPA non-dominant radius</td>
<td>general aerobics plus upper body strengthening</td>
<td>3x/week, 45 min., 10 months</td>
<td>Exercises increased BMC and BMC/BW</td>
</tr>
<tr>
<td>Snow-Harter (1992)</td>
<td>random DPA L2-4, femur</td>
<td>Universal gym running</td>
<td>3x/week, 3 sets of 8-12, 75% IRM, 8 months</td>
<td>Lumbar BMD increased in both groups</td>
</tr>
<tr>
<td>Ryan (1994)</td>
<td>DEXA</td>
<td>resistance training, 14 exercises</td>
<td>3x/week, 2 sets of 15, 16 weeks</td>
<td>2.8% increase in femoral neck BMD</td>
</tr>
</tbody>
</table>
VIIB.II Strength Training Investigations

Recent studies suggest that loads other than those generated by gravity, such as a muscular pull, can actually stimulate bone deposition (102). Male and female weight lifters consistently have a higher bone density in the axial and appendicular skeleton when compared to a control group (103,104). Some studies have examined the relationship between muscle strength and bone mass (105), or between muscle mass and bone mass (106). However, none of these studies attempted to determine the physical activity levels in their study populations. Recently, the relationship of muscle and bone loss in terms of activity level and age has been examined (107). The authors found a significant positive relationship between quadriceps muscle strength and bone mass at all three skeletal sites measured. The changes in bone mass with age varied between the different skeletal sites measured. The spine showed an accelerated period of bone loss over the early post-menopausal period, whereas bone in the distal femur steadily declined from the 3rd decade.

These patterns of bone loss are similar to those found by Schaadt and Bohr at skeletal sites with similar distributions of cortical and trabecular bone (108). However, in this study, with age kept constant, physical activity did not correlate with any of the muscle or bone indices. The relationship between the loss of muscle and bone with age cannot be explained by declining physical activity levels alone, but is also related to declining estrogen levels, growth hormone, and IGF-1.

A positive effect of estrogen on BMD both in the lumbar spine and proximal femur has been recently reported by Heikkinen et al (109). Their placebo controlled, 2 year prospective trial of two different estrogen-progestin regimens prevented bone loss and increased muscle
strength in both treatment groups. Each treatment group was further randomized to non-exercise and exercise subgroups. Unfortunately, no synergistic effect of exercise and estrogen on BMD could be shown. It is of interest that the positive effect of estrogen treatment on muscular strength was particularly pronounced in the women who had a low level of muscle strength at the beginning of the study. The anabolic effect of estrogen on skeletal muscle seems definite.

In contrast, Taaffe and colleagues recently determined that maximal muscle strength of elderly women is not influenced by estrogen status (110). In their study, 85 healthy women aged 65-82 years performed five standard lower body exercises using isotonic equipment. Although individuals receiving ERT had an enhanced bone mass compared with those not receiving ERT, there was no effect of hormone replacement therapy on lower body strength. An explanation for the conflicting results is not readily available, but is most likely related to differences in study design.

A decrease in both the number and size of the type II muscle fibers is related to the decrement in the force generating capacity with age (111). This may explain part of the reason why women are able to maintain, on a relative basis, muscle endurance during activities which rely predominantly on the recruitment of type I fibres. It follows then, that tests of maximal muscle strength which rely largely on type II fibers will be diminished as people age.

It is important to be aware of issues surrounding comparisons involving the initial value of each physical attribute when interpreting the results of studies examining strength training and BMD. In a recent study of post-menopausal women, the increase in vertebral BMD of 1%, when added to a 1.8% decrease in the control group, provided a statistically significant benefit (112).
Also, the femoral neck bone density increased by 0.9% in the exercise group and decreased by 2.5% in the controls. The women in this study were greater than 5 years post-menopause, not older than 70, and had not taken estrogen, or any other factor known to affect bone. They performed strength training exercises at 80% of 1RM max to train the major muscle groups attached to the bones of interest (L2-4, femoral neck). The authors concluded that a high intensity strength training program has a positive effect on bone density, muscle mass, muscle strength, and dynamic balance.

A recent study supported the evidence that post-menopausal bone mass can be significantly increased by a strength regimen that uses high loads and low repetitions (113). In this study, women, aged 60, trained one side of their body using a low weight, high repetition program (performing 3 sets of 20 repetitions, i.e., endurance training), while on the opposite side they trained with a heavier weight, low repetition program (performing 3 sets of 8 repetitions i.e., strength training). The radius and femur on the side in which they strength trained increased BMD by 2.1 %, while there was no change in the BMD on the side that followed the endurance training protocol. The most significant gains in bone mass were achieved from a program that employed a heavy load with fewer repetitions. The authors concluded that the peak load employed in the training is more important than the number of loading cycles in producing an increase in the bone mass in early post-menopausal women.

Another recent study also found a significant difference in lumbar BMD (+1.6%) in the weight trained group compared to a decrease (-3.6%) in the control group over a nine month period (114). In this study, the initial workload corresponded to 60% of 1RM; the subjects were 1-7 years post-menopause and were taking no medication. No significant weight training effect
was detected at the femoral neck or distal wrist site. It has been hypothesized that a skeletal region with a high percentage of trabecular bone would be the first to respond to a weight lifting program (114). The vertebral body consists of greater than 66% of the more metabolically active trabecular bone (115). The estimated composition of bone at the femoral neck is 75% cortical and 25% trabecular (115). Thus, it is plausible that the 9 month training program used in this study was not of a sufficient duration to affect the bone with the lower metabolic rate.

Women who are active and have relatively well maintained bone mass may not accrue the same increase in BMD after initiating a strength training regimen. A recent study of active, post-menopausal, non-estrogen depleted women found no significant increase in BMD at any site compared with control subjects (116).

The general, versus the localized, effects of exercise on BMD in the radius of post-menopausal women has been examined (117). The subjects followed either a general aerobics training program or a general aerobics plus weight training program. The exercise subjects experienced a mean increase of 1.4%, whereas the control group exhibited a decrease of 2.5%. The authors suggested that the effects of exercise may be general, as well as localized, due to the lack of a significant difference between the study groups. Perhaps an increase in muscular strength which occurs in a relatively short time span, precedes the increase in the more slowly developing BMD.

The few prospective strength training intervention studies in young post-menopausal women have shown little or no increase on BMD. Rockwell and colleagues (118) reported detrimental effects of weight training on the lumbar BMD, whereas Gleeson et al. found a positive relationship between weight training and BMD (119). Snow-Harter et al. also reported
similar increases in the lumbar BMD of runners and weightlifters (1.3% and 1.2%), with no change in the BMD of the controls (120). No measure of bone mineralization at the proximal femur changed significantly in any group. Vuori and colleagues assessed the effect of unilateral leg press exercise on the BMD and BMC in young women (121). Their findings indicated that strength training intensive enough to induce a substantial gain in strength, was not an effective stimulus to increase BMD and BMC in young physically active women. Women, who are active and have a relatively well maintained bone mass, may not accrue the same increase in BMD after initiating a strength training program. Again, this demonstrates that those with an average, or above average, bone mass may have the least to gain when initiating an exercise program.

Interestingly, strength training appears to increase regional bone density in middle aged men to a greater extent than in women. In a recent study, males aged 50 to 70 years, experienced increases of 3.8% in the BMD of the femoral neck and 2.0% in the lumbar BMD after 16 weeks of training (122). These researchers were the first to demonstrate specific biochemical indexes of bone formation and absorption. This was demonstrated through the finding of a 19% increase in serum osteocalcin level and a 26% increase in skeletal alkaline phosphatase isoenzyme level, both validated markers of bone formation (123). The increases were not accompanied by a significant increase in tartrate-resistant acid phosphatase, which served as a marker of bone resorption.

The differences in training regime and gender are the only tenable explanations why their results differ from those of others. The men employed a heavier resistance program, and males don’t have the effect of estrogen on bone metabolism.

For individuals seeking to prevent or treat osteoporosis, much of the benefit of an exercise
program may be in the resultant increase in muscle strength, co-ordination and flexibility associated with such a program (124). Perhaps the greatest benefit is the improvement in mobility and balance associated with exercise that leads to a reduction in the incidence of falls.

VIII. Physical Activity and Fractures

Osteoporotic fractures are associated with a low bone mass, and occur most often in the vertebrae and distal radius in the early post-menopausal years (125). Vertebral fractures are the most common; however, the true incidence and prevalence rates are underestimated by clinical data. A recent report from the World Health Council on Osteoporosis has suggested that only 30% of women with vertebral fractures may receive clinical attention (126). This is because many vertebral fractures occur without specific trauma and are also asymptomatic.

As stated previously, the vertebrae and distal radius consist of a large proportion of more metabolically active trabecular bone. A review of the intervention studies reveals that these sites are the most respondent to an exercise program. Therefore, an exercise program designed to strengthen these areas, in particular, should be included as part of the exercise program for middle-aged women.

Hip fractures are more closely associated with age-related type II osteoporosis. These fractures are related not only to a low bone mass, but to other factors, such as decreased balance, lower levels of muscle strength and power in the lower extremities, and reduced soft tissue in the hip region. The results of an earlier study provide increasing evidence that mild activities, such as standing or walking, can prevent falling and hip fractures (127). Therefore, it would appear that an exercise program should be modified for elderly women to place a larger emphasis on
improving balance and lower body strength.

The type of exercise prescribed for post-menopausal women should be directed by their current health status. Weight bearing exercise has been demonstrated to be a necessary type of exercise for osteoporosis (128). Weight bearing exercise produces a mechanical loading, which combined with the force of gravity, creates electrical charges in the bone that can stimulate bone formation (128).

A muscular strength training program must be part of the exercise program for patients with osteoporosis. Recent evidence has suggested that resistance exercise provides a superior stimulus for bone when compared to weight bearing exercise. Also, it has been demonstrated that a high intensity resistance training is a feasible, safe, and effective means of countering muscle weakness and physical frailty even in very elderly people. The extent of improvement can be limited, however, if the principals of progressive resistance are not followed. The ability of women to progressively increase the training load, their compliance to the exercise program, biological variability, and the principle of diminishing returns requires that women on an exercise program must give increasing amounts of effort to achieve smaller and smaller gains.

VIV. CONCLUSIONS

It is important to consider to what extent BMD, by itself, determines bone strength. Current technology used in the quantifying of BMD measures the quantity of bone, but does not consider other aspects of bone physiology and structure, i.e., quality of bone. Although bone strength is highly correlated to BMD, other factors, such as bone quality and bone architecture, may be important factors in determining the risk of fracture and may be influenced by physical activity.
Evidence is now available, based on the observed biochemical effects on bone mass, both from cross-sectional and longitudinal studies, that exercise has a beneficial affect on bone mineral density. Epidemiological studies assert that regular, moderate exercise is likely to decrease the risk for falls, decrease fractures, and improve quality of life.

Many of these conclusions have been based on studies involving only healthy, post-menopausal women. There are few studies which have looked at the ability of women with documented osteoporosis to improve BMD and reduce fractures through an exercise training program. Also, most prospective training studies have been of a relatively short duration, involving a fairly small sample size.

No data are available regarding the minimum level of weekly caloric expenditure required to positively affect bone mass. Questions remain whether women will remain compliant to a prescribed exercise program for a prolonged period (longer than 2 years). It is not clear whether it is necessary for women to attend a supervised exercise program, or can the same benefits be accrued by following an at home program?

In order to attempt to answer the above questions, the following retrospective analysis was undertaken.
RESEARCH METHODS

Design

The purpose of the present study was to determine if patients enrolled in the Queen Elizabeth Hospital PRO Program maintained, or improved, their bone mineral density, over a five-year period. Furthermore, potential differences in clinical outcomes among a group of women who attended a supervised exercise program were compared to a group who chose to exercise on their own at home. Also, each subject completed a physical activity questionnaire in order to estimate weekly caloric expenditure (Appendix 1).

The present study was retrospective in nature, with data being obtained from a detailed review of each patient’s hospital chart. Each patient had an annual clinical assessment by the attending physician (Appendix II). Data was collected at study entry (T1), and periodically via the annual assessment throughout the five year period from 1990-91 to 1995-96 (T2).

It was hypothesized that the home group and the hospital group would have no differences in bone density, incidence of fracture, and loss of height over a five-year period. Confounding variables, such as the number of years post-menopause, the use of estrogen, calcium, or, other medications, and weekly caloric expenditure were taken into account. Also, because some authors have found a positive correlation between the frequency of exercise and BMD (see Review of the Literature), a correlation between the reported weekly caloric expenditure and BMD was also investigated.
Subjects

The patients were referred from their primary physician to the PRO program with the diagnosis of osteoporosis based on bone density below the normal range (i.e., < 2 S.D. below the norm) and/or an incidence of fracture. The subjects completed a consent form to allow information in their hospital chart to be allowed for the study (Appendix III).

As of January 1st, 1997, there were 209 patients enrolled in the PRO Program for a minimum of 5 years. Ninety-four patients enrolled for 5 years or more were identified as still being active in the program (i.e., having attended the exercise program within the previous 6 months of January 1st, 1997). Monthly attendance records at the hospital were consulted in order to identify those individuals who attended an average of 4 times per month. Four women were identified as being “seasonal” attenders, in that they travelled south for the winter. They were therefore excluded from the analysis. The remaining patients that attended the program 40 times per year (average once per week, given program cancellations) for 5 years or more formed the “hospital” group. Of the 94 active patients, 68 met this inclusion criterion. Of these 68 women, some were missing clinical data, or were not reachable, leaving the final “hospital” subject pool at 42. Of the 42 women in the supervised group, 27 attended an average of 2 times per week, while 15 attended an average of once per week. Ninety-four patients that had an annual physician assessment and exercised at home were identified as the home group. Of this group, 47 returned the survey and had sufficient data in their hospital chart for analysis. The 5-year comparison was therefore made on a total of 89 patients (42 hospital program vs. 47 at home program). An equivalent number of patients who did not choose to exercise at home or under supervision was not available, as these women did not have serial bone density measurements.
Data Collection

All patients had an initial clinical assessment, including bone mass measurements. In addition, clinical symptoms, history of fracture, medications being taken, loss of height, and frequency of exercise were included in an annual follow-up assessment. A database was developed for each patient (Appendix II). Fractures were recorded at study entry and new fractures were recorded over the 5-year follow-up period. Fractures that occurred in the year prior to the initial physician assessment were recorded at T1. Fractures that occurred over the five-year study period were recorded at T2.

Estrogen use was entered as a yes/no variable. Other medications known to affect bone homeostasis were classified as "other medications," and were also entered as a yes/no variable. Calcium and vitamin D use were also entered as a yes/no variable.
Exercise Protocol  
All patients were prescribed an exercise program, which was modified to meet individual requirements. All patients were encouraged to attend the exercise program twice per week, and to exercise on their own twice per week. However, some patients, after learning the exercises involved in the program (minimum of 4 classes), choose to carry on their exercise program at home, due to geographical location and/or inconvenience. They were all given an instructional booklet on exercise and osteoporosis, which contained a description of the exercises for them to follow. The exercises in this booklet were the same as the exercises the “hospital” patients were utilizing in the hospital program. The estimated caloric expenditure of completing this prescribed program was 150 kcals/exercise session. All patients continued to visit the attending physician in the program (Dr. R. Chow) on an annual basis for a clinical assessment, and to ensure that the exercises were being done correctly. Thus, the patients were divided into a supervised exercise group (hospital group; n=42) and an independent exercise group (home group; n=47). Both groups attended educational seminars and had annual follow-up appointments. The hospital exercise program consisted of a 20-minute low-load, strength training session and 30 minutes of aerobic activities. The major muscle groups of the upper and lower extremities were strengthened using free weights. Initially, the patients performed 1 set of 10 repetitions for each muscle group. They were instructed to gradually increase the number of repetitions until they could do 1 set of 15. When this could be completed, they were instructed to increase the number of sets to 2, and gradually increase the number of repetitions. After they could safely and effectively perform 2 sets of 15 repetitions for each muscle group, they were instructed to increase the amount of weight. Thus, they were instructed on the principle of progressive resistance exercise training. The aerobic exercises consisted of walking and various
“dancercize” routines, choreographed to music. In order to ensure that the patient achieved the target heart rate (70-80% of age predicted maximum heart rate), heart rates were taken every 10 minutes during the 30-minutes aerobics program.

**Physical Activity Index**

Habitual physical activity was estimated using the Harvard Alumni Questionnaire (Appendix I) to determine weekly activity levels in the two groups. This questionnaire has been validated for use in post-menopausal women (129). It is based on three simple questions: How many flights of stairs do you climb each day?, How many city blocks do you walk each day?, and How many hours per week do you engage in physical activity? For purposes of analysis, a flight of stairs climbed per day was equated to 28 kilocalories (kcal) per week energy expenditure, and a city block (1/12 mi) walked per day was considered to constitute expenditure of 56 kcal per week (130). The number of hours per week of physical activity was classified as “light activity” or “strenuous activity.” A list of approximately 80 kinds of physical activity was compiled, and those activities deemed to be light were rated at 5 kcal/min, and that of a more strenuous nature was rated at 10 kcal/min.

A physical activity index was devised to provide a composite estimate of energy expenditure from the number of stairs climbed, blocks walked, and sports played. This index was compared to the frequency of exercise obtained from the patients’ hospital chart. The two sources of information were combined to obtain an estimate of overall weekly caloric expenditure over the five-year period.
Bone Density Measurements

In post-menopausal osteoporosis, significant bone loss occurs in the spinal vertebrae and femoral neck. Fractures at these sites can be devastating, and result in a high mortality rate in the older population; therefore, measurements were made of these important areas of interest.

At study entry, bone mineral content was measured by Dual Photon Absorptiometry, using a Lunar DPA3, as reported previously (36). The pictorial image generated on the computer during scanning allowed for the determination of degenerative diseases or deformities. The computer produced a numeric printout with the L2-L4 data on one page and the data on the hip on another. Bone mineral content was expressed as g/cm². Percentile scores were given based on age, sex, weight and ethnic matched controls from the Mayo Clinic.

The reliability of the Lunar DPA3 has been reported as 1% for a single female evaluated over 6 months on 121 different scanners with a variety of 153 Gd sources. The precision is reported to be 2% for the spine and 3% for the femur (131).

At study completion (T2), the technology used in the measurement of bone mineral density had become more advanced. Specifically, the patients bone mineral density at T2 was determined by dual energy X-ray absorptiometry (DEXA). DEXA's widespread availability, coupled with it's lower radiation exposure, rapid scan time, and high intrasite reproducibility, led to it being the method of choice (35).

DEXA measurements were made with the Lunar DPX densitometer. DEXA instruments provide high precision and assess total body BMD with coefficients of variation between 0.6 and 1.2% for short- and long-term measurements (132).
Given that the BMD was assessed by two different machines which provide two different kinds of measurement, for the comparison of T1 and T2 data, the bone density was expressed as a percentage of that observed in young adults. Therefore, the percent bone mass at the L2-4 site, and the percent bone mass at the femoral neck site were compared at T1 and T2.

**Statistical Analysis**

**SPSS** (version 6.0) was used to carry out the statistical analysis. Initially, a cross-tabulation of estrogen use was performed to determine whether changes in estrogen use could be used as an independent variable in the analysis (Appendix IV). The results indicated that it could not be used since 82% of the subjects never changed their use of estrogen.

The same cross-tabulation was performed for the other medications (Appendix IV). No differences in the distribution of any medication were found at T1, but the analysis of medication use at T2 did indicate a change in distribution.

As too few subjects were found to be in the yes category for fractures at T2, the fractures at T2 variable did not contribute usable information. Therefore, fracture at T1 was identified as being an independent variable.

A repeated measures, multivariate analysis of variance (ANOVA) was carried out with the dependent variables: bone mass in spine, bone mass in hip, height, and the independent variables: group, medication use at T2, and fractures at T1.
Results

The descriptive characteristics of the 42 subjects in the hospital group and 47 in the home group are shown in Table 5. Subject recruitment was limited by the small number of women who were: a) participants in the PRO Program for a minimum of five years, b) still active in the program, and c) willing to complete the required physical activity questionnaire. Also, the BMD results were not available for many subjects. An attempt was made to retrieve missing data; however, this was not possible in the case of nine potential subjects. They were therefore excluded from the data analysis.

Years Post-Menopausal

The hospital group was 18.4 $\pm$ 7 years post-menopausal at study entry. The home group was 16.2 $\pm$ 9 years post-menopausal at study entry. The slightly younger age of the home group may be due to the fact that many in this group were still working at study entry. This might explain why some individuals chose to carry out the exercise program on their own; as the classes at the hospital were only offered during the daytime.

Change in Height

The average height of the hospital group was 157.6 $\pm$ 6.6 cm at study entry. The average height of the home group was 160.6 $\pm$ 6.1 cm at study entry. Both groups demonstrated an average decrease in height of approximately 1 cm over the five-year follow-up period.

Medication Usage

The two groups were also similar with respect to calcium intake, estrogen usage, and other medications known to affect bone metabolism (Table 6). At study entry there were 36 women
<table>
<thead>
<tr>
<th>PATIENT CHARACTERISTICS</th>
<th>HOSPITAL GROUP</th>
<th>HOME GROUP</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Stud y Entry</td>
<td>5-year Follow-up</td>
</tr>
<tr>
<td>Average Age</td>
<td>63.2</td>
<td>S.D. ±4.3</td>
</tr>
<tr>
<td></td>
<td>60.3</td>
<td>S.D. ±3.8</td>
</tr>
<tr>
<td>Average Years Post-menopausal</td>
<td>18.4</td>
<td>S.D. ±7.8</td>
</tr>
<tr>
<td></td>
<td>16.2</td>
<td>S.D. ±9.4</td>
</tr>
<tr>
<td>Average Height (years)</td>
<td>157.6</td>
<td>S.D. ±6.7</td>
</tr>
<tr>
<td></td>
<td>160.6</td>
<td>S.D. ±6.1</td>
</tr>
<tr>
<td>Number of Fractures</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td></td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>Average DPA Percent-Spine</td>
<td>73.69</td>
<td>S.D. ±11.8</td>
</tr>
<tr>
<td></td>
<td>74.74</td>
<td>S.D. ±10.4</td>
</tr>
<tr>
<td>Average DPA Percent-Femoral neck</td>
<td>74.02</td>
<td>S.D. ±12.0</td>
</tr>
<tr>
<td></td>
<td>74.74</td>
<td>S.D. ±8.4</td>
</tr>
</tbody>
</table>

TOTAL NUMBER OF SUBJECTS

<table>
<thead>
<tr>
<th>Hospital Group</th>
<th>Home Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>42</td>
<td>47</td>
</tr>
<tr>
<td>89</td>
<td></td>
</tr>
</tbody>
</table>
taking adequate calcium in the hospital group, and 42 in the home group. At study conclusion, all subjects reported taking adequate calcium, either through their diet or supplementation. This reveals that during the course of follow-up, a large majority of women were taking adequate calcium (1000 mg elemental calcium daily) and Vitamin D.

At study entry, there were 11 women in the hospital group and 12 in the home group taking estrogen replacement therapy. This represented 26% of the subjects taking estrogen and 74% not taking estrogen (Figure 1). At study conclusion, there were 19 women in the hospital group, and 20 in the home group taking estrogen. This represented 44% of the women taking estrogen and 56% not taking estrogen. Interestingly, all of the women that were taking estrogen at study entry remained on estrogen at the five-year follow-up.

The subset of women taking estrogen at study conclusion was analyzed to determine the change in BMD during the course of the study. The results are summarized in Figure 2. In the hospital group, of the 19 women taking estrogen, 17 demonstrated an average improvement of 7.4% in the lumbar site BMD. Two of the subjects had a decrease of an average of 4.6% in the lumbar site BMD. These two subjects were 25 and 34 years postmenopausal, respectively. Sixteen of the women had an average increase of 2.8% in femoral neck BMD, while 3 had an average decrease of 3.3%.

In the home group, of the 20 women taking estrogen, 18 demonstrated an average increase of 5.4% in the lumbar site BMD. Ten of the women had an average increase of 4.0% in the femoral neck site BMD, while 10 had an average decrease of 4.0%.

There were few women in either group that were taking other medications that affect bone metabolism at study entry. An important shift in both study groups occurred in the use of
### TABLE 6
**MEDICATION USAGE**

<table>
<thead>
<tr>
<th>HOSPITAL GROUP</th>
<th>Taking Calcium</th>
<th>STUDY ENTRY</th>
<th>STUDY COMPLETION</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>36</td>
<td>42</td>
<td></td>
</tr>
<tr>
<td>Not taking Calcium</td>
<td>6</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>HOME GROUP</th>
<th>Taking Calcium</th>
<th>STUDY ENTRY</th>
<th>STUDY COMPLETION</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>42</td>
<td>49</td>
<td></td>
</tr>
<tr>
<td>Not taking Calcium</td>
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<td>0</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>HOSPITAL GROUP</th>
<th>Taking Estrogen</th>
<th>STUDY ENTRY</th>
<th>STUDY COMPLETION</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>11</td>
<td>19</td>
<td></td>
</tr>
<tr>
<td>Not taking Estrogen</td>
<td>31</td>
<td>23</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>HOME GROUP</th>
<th>Taking Estrogen</th>
<th>STUDY ENTRY</th>
<th>STUDY COMPLETION</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>12</td>
<td>20</td>
<td></td>
</tr>
<tr>
<td>Not taking Estrogen</td>
<td>37</td>
<td>29</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>HOSPITAL GROUP</th>
<th>Taking other medications</th>
<th>STUDY ENTRY</th>
<th>STUDY COMPLETION</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>7</td>
<td>13</td>
<td></td>
</tr>
<tr>
<td>Not taking other medications</td>
<td>35</td>
<td>29</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>HOME GROUP</th>
<th>Taking other medications</th>
<th>STUDY ENTRY</th>
<th>STUDY COMPLETION</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>7</td>
<td>16</td>
<td></td>
</tr>
<tr>
<td>Not taking other medications</td>
<td>42</td>
<td>33</td>
<td></td>
</tr>
</tbody>
</table>
“other” medications. Because of the recent shift in the use of bisphosphonates, this information was analyzed separately. Seven women in each group were taking didronel. At study conclusion, 5 women were taking didronel and 7 were taking fosamax in the hospital group. In the home group, 7 were taking didronel, and 10 were taking fosamax. Given, the small sample size in each group, the hospital and home groups were analyzed collectively. Fosamax was not available as a treatment option for osteoporosis at study entry, as it had not yet received federal approval.

In the current study, the 12 women taking didronel for the 5 year period had an average improvement of 4% in the spinal BMD. There were no significant changes in the femoral neck BMD in this group. No subjects were initially taking Fosamax; however, 17 women were taking this medication for an average of 14.3 months at study conclusion. These women had an average improvement of 6.6% in the lumbar spine, and 4.5% in the femoral neck.

**Bone Mineral Density**

The average percentage change in BMD over the five-year study is summarized in Figure 3. In the hospital group, the DPA in the spine was 73.7% of that reported for young healthy women, whereas at study conclusion, as measured by DEXA, the BMD had increased to 78.1%. In the home group, the initial bone density of the spine, as measured by DPA was 74.1% of that reported for young healthy women, and at study conclusion, as measured by DEXA, the BMD had increased to 77.5%. The percentage of individuals in each group that exhibited a change spinal BMD is summarized in Figure 4.

In the femoral neck, the BMD, as measured by DEXA was 74.0% at study entry in the hospital group, which improved to 75.1% at study conclusion. In the home group, the initial
FIGURE 1

ESTROGEN USAGE

STUDY ENTRY

TAKING ESTROGEN

NOT TAKING ESTROGEN

74%

56%

STUDY CONCLUSION

TAKING ESTROGEN

NOT TAKING ESTROGEN

FIGURE 2

ESTROGEN USAGE & BONE MINERAL DENSITY

PERCENT IMPROVEMENT

HOSPITAL GROUP

N=17

N=2

N=16

N=3

SPINE L2-L4 BMD

HIP-FEMORAL NECK BMD

PERCENT IMPROVEMENT

HOME GROUP

N=18

N=2

N=10

51

SPINE L2-L4 BMD

HIP-FEMORAL NECK BMD
BMD in the femoral neck was 74.7%, which decreased to 73.8% after the five-year follow-up period. The percentage of individuals in each group that changed femoral neck BMD is summarized in Figure 5.

**Incidence of Fracture**

The incidence of fracture of both groups at study entry and conclusion is summarized in Table 7. At study entry, 11 subjects in each group reported having had at least one fracture in the previous 12 months. This group of 22 women was analyzed to determine medication usage. Thirteen of the 22 women were taking no medication for osteoporosis at study entry. At study conclusion, only 4 of the 22 women with fractures at study entry reported having had a fracture over the course of the study period. Only 1 of these 22 women were not taking any medication for osteoporosis at the five-year follow-up. Both groups reported having increased their weekly caloric expenditure during their time in the program.

**Statistics**

In the statistical analysis, the only significant factor arriving from the ANOVA was time, i.e., the change from the start to the finish of the study. In particular, the groups did not differ significantly in terms of any of the dependent variables. Therefore, the hypothesis was proven true, as there were no differences in the clinical outcomes between the two groups.

The effects tested for in the ANOVA included: main effects of group, other medications at time 2, fractures at time 1; also evaluated were the interactions between group and medications at T2, group and fractures at T1, fractures at T1 and medications at T22 and all interactions between the time factor and the above effects. There was no evidence that any of these factors was important in distinguishing the levels of significance of the independent variables.
5-YEAR CHANGE IN BMD
Average Percentage Change in BMD

Figure 3
Percentage of Each Group that Changed Spinal BMD (L2-L4)

HOSPITAL GROUP

HOME GROUP

PERCENT THAT IMPROVED BMD

PERCENT THAT DECREASED BMD

FIVE YEAR FOLLOW-UP PERIOD

STUDY ENTRY

STUDY CONCLUSION
Figure 5

Percentage of Each Group that Changed Femoral Neck BMD

[Bar chart showing percentage change in femoral neck BMD between study entry and conclusion for hospital and home groups over a five-year follow-up period.]
### Table 7

#### Incidence of Fracture

<table>
<thead>
<tr>
<th></th>
<th>Hospital Group</th>
<th>Home Group</th>
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</thead>
<tbody>
<tr>
<td><strong>Study Entry</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of subjects with fractures</td>
<td>11</td>
<td>11</td>
</tr>
<tr>
<td>Taking Estrogen</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Taking other medication (incl. Calcium)</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Taking no medication</td>
<td>6</td>
<td>7</td>
</tr>
<tr>
<td>Weekly caloric expenditure</td>
<td>797</td>
<td>787</td>
</tr>
</tbody>
</table>

|                          |                |            |
| **Study Conclusion**     |                |            |
| Number of subjects with fractures at Study Entry having subsequent fractures | 2              | 2          |
| Taking Estrogen          | 5              | 4          |
| Taking other medication  | 6              | 6          |
| Taking no medication     | 0              | 1          |
| Weekly caloric expenditure | 950            | 905        |
Discussion

The results from the current study indicate that for the post-menopausal women with osteoporosis who participated in The PRO Program it was possible to stabilize the BMD of the lumbar site over the five-year study period. The study group that participated in the supervised exercise program were also found to sustain the BMD of the femoral neck site. The home exercise group had a slight decrease in the BMD of the femoral neck site. No significant differences existed between the two groups at study entry in terms of BMD, years post-menopause, calcium intake, weekly caloric expenditure, (or use of medications for the treatment of osteoporosis.) The difference in BMD found between the two study groups at study conclusion was not statistically different.

The effect of regular exercise on the osteoporotic process is difficult to establish. In the elderly, the value of exercise to improve bone mass to a clinically useful level is uncertain. The optimal, or even the minimal, level of exercise necessary to retard or ameliorate bone loss has yet to be determined. Presently, there is a paucity of long-term longitudinal studies on the effects of exercise on bone in post-menopausal women. Although there have been many studies looking at the effects of exercise on bone density in the distal radius and lumbar spine, few studies have examined the long-term changes in the proximal femur. This makes comparisons to the literature rather limited. In the current study, bone mineral density of the femoral neck was examined because most hip fractures occur at the femoral neck and at an earlier age than those at other sites (133). Mechanical factors do not have a great effect on Ward's triangle because it lacks muscle attachments (133).
The majority of cross-sectional studies examining the effects of exercise on BMD have compared the bone mass in athletes to a group of sedentary subjects. Shimegi et al. examined BMD in 3 groups of healthy post-menopausal women aged 49-61 years (82). The three subject groups included volleyball players, joggers, and sedentary controls. Bone mineral density of L2-L4, as measured by DEXA, in the volleyball players and joggers was significantly greater than that of the control group.

Dook et al. recently examined the effects of 20 or more years of consistent athletic training in mature women (42-50 years old) (84). Four contrasting groups of netball/basketball players (high impact), runners/filed hockey players (medium impact), swimmers (non impact), and sedentary controls were examined. A major finding of the study was that long-term involvement in a high and medium impact loading activity was associated with greater whole body and regional leg BMD than both swimmers and abstinence from athletic participation.

The majority of cross-sectional studies have examined long-term habitual exercisers engaged in intense activities. It is unclear, therefore, how these results can be extrapolated to the general population who tend to engage in a more moderate exercise program. Nevertheless, these results provide further evidence of the beneficial effects of exercise and provides a basis for the development of long-term exercise programs for skeletal maintenance.

In the current study, the exercise program was of a moderate intensity, in that there were no high impact activities. Grove et al. recently compared the bone density in 2 groups of post-menopausal women: one engaging in high impact exercise, and one following a low impact program (96). The difference in BMD between the two groups was not significant. The authors concluded that 20 minutes of moderate intensity, low impact exercise, 3 days per
week, for 1 year is effective in maintaining BMD in early post-menopausal women. The results of the current study are in agreement with that of Grove et al. Many of the subjects in the current study were also taking medications known to affect bone homeostasis, which possibly played a synergistic role.

In a recent placebo controlled, 2 year prospective trial of two estrogen-progestin regimens in healthy post-menopausal women no synergistic effect of exercise and estrogen on BMD could be shown (110). The exercise program alone did not increase BMD over 1 year and did not add to the effects of estrogen. The mean time after the menopause was 2.75 years, therefore, subjects were much younger than those in the current study. Also the initial BMD values were much higher in this study, which makes comparisons to the current study rather limited.

Cross-sectional studies have found a greater lumbar spine bone density in exercisers than in non-exercisers (87). In an extensive four-year study in women 35 to 65 years of age, Smith et al. were able to show that the rate of decline in bone mineral content was significantly less in a group doing aerobic exercise than in a control group (134). A recent two-year longitudinal study of elderly athletes supports a strong relationship between changes in weight bearing exercise and lumbar BMD in females over age 50 (135). The group of 27 exercisers maintained an average of 197.8, +43.7 minutes per week of aerobic exercise (which consisted of running and aerobic dancing). Reductions in exercise habits were associated with a significant bone loss, while continuation of the exercise program at a given level appeared to offer protection from rapid bone loss. The current study supports this concept, as the weekly caloric expenditure was similar between the two groups at study entry, increased slightly in
both at study conclusion, and both groups exhibited an maintained lumbar BMD.

Not only is bone density higher in physically active people, but increased activity is associated with a lower rate of age-related bone loss. Jacobson et. al. reported a 0.7 % decrease per year in spine density in a control population of women older than 50 years that was not exhibited in a group of more active subjects (85). The “active” women exercised 3 times per week for a minimum of 3 years. This is a similar training protocol to the exercise program in the current study, and the results are in agreement.

Harrison et. al. investigated the value of a program for the rehabilitation of osteoporotic patients in 1993 (136). The program was assessed, based on a four-year follow-up of 139 patients referred to the program over its initial 2 years of operation. Patients had annual clinical assessments, and bone mass measurements by neutron activation analysis. Seventy-eight of the 139 patients remained in the program over the four-year follow-up. The effect of the program on the osteoporosis process was inconclusive. The 37 patients (Group 2) that obtained the greatest improvement in fitness (VO2 max > 6 ml/kg/min), had a significantly greater reduction in back pain than did the 36 (Group 1) with a less significant improvement (VO2 max < 6 ml/kg/min.). Group 2 also had, on average, a greater increase in bone mass over the 4 years, and had fewer new vertebral fractures. While these findings were encouraging, they did not reach significance at the p<0.5 level.

In their study, the improvement in bone mass can be attributed to fluoride treatment. Increases in bone mass of the axial skeleton have been established with fluoride treatment (137). It is possible that the patients taking medication were more concerned with their disease, and therefore, were more committed to the exercise program. Therefore, it is
impossible, from this study, to determine whether improved fitness, as a result of regular exercise, had a beneficial effect on the prevention of fractures. Alternatively, improved fitness may have been possible only in those patients in whom few or no fractures occurred. A well-

Caplan et. al. assessed the effects of twice-weekly aerobic weight-bearing exercise on bone density in post-menopausal women (95). The mean percentage change in the lumbar BMD was −0.8% in exercisers and −3.8% in controls. The mean percentage change in the trochanteric BMD was +9.6% in exercisers and −4.4% in controls. They found an age-related reduction in both the vertebral and femoral BMD, which seemed to occur in steps, particularly in the vertebral BMD between the fifty-fifty nine year age groups, and in the femoral neck BMD between the seventh and eighth decades. This likely corresponds to the two phases of post-menopausal and senile bone loss (37).

The majority of cross-sectional and prospective training studies in post-menopausal women have used healthy women as their subjects. It is believed that after the initial acceleration in bone loss following menopause, the effects of aging predominate. In the current study, the average years post-menopause were 18.4 in the hospital group and 16.2 in the home group. It is worth highlighting that both groups achieved some stability in their BMD values over the course of the study.

Two population-based studies failed to find a relationship between level of physical activity and bone mass (134). In a study of young women, Sowers et. al. found that bone mass in the radius, measured by SPA, was not correlated with physical activity. Physical activity, however, was measured using a questionnaire developed for a previous study involving elderly individuals. Smith et. al. has postulated that decreased physical activity in the aged plays only
a limited role in the overall pattern of age-related bone loss (134). They compared the levels of activity between two distinct age groups, where influences from unidentified cohort differences may have been substantial. This study also failed to account for the effects of estrogen deprivation at the time of menopause.

A factor, which is believed to increase BMD, is body weight acting through a local mechanical effect (138). The home group did gain, on average, 6.2 kilograms over the course of the five-year follow-up. The hospital group gained 1.6 kilograms over the study period. Both groups had a similar improvement in spinal BMD; therefore, weight gain, in itself, is not the likely reason for the increase in BMD.

Current Treatment Options

The bone density data arising from the PEPI trial showed that all protocols of estrogen replacement therapy (ERT) resulted in similar improvements in spinal bone mass (139). The placebo group had a mean loss of 2.7% in bone mass. This indicates that conventional ERT, regardless of the type of protocol, acts similarly to protect against post-menopausal bone loss. Therefore, in the current study, it was simply noted whether or not each subject was taking estrogen, and the specific dosages were not examined.

Although ERT may be appropriate for the majority of women, many are reluctant to initiate treatment, or remain on ERT (140). In the current study, all of the patients that were initially taking ERT at study entry remained on ERT at study conclusion five years later. It is unclear as to why the group exhibited this high compliance to the prescribed regimen. Perhaps they did not experience the common side effects of ERT, such as withdrawal bleeding, headache, and nausea. The majority of the women taking ERT exhibited a large improvement in BMD
over the course of the study. It is possible that the benefit of their therapy outweighed the bothersome side effects. This indicates that with specific education and reassurance by the patient’s pharmacist and physician, patient acceptance of ERT can be improved.

An interesting finding in the current study is that at study conclusion 100 % of subjects reported taking a minimum of 1000 mg of elemental calcium daily. This was determined during their annual clinical assessment, which did not include a nutritional analysis, therefore, this finding must be viewed with caution. Nevertheless, it is important to note, as Dawson-Hughes et. al. demonstrated that calcium supplementation of women five years beyond the menopause resulted in significant gains in BMD at several sites measured compared to placebo-treated control subjects (66). The women in the current study had the opportunity to attend numerous lectures by nutritionists, pharmacists, and physicians on the benefits of calcium supplementation. This may, in part, explain their high compliance to following calcium intake recommendations.

Recently, two oral bisphosphonates, etidronate disodium (didronel) plus calcium carbonate and alendronate disodium (Fosamax), have clearly demonstrated an ability to increase BMD (140). Etidronate is the longest-studied bisphosphonate, with seven years of clinical trial experience. Evidence from a number of randomized trials shows a significant increase in spinal bone density over pretreatment values, and an accompanying fifty percent reduction in the incidence of new vertebral fractures (141). A gradual increase in bone density has been reported, averaging approximately 5 % in the lumbar spine after 3 years of use (141). In the current study, the 7 women in the hospital group and the 7 women in the home group, who were taking didronel at study entry, had a similar improvement of approximately 4 % in the
spinal BMD. There was no significant change in the femoral neck BMD in this group, which is in agreement with other studies (140).

In a recent three-year study, alendronate was found to increase the BMD of the lumbar spine by 8% and the femoral neck by 5% (142). In the current study, no subjects were taking alendronate at study entry, as it had not yet received federal approval for the treatment of osteoporosis. At study conclusion, there was a significant shift in the use of Fosamax. Seventeen women were taking this medication for an average of 14.3 months. They had similar improvements in BMD values to that reported in the literature (142).

Focusing solely on improving the BMD is addressing only part of the problem; prevention of falls is likely to contribute substantially to reducing fracture rates. While the current study did not have information in the patient's chart to record the number of falls, there was a significant reduction in the number of fractures over the five-year-follow-up period. In a recent controlled trial of weight-bearing exercise in 92 older women (mean age 64.5), only 2 fractures were recorded during the two year study period (125). They found that the study group taking calcium and engaging in exercise experienced fewer falls than the women taking calcium only. This finding supports the view that improving balance, strength, and flexibility through exercise may make falls less likely (143).

Meunier recently published the results of a cross-sectional study, during which the femoral BMD was measured in 128 females living in retirement homes. They found that the annual rate of bone loss in this population was between 1-8% per year. A reduction in one standard deviation corresponds to a about a 10% reduction in bone mass. This means that in about 6 years, these elderly people will have a relative risk of fracture which is multiplied by about
2.6. It also means that if one can stop the bone loss and maintain the incidence at age 85 at the age 75 level, one could probably prevent 20-40% of the hip fractures.

The present study cannot elucidate which training program is most appropriate for preventing bone loss. Both groups employed an exercise regime consisting of weight-bearing and muscle strengthening exercise. The investigation of the effects of exercise on bone requires consideration of the exercise intensity. The hormonal response to varying intensities has been shown to be different (144). For example, growth hormone, which has an anabolic effect on bone is acutely increased to a greater extent with intermittent bouts of exercise, compared to continuous aerobic exercise (144). In the present study, the subjects were instructed to carry on aerobic exercise at 70-80% of their maximal predicted heart rate for a continuous 20 minutes. All subjects used different weights, ranging from one to five pounds; therefore, the intensity of the muscle strength training program was not controlled for in the program.

Many studies have demonstrated a relationship between physical activity and bone density, but it is extremely important to use reliable and valid methods to draw meaningful conclusions. The validity and reproducibility of the Physical Activity Index (PAI) from the College Alumnus Questionnaire (CAQ) was recently determined in 78 men and women with a broad range of physical activity habits (129). The results suggested that the CAQ is a moderately good instrument for classifying people for habitual activity levels, and that the instrument has acceptable reproducibility. The questionnaire items are recalled reasonably well, and they contribute to the validity of the questionnaire as a measure of overall leisure-time physical activity expenditure. These results are consistent with earlier validation studies.
that showed statistically significant associations among the PAI and measures of cardiorespiratory fitness (145). The capacity of a questionnaire to perform well against validation measures does not appear to be solely related to its length or attention to detail (146). More important seems to be the logic with which its questions are answered. This point is particularly well borne out with the CAQ.

A review of six studies measuring physical activity by questionnaire revealed that more dissimilarities than similarities exist between questionnaires used to measure physical activity (147). Caution should therefore be used in the comparison of studies measuring physical activity by questionnaire because of differences in the time frame of the activity measured and variations in the calculation methods.

It has been previously reported that subjects under estimated the amount of walking and stair climbing they reported in the questionnaire (146). The under estimation of walking may be related to the wording in the questionnaire, which asks “the number of blocks walked in a day.” This wording may cause subjects to think only about walking in the context of city blocks and does not reflect the majority of walking each day, which occurs, around the house and for transportation. In an effort to control for this, the hospital attendance records were consulted to determine the amount of times per week that the subjects engaged in exercise. This was possible for the hospital group, but obviously not feasible for the home group.

Black-Sandler et al. previously employed the Paffenbarger questionnaire as a measurement tool of physical activity (148). They defined exercise in terms of weekly caloric expenditure. They found no significant correlation between kcal/week expended and bone mineral content. In their study, however, the time frame for assessing physical activity was only three days. It
is likely that bone mass is dependent upon long-term physical activity, as the effects of activity on bone are cumulative. Therefore, self-reports of physical activity over a three day time span may not be at all representative of activity during the preceding years. It may be more valid to correlate bone density with historical levels of activity as opposed to short-term activity (149).

The cross-sectional nature of the present study allowed observations to be made without the large investment of time and resources required for a five-year longitudinal study. Another advantage of the design is that it is not susceptible to drop out because the subjects had already completed the training and the measurements had already been made.

In most cross-sectional studies, there is an inherent absence of bone mass measurements prior to the onset of exercise. Therefore, the difference in bone mass demonstrated between exercisers and controls can be attributed to either the exercise or to selection differences. An advantage of the current study was that it was a repeated measures design, therefore the differences noted in BMD between groups cannot be attributed to selection differences. Also, few studies have used sufficient matching as a method of increasing comparability between study groups. In the current study, groups were matched based on years post-menopause, average height, average BMD measurement, and medication status.

Limitations of the study

Several limitations of this study are apparent. The study groups were determined by identifying those patients who chose one of two exercise rehabilitation programs upon study entry; the patients were not prospectively assigned to the two groups. However, a comparison of group characteristics at program entry revealed no significant differences between the two
groups, which might have resulted from the non-random assignment.

Another potential effect of the non-random assignment of subjects is the problem presented by self-selection. Patients who are capable of working independently and successfully on their own may choose the home-exercise program, while patients who recognize their need for supervision and group support to comply to an exercise program may choose the hospital-based group program. It is possible that, as a result of self-selection, one type of exercise program, undertaken by a particular subject, produces different results than would occur with random assignment. A stronger experimental design is one in which a random allocation of subjects is used.

Another limitation of this study is the lack of a control group of osteoporotic patients. This would identify the contribution of exercise alone to the demonstrated improvement in bone mineral density. The rate of bone loss for the lumbar and trochanteric regions in the study group was not consistent with the published data, which shows an annual rate of bone loss of some 2.2 to 3.0% per year at the beginning of menopause, which declines to about 0.3% per year by age 70 (8).

A potential difficulty exists in terms of the validity of the retrospective measurement of the physical activity. It is difficult to directly measure activity and ensure reliability and validity without impacting behavior (150). When relying on memory, biased estimates of activity often occur. The subject's ability to recall activity, and weekly and seasonal variations in activity patterns can impact results. In an attempt to control for this, the attendance records at the hospital classes, the physician assessments, and the physical activity questionnaire were all consulted to obtain "as true a picture" of weekly caloric expenditure as possible.
One limitation of this study that could have influenced the outcome is the actual amount of supervision provided by the group exercise program. Of the 42 women in the supervised program, 27 attended an average of two times per week, while the remaining 15 attended only one class per week. The remainder of their program was conducted at home. Therefore, there was an additional "hybrid" group of supervised/independent exercisers (n=15). This subset of women was analyzed separately, as it is possible that if provided with more frequent supervision, the patients may have achieved better results in the hospital-based program. This was not the case in the current study, as there was no significant difference in any of the clinical outcomes measured between the women that attended the program twice per week and those that attended only one time per week. If patients can actually achieve equitable and safe results in an unsupervised, or even a minimally supervised program, considerable savings of health care dollars could be actualized in terms of the potential diminished morbidity associated with the initiation of an exercise program.

Finally, the quality of the performance of the exercise program is not known for the patients that exercised at home. Although every participant initially attended four supervised exercise classes at the start of the program, their performance was not checked clinically on an ongoing basis, due to the limited time constraint of their annual assessment.

Even in the absence of any significant improvement in bone mass, regular exercise may be beneficial in many other ways. Regular exercise undertaken by the elderly individual has been reported to have a beneficial effect on various psychological factors and a general sense of well-being (151). Furthermore, good muscle tone should reduce the probability of falls that result from unsteadiness. Unfortunately, the incidence of falls was not available in each
patient's chart to clarify this relationship in the current study.

Osteoporosis steals more than bone; it can rob independence. Loss of independence is the consequence of osteoporosis-related fractures that patients dread most. These fears have a foundation fact. Results of a six-year follow-up of 185 patients showed that only 9% were able to walk on their own outside following a hip fracture (152). This can leave patients isolated, alone, and out of contact with the world. Many osteoporotic patients remain indoors, in fear of venturing outdoors and having a fall. Most falls, however, occur indoors, usually in the bathroom or kitchen, contrary to many patient's fears.

Much of the benefit of participating in the PRO program may be attributed to the moral support derived from the social interactions with other patients and with health professionals. In the group setting of the PRO program, the patients were encouraged to leave their homes, to participate in the group activities, and to return to a more physically active lifestyle.

A great number of the patients found the PRO program of sufficient benefit to continue in it for at least five years. Based on the results of the patient status questionnaire completed at study end (Table 8), it can be said that most patients felt that they had benefited significantly as a result of their participation in the program. The majority of the women indicated that their mobility and balance improved as a result of the exercise program. They also reported an improvement in their co-ordination and an overall decrease in pain from osteoporosis. Based on the encouragement of their fellow patients with osteoporosis, many found that, with perseverance, they were able to carry out progressively more vigorous exercises without pain. This gives each individual the confidence to return to more energetic and interesting activities, and greatly improves their quality of life.
### TABLE 8

**PATIENT QUESTIONNAIRE**

<table>
<thead>
<tr>
<th></th>
<th>HOSPITAL GROUP</th>
<th>HOME GROUP</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Q.1 If the PRO Program did not exist, do you think you would exercise:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>a) Less often</td>
<td>32</td>
<td>26</td>
</tr>
<tr>
<td>b) More often</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>c) About the same</td>
<td>10</td>
<td>21</td>
</tr>
</tbody>
</table>

| **Q.2 How has the PRO program affected your ability to move around (mobility)?** |                      |
| a) Caused an increase | 36 | 37 |
| b) Caused a decrease  | 2  | 10 |
| c) No change          | 4  | 12 |

| **Q.3 How has the PRO Program affected your tendency to fall (balance)?** |                      |
| a) Caused an increase | 2  | 10 |
| b) Caused a decrease  | 22 | 14 |
| c) No change          | 18 | 23 |

| **Q.4 How has the PRO Program affected the co-ordination of your movements?** |                      |
| a) Caused an increase | 36 | 27 |
| b) Caused a decrease  | 2  | 2  |
| c) No change          | 4  | 18 |

| **Q.5 Since starting the PRO Program, what has been with your experience with pain from osteoporosis?** |                      |
| a) Overall increase in pain | 4  | 12 |
| b) Overall decrease in pain  | 24 | 12 |
| c) No pain experienced       | 14 | 23 |
The length of the study is important as it shows the acceptability of such an exercise program in this age group. The finding of a beneficial effect adds weight to the calls for other patients to start exercising, and for an increased range of facilities to be made available for older individuals in the community.

Exercise therapy has been shown to contribute to many psychological improvements, such as decreasing anxiety and depression, enhancing self-confidence and esteem, and producing a general sense of well-being (95). The contribution of exercise towards the psychological well-being may be the single most important component of the rehabilitation, especially if it permits the individual to resume a normal vocational and social life.

There are a host of other variables that could be beneficially influenced by supervised group exercise, but these were not included in this study. Heath, in a long-term follow-up of bypass patients discharged from an exercise rehabilitation program, found that the physical activity patterns of the patients in the supervised program were significantly more vigorous than the patients in the unsupervised program (153). Traits, such as motivation, depression, and socio-economic status, may contribute greatly to the effectiveness of a supervised, versus an unsupervised, exercise rehabilitation program and should be considered in the future.

The majority of the exercise rehabilitation studies have been small. The focus of these studies has been quite narrow in that they investigated predominantly male post-bypass patients participating in a supervised group exercise program. The research has mainly focused on the cardiovascular and aerobic benefits of exercise, and has virtually ignored other indices of physical health, such as bone mineral density.

The direct cost of osteoporosis to society has been estimated to be $20 billion annually in
the United States (population 250 million). The greatest proportion of these costs comes from hip fractures. Such numbers, of course, do not take into account the morbidity and impaired quality of life for the individuals who suffer fractures (154).

A number of cost-effective delivery systems are now being sought in many countries; home exercise seems to be an attractive alternative to clinically supervised exercise programs. The benefits of supervised versus unsupervised exercise has just recently been addressed. To date, two studies have investigated this issue, and have presented widely different results. Stevens et al. (155) found no significant difference between supervised and unsupervised exercise in improving exercise capacity in their post-bypass sample, whereas Heath et. al. (153) found supervised exercise to be significantly more beneficial. However, the follow-up period for both studies was short, lasting only 10 to 12 weeks in duration.

The question as to whether a supervised exercise program is required to assist patients in achieving their optimal functional capacity is an important one to answer at this time, due to the increasing costs of providing healthcare services. The duration for which these services should be provided is another important factor to consider.

The results from the current study clearly demonstrate that the women received a significant benefit as a result of their participation in the PRO Program. It was not important whether or not the women exercised in a supervised program or in an unsupervised environment. They both enjoyed similar benefits. It would appear that the most important factor involves the referral to the program. This often involves a referral to see an endocrinologist. It was noted that a large percentage of the women at study entry were not taking estrogen or any other medications for osteoporosis. At study conclusion, these numbers had improved significantly,
and this was associated with a reduction in the number of fractures over the study period.

Interestingly, no subjects that had fractures at study entry, experienced a new fracture by the study conclusion. Thus, it was likely a combination of medical therapy and the exercise programs that resulted in the significant gains in spinal BMD and the reduction in fractures in the groups studied.

In the future, studies should be designed to define the effect of mechanical loading on bone resorption and formation. These are required to define the cellular mechanisms by which mechanical loads are transduce and lead to an increase in bone mass. Also, studies should be designed to quantify the interactive effect of physical activity, nutrition, medications, and bone mass. Finally, further randomized exercise intervention trials are necessary to quantify the effect of specific physical activities in balance, co-ordination, and strength of muscle groups that may affect the risk of falling.

Conclusion

It is quite likely that bone mass is more closely related to the type of activity (e.g., weight-bearing) performed, rather than the level of energy expenditure. Physical activity has been defined as the level of energy expenditure; exercise has been defined as a subset of physical activity involving repetitive, purposeful movement (156). Therefore, whereas defining activity in terms of energy expenditure has been appropriate for studying obesity, defining activity in terms of weight-bearing exercise may be more appropriate for studying a program directed at influencing bone mass.

The correlation between the BMD and the weekly caloric expenditure of the subjects in the present study was not strong; therefore, no conclusion can be drawn as to the minimum level
of caloric expenditure necessary in order to retard bone loss. It can be concluded that post-menopausal women with osteoporosis can maintain spinal and femoral neck BMD provided that they engage in an exercise program and are followed very closely by their physician. These findings are promising and bode well for women with osteoporosis, particularly in light of the recent advances in the medical treatment of this crippling disease.
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Appendix I

Physical Activity Questionnaire
PRO PROGRAM PHYSICAL ACTIVITY QUESTIONNAIRE

1. Approximately how many flights of stairs do you climb each day (10 steps equals one flight)?

2. How many city blocks or equivalent do you walk each day (12 blocks equals one mile)?

3. Approximately how many hours per week do you engage in physical activity (for example bowling, dancing, yardwork, housework, etc.)

4. How often do you do formal exercises at home?
   - [ ] never
   - [ ] less than one per week
   - [ ] between one and two times per week
   - [ ] three times per week or more

5. If the PRO Program did not exist, do you think you would do physical exercise less often, about the same, or more often?
   - [ ] less often
   - [ ] about the same amount
   - [ ] more often

6. Has the PRO Program affected the following aspects of your fitness:
<table>
<thead>
<tr>
<th>Caused an Increase</th>
<th>Caused a Decrease</th>
<th>No Impact</th>
</tr>
</thead>
<tbody>
<tr>
<td>• ability to move around (mobility)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• tendency to fall (balance)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• co-ordination of your movements</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

7. Please indicate by checking the corresponding box if any of the following have happened to you, and how often since you started the PRO Program.

<table>
<thead>
<tr>
<th>Hip fracture</th>
<th>Wrist fracture</th>
<th>Vertebal fracture</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

8. Since starting the PRO Program, what has been your experience with pain from osteoporosis

- [ ] overall increase in pain
- [ ] overall decrease in pain
- [ ] pain about the same
Thank you for agreeing to be a part of The Queen Elizabeth Hospital’s study into the benefits of exercise in patients enrolled in the PRO Program. Some of the information about the study is as follows:

WHAT IS THE PURPOSE OF THIS SURVEY?

The survey asks you to answer as accurately as possible questions regarding your level of physical activity. From your response and surveys completed by more than 90 other participants in the PRO Program, we hope to increase our knowledge of the optimal amount of physical activity required in the prevention and treatment of osteoporosis.

HOW DID WE CHOOSE YOUR NAME?

Names of the clients of the PRO Program that have been enrolled in the program for five years or more were randomly selected to be part of the study. It is strictly by chance that you are one of them.

WILL MY RESPONSES BE CONFIDENTIAL?

Yes, most definitely! There will be no way for anyone to know which survey was yours. Also, we will be grouping the information received from the survey and no individual responses will be identified in the result.

WHO IS THE PERSON RESPONSIBLE FOR THE SURVEY?

We ask for your assistance by completing and returning the enclosed survey by ________________. If you have any questions or concerns, please call Mike Walker at 597-3005. Thank you.
Appendix II

Yearly Physician Assessment
### 3. Yearly Assessment Database (ASSESSMENT)

<table>
<thead>
<tr>
<th>Field</th>
<th>VarName</th>
<th>Definition</th>
<th>Type</th>
<th>Size</th>
</tr>
</thead>
<tbody>
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Appendix III
Patient Consent Form
Consent to Exercise Program for Osteoporosis
THE REHABILITATION INSTITUTE OF TORONTO
PREVENTION AND REHABILITATION OF OSTEOPOROSIS
PROGRAM

Patient Consent Form

I understand that I will be asked to participate in a study to examine the efficacy of a supervised exercise program in the prevention and treatment of osteoporosis.

I understand that I will be asked to complete a questionnaire detailing my daily physical activity and experiences with osteoporosis and that the information submitted will remain absolutely confidential and will not appear or be identified in any part of the study.

I also understand that I am under no obligation to participate in the study and that I am free to refuse to answer specific questions. Refusal to participate will not affect my care at The Rehabilitation Institute of Toronto in any way.

I understand that the findings from this study may assist the PRO Program in enhancing patient care and management.

I understand that any questions or concerns may be forwarded to the researchers, Dr. Chow or Mike Walker at (416) 597-3005.

I, ____________________________, consent to participate in the aforementioned study.

Dated: ____________________________

Signature: ____________________________
CONSENT TO EXERCISE PROGRAMME FOR
OSTEOPOROSIS

I, ____________________________ (Patient's Name), hereby consent to participate in
an Exercise Programme under the Title of Prevention and Rehabilitation for
Osteoporosis being conducted by ____________________________ (Physician), and his
assistants and the staff of ____________________________ (Hospital’s Name) and the Bone
and Mineral Metabolism Unit.

The Research Programme has been fully explained to my understanding by
__________________________ (Physician). I fully understand that the nature of the
research is to determine the aspects of exercise upon my diagnosed condition
of Osteoporosis. While exercise is believed to be beneficial, the optimal
exercise programme needs to be established. I understand that all data
gathered will be used as part of a research study, and that any
identification of myself will be kept in strictest confidence by the
research team. Publishable data is the sole property of the programme and
may not necessarily be revealed to me. That the release of information in
this programme will be restricted only to the Osteoporosis Rehabilitation
Exercise Team, unless specifically consented to by me.

Date at Toronto, this __________ day of ___________ 19___.

__________________________ Witness ____________________________ Signature of Patient
Appendix IV

Medication Analysis
### E1 * E2 Crosstabulation

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### Oth1 * Oth2 Crosstabulation

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Appendix V

Research Proposal Approval
University of Toronto  

OFFICE OF RESEARCH SERVICES

PROTOCOL REFERENCE #2620

August 14, 1997

Dr. M. Plyley  
School of Physical & Health Education  
320 Huron Street  
University of Toronto

Dear Dr. Plyley:

We are writing to advise you that a Review Committee composed of Drs. E. Thorsen, C. Rodgers and G. Regehr has granted approval to the research study entitled, "A Cross-Sectional Analysis of the Efficacy of a Supervised Exercise Program in the Prevention of Osteoporosis".

During the course of the research, any significant deviations from the approved protocol (that is, any deviation which would lead to an increase in risk or a decrease in benefit to human subjects) and/or any unanticipated developments within the research should be brought to the attention of the Office of Research Services.

Best wishes for the successful completion of your project.

Yours sincerely,

Susan Pilon  
Executive Officer  
Human Subjects Review Committee

SP/mr  
Enclosure

cc: Professor B. Kidd, R. Chow, M. Walker
16 October 1997

Dr. R. Chow
c/o PRO Program
Rehabilitation Institute of Toronto

Dear Dr. Chow,

Re: A Cross-Sectional Study of the Efficacy of a Supervised Exercise Program in the Prevention and Treatment of Osteoporosis

At its most recent meeting of 15 October 1997, the Research Sub-Committee of the Rehabilitation Institute of Toronto reviewed the above research proposal. I am pleased to inform you that the proposal was approved.

I wish you well in your research endeavors.

Yours sincerely,

M.E. Charlton
Acting Chair, Research Sub-Committee

cc: Dr. M. Plyley
    Mr. M. Walker