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Exercise for Optimising Bone Health

in Premenopausal Women

By

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ABSTRACT

Osteoporotic fractures in the elderly are a worldwide epidemic and the increasing ageing of the global population means that the economic cost of these fractures will continue to rise. Leading a physically active lifestyle offers one preventative measure, so it is important that the general public know precisely how to exercise. This thesis describes investigations into the effects of brief, high-impact, unilateral exercise on neuromuscular and bone health, concentrating on defining the optimum weekly frequency of exercise required for healthy but sedentary premenopausal women to maximise their peak bone mass.

A 6 week-long pilot study involving 13 participants first assessed the effectiveness and feasibility of a high-impact, unilateral exercise program in terms of ground impact forces and subject acceptability, with the aim to use this exercise design in a long-term intervention. Firstly, ground reaction forces during a maximal vertical hop (mean(SD) 3.7(0.4) times body weight) exceeded those acting on one leg during a maximal jump (mean 2.1(0.4) times body weight per leg, assuming symmetrical distribution of body weight on each foot), which were also greater than impact forces measured in previous studies that demonstrated significant increases in hip BMD following a jumping intervention. These comparisons indicated that the proposed exercise design could generate sufficient loading to produce significant gains in bone mass. Secondly, preliminary results suggested that the exercises would be feasible to use in a long-term intervention, as reflected by the high short-term compliance rate (99%), absence of injury, and positive feedback received from the non-athletic women involved in the pilot study.

The main experimental study initially recruited 97 women, of whom 89 (age 33.6(11.1) years) were eligible. They were randomly assigned to perform 50 multidirectional hops on the same leg 0, 2, 4, or 7 days per week. Compliance amongst exercisers was 86.7(10.6)% for the 6-month intervention and measurements were taken at baseline and post-intervention. By the end of the intervention, they were hopping at a height of 73.4(27.9)mm that corresponded to ground reaction forces of 2.8(0.5) times body weight. BMD increased significantly in the exercise relative to the control limb in women exercising daily at the femoral neck, upper neck, and Ward’s triangle regions of the hip. The difference in response between legs at the femoral neck was significantly greater in those exercising daily than in those exercising 0 or 2 days per week. Significant improvements in neuromuscular function were also observed.

Examination of correlations between variables indicated that hip BMD was related to muscle function, whilst hip geometry was most strongly predicted by fat-free mass, thereby suggesting that in addition to regular exercise, maintaining a healthy musculature has positive benefits on the skeleton.
In conclusion, the most important finding of this research is that more frequent loading appears to produce the greatest changes in BMD, thereby suggesting that exercise may need to be performed more frequently than currently recommended. A high-impact, unilateral exercise design was found to be a feasible method to investigate the effects of mechanical loading on bone and can now be used in future intervention studies to further refine exercise recommendations that may serve to prevent osteoporosis-related fractures in different populations.

KEY WORDS: EXERCISE; BONE MINERAL DENSITY; BONE GEOMETRY; PREMENOPAUSAL WOMEN; IMPACT; MUSCLE FUNCTION
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<td>BMD</td>
<td>Bone mineral density</td>
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<td>BMC</td>
<td>Bone mineral content</td>
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<td>BMI</td>
<td>Body mass index</td>
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<tr>
<td>CSA</td>
<td>Cross-sectional area</td>
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<td>CSMI</td>
<td>Cross-sectional moment of inertia</td>
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<td>CV</td>
<td>Coefficient of variation</td>
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<td>DXA</td>
<td>Dual X-ray absorptiometry</td>
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<td>FM</td>
<td>Fat mass</td>
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<td>FFM</td>
<td>Fat-free mass</td>
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<td>FSI</td>
<td>Femoral strength index</td>
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<td>GRF</td>
<td>Ground reaction force</td>
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<td>IKES</td>
<td>Isometric knee extension strength</td>
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<td>MES</td>
<td>Minimum effective strain</td>
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<td>pQCT</td>
<td>Peripheral quantitative computerised tomography</td>
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<td>RCT</td>
<td>Randomised controlled trial</td>
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<td>RT</td>
<td>Resistance training</td>
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CHAPTER ONE

Introduction

Osteoporosis is defined as “a systemic skeletal disease characterised by low bone mass and microarchitectural deterioration of bone tissue, with a consequent increase in bone fragility and susceptibility to fracture” (World Health Organisation 1994). The term “microarchitectural deterioration” refers to the thinning of trabeculae and the loss of intertrabecular connections in bone; changes in bone mass and structure that reduce the overall strength of bone and make it prone to fracture, which is the clinical manifestation of the disease. Osteoporosis is commonly only diagnosed after a fracture has occurred, which is unsatisfactory, as the condition should ideally be diagnosed beforehand or, even better, preventative measures should be taken so that fracture never occurs. Being the outcome of a dysfunctional form-function relationship, the common sites of osteoporotic fracture are those sites that come under loading from the weight of gravity or the weight of the body during a fall, i.e. predominantly the lumbar spine, proximal femur, and radius (Chan et al. 2003).

Bone mineral density (BMD) is the amount of bone per square centimetre of cross-sectional area and is expressed by a T-score, thus providing a relative comparison to the BMD of a healthy, sex-matched young adult at peak BMD. The World Health Organisation (WHO) classifies a T-score of ≤−2.5 (2.5 standard deviations below the young, healthy mean) as representative of osteoporosis and severe or established osteoporosis is diagnosed when this low T-value is accompanied by one or more fragility fractures (World Health Organisation 1994). The WHO intended to use these reference ranges to compare the prevalence of osteoporosis in different countries, but it has become common-use for their classification to be adopted in a clinical setting to decide whether or not an individual requires treatment. In conjunction with the risk factors for falling, BMD is recognised as one of the most important determinants of fracture risk, with fracture risk increasing 50% for each standard deviation decrease in BMD (Marshall et al. 1996).

Bone loss is a universal phenomenon that is part of the ageing process, but due to differences in bone and endocrine physiology, women lose more than men over their lifetime. The disease is a major public health problem with great social and economic significance. One in five men and one in two women in the U.K. over 50 years of age will suffer an osteoporosis-related fracture in their lifetime (van Staa et al. 2001) and the annual cost for all fractures is £1.5 billion (Torgerson and Dolan 2000). This includes providing treatment and nursing home care for patients whose disabilities
have cost them their independence in daily living. Hip fracture is the most severe cause of mortality and morbidity, with 1 in every 2 patients never regaining full pre-fracture functional ability and hence requiring institutional care (Osnes et al. 2004), and 1 in 5 dying within the first year of sustaining the fracture (Forsen et al. 1999). Because of the ageing of the global population, these figures are set to continually increase.

The primary focus on osteoporosis tends to be on older women who have diminished menopausal levels of oestrogen. However, two mechanisms that principally determine adult bone health are peak bone mineral density (BMD) at skeletal maturity and the rate of bone loss with advancing age, thus maximising premenopausal BMD is a critical strategy for the prevention of osteoporosis and resultant fractures later in life. A substantial body of literature has resulted in the consensus that participating in regular physical activity can positively improve bone mineral status (Kohrt et al. 2004). The advantage of exercise over methods such as dietary intervention is that it increases the skeleton’s resistance to fracture by improving and maintaining both BMD and neuromuscular competency, thus reducing skeletal fragility and predisposition to falls (Drinkwater et al. 1995, Smith and Gilligan 1996).

As stressed by the WHO, “encouraging physical activity at all ages is therefore a top priority to prevent osteoporosis” (Chan et al. 2003) but unfortunately, a mere 24% of British women aged 18 years and over meet the current recommended target of 30 minutes of moderate exercise on at least five days per week, and 16% do not spend any time at all in activities of at least moderate intensity (Department of Health 2004), thereby indicating that very few women take advantage of the most effective method of delaying bone loss offered by physical activity. Furthermore, physical activity levels decline dramatically as women get older (Figure 1.1), which is the time when maintaining bone mass is most critical. Although exercise recommendations for cardiovascular fitness have already been precisely defined (Pollock et al. 1998), it is unlikely that the same exercise prescription applies to cardiovascular health and skeletal health, and to both pre- and postmenopausal women. Bone’s response to exercise differs across the lifespan according to the age and health of the individual (Beck and Snow 2003), yet in the past research has predominantly involved preventing bone loss in postmenopausal women, rather than optimising peak bone mass in premenopausal women (Wallace and Cumming 2000).
From a clinical viewpoint, it is important to determine the optimal conditions of exercise to maximise BMD before the menopause so that the effects of its loss post menopause will not be as severe. It is therefore the overall aim of this PhD to more precisely define the exercise prescription for young women to ensure that they attain their peak BMD.

The thesis is presented in the following sections:

1. A comprehensive literature review first covers what is already known about the effects of exercise on bone and what still needs to be established. A rationale for the present research is consequently developed.
2. Justification for the materials and methods predominantly employed for the proposed studies is described in the General Methods chapter.
3. The purpose of the pilot study is to assess the effectiveness and feasibility of unilateral exercise to use as a model to determine exercise effects on bone.
4. Chapter five presents a 6 month-long intervention that used the proposed unilateral exercise programme to clarify the exercise prescription required for optimum bone health in premenopausal women.
5. Following this, the study comprising chapter six examined the associations between bone variables, neuromuscular function, and body composition; and identified the main predictors of bone status in non-athletic women.

6. Finally, overall conclusions draw together the findings and their implications for public health strategies are considered. Limitations of the research are also highlighted and avenues of future research are suggested.
Figure 2.1: Bone architecture of a typical long bone
(Image taken from www.shoppingtrolley.net/images/long-bone)
2.1 Background

2.1.1 Bone Biology

The human skeleton serves several functions. These include support and protection for the soft tissues vital for immediate maintenance of life (the central nervous system and cardiovascular system), a cavity for bone-forming cells, a large reservoir for key minerals (especially calcium), and a rigid structure that provides sites of attachment for muscles to produce locomotion.

There are two types of bone: cortical (or compact) and trabecular (or spongy). The dense structure of cortical bone is well suited to the supportive, protective, and mechanical functions of the skeleton. It makes up the outer layer of all bones and the shafts of long bones, resulting in over 80% of total skeletal mass (Einhorn 2001). The remainder is trabecular bone, which forms the inner part of axial bones and the ends of long bones. Due to its internal network of crossbridges that are filled with marrow, trabecular bone provides the site for bone metabolism and for the storage of minerals. Figure 2.1 on the opposite page illustrates the composition of a typical long bone.

2.1.2 Bone Remodelling

Throughout life, the skeleton undergoes continuous remodelling that involves the removal of old bone and replacement with new bone. It is an essential process that enables growth, adaptation of bone’s mass and structure, the maintenance of serum calcium levels, and the continuous repair of the micro fractures and fatigue damage that bone sustains daily thus keeping its structure sufficiently strong to support the body. Remodelling is a complicated process of many interactions regulated by local and systemic factors that comprise electrical and mechanical forces, hormones, growth factors, and cytokines (Lanyon 1996).
The remodelling process (Figure 2.2) is initiated by the activation of osteoblastic lining cells that secrete collagenase to remove the thin layer of non-mineralised bone typical of a resting bone surface. This exposes the mineralised bone underneath to the resorbing osteoclasts, which excavate the bone matrix to a maximum depth of 50-60µm by releasing acids and enzymes. As bone is resorbed, osteoclasts release cytokines (signalling molecules) that attract and stimulate osteoblasts to lay down new bone. There is a short reversal phase when a cement line is formed, then the osteoblasts produce osteoids (collagen and ground substance) at a rate of 0.5-1.0µm/day (hence one cycle taking 3-4 months to complete (Drnkwater 1994)). When the thickness of osteoids reaches 12-15µm, bone begins to mineralise from the bottom up until the resting bone surface is again covered by a thin layer of non-mineralised bone and lining cells. During formation, some osteoblasts are trapped in the bone matrix and thus become osteocytes, the pathway of communication through which stresses and strains are detected (mechanotransduction). The amount of new bone that is formed is controlled by the number of osteoblasts present and the amount of mineral that each cell produces. Mechanical loading results in increases in
both the number of osteoblasts recruited and their synthetic activity (Lanyon 1996). In a young, healthy skeleton the coupling of bone resorption and formation is balanced so that bone mass is maintained, but many influencing factors either negatively or positively cause an imbalance, thereby leading to an overall loss of bone mass (e.g. from oestrogen deficiency) or to an overall gain (e.g. from weight-bearing exercise). In the elderly, bone resorption usually exceeds formation so that removed bone is not replaced, thus leading to a thinning of the internal trabecular network.

Heredity determines between 50% and 85% (depending on the skeletal site) of peak BMD variance (Heaney et al. 2000) and common determinants of BMD such as age exist, but a range of environmental factors; notably, exercise, hormones, and nutrition can greatly determine attainment of peak bone mass and the rate of age-related bone loss (Nichols et al. 2000). Figure 2.3 displays the difference in fracture risk between people who both achieve their (genetically-determined) peak bone mass and then endeavour to maintain it through environmental influences such as physical activity and diet, and those who do not. The relative influence of these factors also varies from site to site, with those predominantly composed of trabecular bone (e.g. the spine) responding more rapidly to a change in the environment than those predominantly made up of cortical bone (e.g. the hip) (Einhorn 2001).

**Figure 2.3: Graph illustrating how attainment of peak bone mass determines fracture risk later in life (taken from Heaney et al. 2000)**
2.2 The effects of exercise on bone health

Bone strength and resistance to fracture are determined by bone's material and structural properties, and these properties are the consequence of the independent and interdependent expressions of multiple genetic, physical, hormonal, and nutritional factors. A substantial body of literature has led to the consensus that participating in regular physical activity can positively improve bone health and the advantage of exercise is that it also improves neuromuscular competency, thus reducing predisposition to falls and subsequent fracture risk (Kohrt et al. 2004), which is the clinical endpoint of osteoporosis. The rest of this chapter will review the existing evidence that supports the positive effects of exercise on bone properties and, after highlighting gaps in current knowledge, the rationale for researching the effects of exercise on bone health will be developed.

2.2.1 Bone as a mechanostat

It is hypothesised that bone cells have sensors within the cell membrane where mechanical strain, fluid/pressure shifts, or electrical charges are converted into a biochemical signal, subsequently modifying bone structure as well as mass to enhance skeletal fatigue resistance (Smith and Clark 2005). Even though the precise stimuli to which osteoblasts and osteoclasts respond remains unconfirmed, it is understood that there is a dynamic regulatory system in bone that adapts its strength to its mechanical environment by alterations in the amount and architecture of bone at each skeletal site. This mechanism for functional adaptation in the skeleton is described as Wolff’s Law after the German scientist who first recognised in 1892 how “every change in environment is followed by change in internal architecture”. Since then, the principle has further developed into the mechanostat theory (Frost 1987), which describes the mechanism of bone adaptation like a thermostat (Figure 2.4): Bone has various set points of minimum effective strain (MES) that are independently and interdependently determined by local (e.g. previous load-bearing), systemic (e.g. hormones), and external (e.g. diet) factors, and those of age and genetics (Skerry 2006). If mechanical loading increases and exceeds the relative MES (i.e. what bone is accustomed to), the ratio of bone formation to bone resorption is temporarily unbalanced until mineral mass increases and structural adaptation occurs so that bone becomes strong enough to support the greater functional demands being placed upon it. A new MES is then established. Conversely, if strain on bone decreases and falls below the MES threshold or if disuse follows a period of hyperactivity, bone becomes
less mechanically competent because a less demanding external environment allows bone to reduce the metabolic cost of maintaining mineral that is needed to support greater loading (Lanyon 1996). It must be stressed that substantial bone loss accompanies unloading. Krolner and Toft (1983) documented spine BMD to deteriorate by 3.6% following only 27 days bed rest during hospitalisation, femoral neck BMD has been seen to decrease 8.7% following 8 months immobilisation due to injury (Sievänen et al. 1994), and during spaceflight spine and femoral neck BMD were reported to diminish by a considerable 1.06% and 1.15% per month, respectively (LeBlanc et al. 2000).

Figure 2.4: Diagrammatic representation of the mechanostat theory (Frost 1987)

2.2.2 Site-specificity of exercise

Wolff's Law and the process of functional adaptation puts forward that bones respond to increased loads by becoming stronger and hence more mechanically competent. It then follows that it is the specific sites of the skeleton that come under the greatest loads which will undergo the most changes. Further developing the concept of the mechanostat theory (Frost 1987), it has been proposed that each location in the skeleton has its own set point threshold for mechanical loading (Skerry 2006). For
example, if the tibia was to regularly experience the stress to which the ribs are exposed, then there would be substantial bone loss due to disuse.

The theoretical basis of the site-specificity of exercise on bone has been displayed in human studies. In premenopausal women who completed a year-long intervention study, those who undertook lower body exercise training along with upper body training increased BMD at their hips and spine. On the other hand, participants who trained only their lower body benefited the BMD at their hips but not their spine (Winters-Stone and Snow 2006). These findings were explained by bone’s response to site-specific exercise, a principle that is consistent with other exercise interventions (Kannus et al. 1994, Kerr et al. 1996). Even when ground impacts and muscle contraction provide a strong bone stimulus, as during jumping interventions, detectable increases in BMD occur only at the hip, not the spine (Bassey and Ramsdale 1994, Bassey et al. 1998). Although these findings are weakened by self-selection, inter-individual differences, or the possibility that activity outside the intervention contributed to BMD gains; the site-specificity of bone to loading is reinforced by the cross-sectional comparisons of racquet-sport athletes who have greater BMD in their dominant, playing limbs compared to their non-playing limbs (Haapasalo et al. 1998, Huddleston et al. 1980, Kannus et al. 1994), as well as by the significant increases in BMD of the trained limb following a long-term, unilateral exercise intervention (Kerr et al. 1996).

2.2.3 Principle of baseline values

The "initial values" principle of exercise training states that individuals with the lowest values of a physiological system have the greatest capacity for improving (Drnkwater et al. 1995, Sheth 1999). This theory also applies to the skeletal system because exercise appears to be most effective in people with low BMD, with attenuation of effect for progressively more athletic individuals (Heaney et al. 2000); a phenomenon reiterated by the mechanostat theory. Baseline BMD is noted to be the most significant predictor of BMD change in response to training (Valnionpää et al. 2006), with individuals having baseline BMD values in the lowest quartile undergoing 2-5 times greater increases than those in the upper quartile (Winters-Stone and Snow 2003). In contrast, there is data that demonstrate an exception to the principle of initial values. Following less intensive training during the off-season, gymnasts can successfully increase their BMD despite having baseline values well above the mean, which demonstrates that bone will respond regardless of its initial value if the load-induced strain on bone is sufficiently high (Nichols et al. 1994). Unfortunately, it is
argued that such analyses are susceptible to the effects of regression to the mean, which can bias any investigation where the response to treatment is classified relative to initial values for a given variable without the use of an appropriate control group (Shephard 2003).

2.2.4 Principle of diminishing returns

Related to the principle of baseline values is the principle of diminishing returns, which describes bone’s curvilinear nature of adaptation to mechanical loading (Figure 2.5). Bone is initially very sensitive to an increase in functional loading, but once it has adapted to a certain level of strain, further changes in bone mass and geometry are small and slow. Dalsky et al. reported a 4.2% increase in spinal BMD in postmenopausal women after 9 months of exercise, but then observed that the rate of increase fell to 1.6% during the subsequent 13 months (Dalsky et al. 1988). Because an adaptive response occurs only when a loading stimulus exceeds the usual loading conditions, continued adaptation requires a progressively increasing overload. Therefore, progression is a crucial requirement for any long-term exercise programme that aims to increase BMD (Lanyon 1996).

Figure 2.5: Graph illustrating bone’s diminishing response to exercise over time

2.2.5 Strain magnitude

Strain magnitude refers to the amount of deformation in bone caused by mechanical loading and the intensity of skeletal exercise has been suggested to be defined by the loads applied to the bone (Turner and Robling 2002). As explained previously by the mechanostat theory, strain needs to exceed the set MES, which animal studies have demonstrated to be about 2000-3000 microstrain. After this point and until the upper
MES threshold where excessive loading causes damage to bone, there is a graded dose-response relationship between the peak strain magnitude and the change in the mass of bone tissue present (Lanyon 1987, Rubin and Lanyon 1985). Whether the same thresholds exist in humans is less clear, but evidence for the importance of magnitude of mechanical loading comes from numerous studies that have compared the BMD values of individuals who take part in different types of sports. Significant BMD differences in the weight-bearing bones between athletes of sports involving high GRF and athletes participating in low- or no-Impact sports have consistently been shown (Kerr et al. 2001, Lee et al. 1995, Nikander et al. 2006, Pettersson et al. 2000). Large differences are regularly observed between gymnasts whose hip and spine BMD values are 30-40% higher than those of long-distance runners (Robinson et al. 1995), and although the cross-sectional nature of such observations mean that it could be argued that dense bones make for poor runners, a more plausible explanation is that the movements in gymnastics involve higher impact forces (10-12 times body weight) (McNitt-Gray 1993) compared to running (2-3 times body weight) (Cavanagh and Lafontune 1980). Moreover, not only are high-Impact sports associated with a greater amount of internal mineral, but athletes involved in high-Impact sports have bone that is superior in structure (Nikander et al. 2006) (Figure 2.6). On the other hand, the bone properties of swimmers are no different from those of sedentary controls (Fehling et al. 1995, Nikander et al. 2006). Cross-sectional comparisons cannot rule out that individuals with genetically favourable BMD are more likely to participate in sport and exercise (Chilibeck et al. 1995), though support for the importance of peak load in increasing bone mass also comes from a randomised intervention trial conducted by Kerr and colleagues. They concluded that postmenopausal bone mass can be significantly increased by a strength regimen of high-loads and low repetitions but not by an endurance regimen that uses low-loads and high repetitions (Kerr et al. 1996).
Figure 2.6: Differences in BMC and polar section modulus (an index of bone strength against torsion and bending) between athletes participating in sports of different loading modalities. Where the 95% confidence interval does not cross the zero line (the value of the controls), the difference is statistically significant (p<0.05). (Figures taken from Nikander et al. 2006)

2.2.6 Strain rate

Strain rate refers to the rate at which peak mechanical strain increases and decreases. A high rate of strain provides a greater osteogenic stimulus than the same peak strain achieved more slowly. Under the same amount of strain, rat ulnae subjected to in vivo loading of a high strain rate (0.1 με/s) were shown to have a 54% greater osteogenic response than the moderate strain rate group (0.03 με/s), who in turn demonstrated a 13% larger response than the low strain rate group (0.018 με/s) (Mosley and Lanyon 1998). It has also been proposed that the required magnitude of strain to initiate new bone formation decreases as the rate of strain increases (Turner and Robling 2005).

In humans, the lack of consensus that exists amongst resistance training (RT) studies in enhancing BMD (Friedlander et al. 1995, Gleeson et al. 1990, Pruitt et al. 1995, Snow-Harter et al. 1992) may be due to the predominant use of machine weights, which are safer than free weights but possibly too controlled, thereby generating an inadequate rate of strain on the loaded bones. Consequently, it may be preferential to design exercise studies that involve free, high-velocity movements, e.g. weights.

2.2.7 Strain distribution

The "error strain distribution hypothesis" (Lanyon 1996) proposes that bone adaptation is driven by unusual strain distributions as bone cells enhance the skeleton's structural competence by adjusting to perceived deviations from normal in
the distribution of dynamic strains. For example, strain produced by loading in torsion appears to be less osteogenic than the same strain produced by loading in longitudinal compression (Boyce et al. 1998). Furthermore, it has been suggested that the distribution of strain may too be more important than its magnitude (Turner and Robling 2002), as unusual patterns of strain can stimulate an osteogenic response at a lower MES (Lanyon 1987).

Milgrom et al. found that zig-zag hopping generated the highest compression, tension, and shear strains in the tibiae compared to those of jogging and walking, and hence it was proposed that this kind of activity may be an optimal tibial bone-strengthening exercise (Milgrom et al. 2001). Accordingly, sports such as squash, volleyball, and gymnastics, which stress bone in a variety of directions, may be more osteogenic activities than sports consisting of only one direction of movement, such as running (Nikander et al. 2005).

2.2.8 Strain duration

Strain cycles are the number of loading repetitions at a given magnitude that change bone’s dimensions, i.e. produce an osteogenic response. However, evidence from animal models suggests that this time it is the intensity (i.e. strain magnitude) rather than the duration of exercise that is the main determinant of increasing BMD (Block et al. 1989, Fehling et al. 1995). The number of cycles of loading applied to bones appears to become unimportant once a certain threshold level has been reached (Rubin and Lanyon 1985). As few as 36 loading cycles that lasted only 72s stimulated maximal bone formation in turkey ulnae (Lanyon 1987) and 100 jumps per day produced the same bone response in rats as 40 jumps (Umemura et al. 1997).

Evidence of a threshold volume of strain in humans is not so clear as observations made in animal studies, though Vainionpaa and colleagues (2006) reported that less than 100 accelerations per day are positively associated with higher BMD providing they exceed 3.9g. It seems that the skeleton will adapt to the current loading to maintain strength and that increasing the duration of exercise above the established level confers no additional benefit. Rather, prolonged periods of mechanical loading saturate bone’s adaptive response to mechanical load because, like mechanoreceptor cells that sense touch and sound, bone cells exhibit a desensitisation phenomenon in the presence of prolonged mechanical loading (Robling et al. 2001, Umemura et al. 1997).
2.2.9 Strain frequency

Subsequently, experimental protocols that insert rest periods between each load cycle appear to restore mechanosensitivity to bone cells and considerably increase bone's anabolic response to loading (Robling et al. 2001, Turner and Robling 2005), whereas static load applied continuously produces no effect different from disuse (LaMothe and Zernicke 2004). In rats allowed time to recover between 36 identical daily loading cycles, 14s of recovery resulted in significantly higher (66-190%) relative bone formation rates compared to any of the three shorter recovery periods (0.5, 3.5, and 7s). Likewise, 5 consecutive days of 100 low-magnitude loading cycles in avian ulnae did not significantly elevate the rate of bone formation compared to contralateral bones, but separating the 100 cycles into 10 bouts with 10s rest did (Srinivasan et al. 2002).

Mechanical loading is not only more osteogenic if short rest intervals are inserted between cycles, but also if each bout of loading is separated by several hours. Four hours rest have been shown to double bone formation in animal models and after 24 hours rest, 98% mechanosensitivity returns (Robling et al. 2001). Some authors have demonstrated that mechanical loading is more effective with an even longer duration of “time off”. For a period of 15 weeks, Saxon et al. loaded one group of rat ulnae for a total of 10 weeks with 5 weeks rest in the middle of the intervention period, whereas another group were loaded continuously for the whole 15 weeks. Both groups experienced significant bone gains during the first 5 weeks but after initial adaptation to the mechanical loading, bone's responsiveness decreased, as the bones of the group who had 5 weeks off were significantly more resistant to fracture at the end of the intervention period (Saxon et al. 2005). Such animal studies indicate that the osteogenic response can be improved by adding more exercise sessions rather than lengthening the duration of individual sessions (Turner and Robling 2002).

It is likely that human bone would also become less desensitised to loading if regular rest intervals interspersed loading cycles, yet as with animal studies, the optimum frequency of loading bouts, i.e. the number of times per week that is required for maximising bone accrual has not yet been defined. To-date, no single study has compared the effects of different frequencies of the same exercise programme on bone. There are reports of significant improvements in spinal and hip BMD in women resulting from exercise sessions that range from twice a week (Sugiyama et al. 2002) to six times a week (Bassey et al. 1998), but simply comparing separate studies of different weekly frequencies is inadequate due to variations in the methodology (e.g.
the type, intensity, and duration of the different exercise programmes) and the participants involved (e.g. age, hormone status, and calcium intake). Moreover, there does not appear to be much variation in the prescribed exercise frequency of existing randomised controlled trials (RCTs), as the majority of exercise interventions select a training frequency of 3 days per week. The very few RCTs that consist of more frequent exercise sessions are those whose intervention involves a short-lasting bout of exercise (Bassey and Ramsdale 1994, Bassey et al. 1998, Sinaki et al. 1989), understandably to maintain compliance. Bassey (Bassey et al. 1998) and Kato (Kato et al. 2006) both used vertical jumping as an exercise intervention, which lasted a similar length of time (5 and 6 months, respectively), although the total number of jumps performed on each occasion was considerably different (50 vs. 10). Femoral neck BMD increased 2.1% in Bassey’s study, which could be regarded as a comparable amount to the 2.6% increase in Kato’s study, but the difference in spinal BMD was noticeably different (1.1% vs. 2.4%). Confidence intervals may have overlapped, thus suggesting that the difference is not as large as it appears, but unfortunately this cannot be confirmed because the authors did not report confidence intervals or standard deviations of the change. As a result, even when trying to match studies as closely as possible it is impossible to explain differences in BMD response by the exercise frequency of the intervention; a difficulty caused by the heterogeneity of study design and participants.

2.2.10 Exercise type and bone

Resistance exercise

In addition to high-impact exercise, resistance exercise is offered as another method to increase or maintain BMD (Kohrt et al., 2004), although evidence from RCTs is not consistent with this suggestion. The type, intensity, and duration of RT appears to significantly determine the overall treatment effect on BMD (Martyn-St James and Carroll 2006a), as does the age and consequent hormonal levels of the individual (Martyn-St James and Carroll 2006b). The observation of pre- and postmenopausal women having different BMD responses to the same intervention has also been noted with other forms of exercise (Bassey et al. 1998), which is thought to be principally due to their differing levels of circulating oestrogen – RT appears to provide the necessary stimulus for increased skeletal incorporation of dietary calcium, while adequate oestrogen permits bone mineralisation to take place (Layne and Nelson 1999). The ability of many studies involving postmenopausal women to show training-associated increases in BMD is largely determined by their hormonal and nutritional
profiles along with the intensity of exercise. Only high-intensity RT can improve BMD in postmenopausal women not on HRT (Kerr et al. 1996), whereas moderate intensity RT is effective in those who do take HRT (Judge et al. 2005).

Aside from the overriding influence of oestrogen and calcium availability, the type and intensity of RT are important considerations if positive changes in BMD are to be observed. In general, protocols involving higher exercise intensities are more likely to produce increases in BMD, especially in postmenopausal women in whom training with loads of <80% of 1RM tend to be ineffective (Maddalozzo and Snow 2000, Rhodes et al. 2000a). Peak load is more important than the number of repetitions (Kerr et al. 1996) and it has recently been found that power training is a more effective osteogenic stimulus than conventional strength training, since rapidly performed movements have been demonstrated to maintain BMD at the spine and hip in older women while slow movements resulted in loss of BMD at these sites (Stengel et al. 2005). In younger women, most RT studies are intensive enough to induce substantial gains in muscular strength, yet few detected simultaneous gains in BMD. The lack of response in bone could be due to the majority of study participants being healthy and physically active, which confers pre-training values that are already high and less sensitive to the initiation of training (Vuori et al. 1994). This emphasises that RT protocols for young women need to provide uncustomary as well as challenging loading patterns in order to elicit a maximal osteogenic response.

The weekly frequency of training does not seem to distinguish the strength of effect on bone. The majority of RT studies involve participants training three days per week, but there is an approximately equal number of significant and non significant results from lower training frequencies (Maddalozzo and Snow, 2000; Kohrt et al, 1997; Nelson et al, 1994). Although the optimum frequency is yet to be defined, training needs to be continued regularly because increases in BMD are reversed upon cessation (Winters and Snow 2000). Additionally, due to the physiology of bone, it is likely that the 8-12 months duration of most trials is not long enough for bone to establish a new basal state of bone remodelling and hence produce significant changes in BMD (Chilibeck et al. 1995).

However, a major issue that has been overlooked is the influence of bone’s geometric and structural properties on overall bone resistive strength. Bone’s response to RT is underestimated because the outcome of most exercise studies is BMD or BMC, which are only measurements of bone mass. With the increased use of the pQCT technique meaningful changes in bone cortex and the ratio of cortical to trabecular bone could
represent improvements in bending strength despite an absence of changes in BMD, as has been the case in high-impact exercise studies (Uusi-Rasi et al. 2003).

Overall, RCTs indicate that RT has the potential to benefit the skeleton of pre- and postmenopausal women (Kelley 1998, Layne and Nelson 1999). Increases in bone mass following training interventions may be small due to the training protocol being insufficiently osteogenic; inadequately long; in premenopausal women, not exceeding their already-high rate of bone mass accretion; and in postmenopausal women, having limiting amounts of oestrogen and calcium (Borer 2005). However, ensuring that young women successfully achieve their highest possible peak BMD and simply suppressing bone loss in older women are valuable means of reducing both populations’ risk of developing osteoporosis (Rhodes et al. 2000b). Moreover, in preventing fall-related fracture, which is the significant end-point of osteoporosis, the importance of balance, muscle strength, postural stability, and coordination cannot be overemphasised. Therefore, in addition to potentially increasing or maintaining BMD, RT has great value in effectively influencing these related risk factors and significantly enhancing health-related quality of life, especially in older individuals (Liu-Ambrose et al. 2005)

*Aerobic exercise*

Measuring aerobic capacity has been used as an indirect way of quantifying physical activity and has been demonstrated to be higher in athletes with high BMD than in controls with lower BMD, thereby leading to the suggestion that fitness-related variables could be used to detect individuals with reduced bone mass (Vicente-Rodriguez et al. 2004). However, it is likely that these cross-sectional comparisons between athletes and controls are simply detecting a positive association that has been caused by the athletes experiencing greater mechanical loading from spending longer doing physical activity, which would confer their greater aerobic fitness. There are mixed findings in non-athletic individuals, with some studies not detecting significant associations between aerobic capacity and hip or spine BMD (Kemmler et al. 2004), while others report that aerobic capacity was the only predictor of hip BMD (Pocock et al. 1986). These discrepancies may result from variations in the habitual physical activity levels of the subjects in the two studies, since those in the former did not have a history of athletic training whereas those in the latter were defined as “normal”, hence they may have formerly participated in more exercise and have continued doing habitual activity. Again, the best way to determine a true association is by conducting a RCT. Stewart et al. had men and women between 55 and 75 years
of age perform 6 months of resistance and aerobic training 3 times per week for 6 months. It was calculated that change in aerobic fitness explained the 13% change in femoral neck BMD in women, but that in the men it was change in lean mass, not fitness, which explained their increased BMD (Stewart et al. 2005). Nevertheless, these findings still fail to distinguish the contribution of impact and muscle loading to BMD from fitness per se, as the aerobic component of the exercise intervention involved running on a treadmill or stair stepping, which, along with resistance exercise, are high-impact activities that generate osteogenic loading.

The cardiovascular intensity of exercise seems to exert an influence on bone metabolism. Results of an eight-week aerobic and anaerobic running intervention found aerobic training to lead to a reduced rate of bone resorption, whilst anaerobic training led to accelerated bone turnover (Woitge et al. 1998). A similar observation was made by Nowak et al. during their investigation into levels of bone markers during the annual training cycle of young male runners. The authors found that aerobic training during the athletes’ preparatory phase improved bone metabolism, whereas intensive endurance training containing a high proportion of anaerobic work during the pre-competition and competition periods resulted in deterioration in bone formation (Nowak et al. 2002).

Aerobic vs. resistance exercise

Applying the findings from animal studies to a human model that the most effective strain for a maximal osteogenic response are not only high in magnitude but also unusually distributed, of a high rate, and brief in duration, then a diverse RT programme would be expected to produce greater increases in BMD than an endurance training programme such as running, even though high-impacts are involved. There have been few RCTs that have directly compared aerobic, impact exercise and RT, and results are inconclusive. There is evidence that both types of exercise are equally effective in increasing BMD in pre- and post-menopausal women (Chow et al. 1987, Rikli and McManis 1990, Snow-Harter et al. 1992), and some authors have suggested that their combination is more effective than either intervention alone (Davee et al. 1990, Friedlander et al. 1995). Even meta-analyses that combine the treatment effect of several studies have mixed outcomes. Wallace and Cumming did not find a difference in effectiveness between endurance, impact exercise and RT (Wallace and Cumming 2000), yet Wolff and colleagues showed endurance exercise was superior to RT in increasing postmenopausal BMD (Wolff et al. 1999). A probable explanation may be that they included RT studies whose
prescription for older individuals did not fulfil all the necessary requirements of high strains and high strain rates.

2.2.11 Exercise and bone geometry

Compared to BMD, relatively little is known about the relationships between mechanical loading and bone geometry. It has been proposed that whole bone functional capacity is principally determined by structural characteristics such as bone size and shape, cortical thickness, cortical geometry, and trabecular architecture, rather than the amount of bone mass present (Jarvínén et al. 2005). For the same bone area and density, small increases in the cross-sectional moment of inertia of bone (CSMI) have been seen to effect a disproportionate influence on estimated torsional and bending strength (Forwood 2001), but this contribution of altered geometry to fracture risk is not detected by clinical assessment of bone using DXA because it fails to distinguish geometry from density (Jarvínén et al. 1999). This is exemplified by results of a 6-month strength training programme of the upper limb that beneficially redistributed bone resulting in improved structural rigidity, despite no evidence of an increase in BMD (Adami et al. 1999). The interaction between material (i.e. mineral mass) and structural properties is important because the two parameters appear to vary independently in response to a given treatment, in this case, exercise.

Cross-sectional comparisons of the playing and non-playing arms of racquet-sport players consistently demonstrate evidence of site-specific, favourable geometrical adaptation (Haapasalo et al. 2000, Kontulainen et al. 2003). Cross-sectional area of the humerus in tennis players has been shown to be as much as 35% bigger in the dominant arm of males and 28% in females (Jones et al. 1977); changes that have more recently been explained by a combination of periosteal and endocortical adaptations that result in increased CSMI (Haapasalo et al. 1996). Comparisons of athletes involved in different sports have also recognised certain qualities in bone structural measurements that relate to the nature of the mechanical loading. Weight-bearing bones in athletes appear to be characterised by greater CSMI and indices of strength (Forwood 2001), larger diaphyses and thicker cortices, as well as denser trabecular bone (Nikander et al. 2006); a feature that enables bone to absorb more load energy per unit volume (Currey 2002). The effect of different loading patterns of exercise on bone geometry is reinforced by longitudinal studies in animals, whereby the largest strains were associated with increased periosteal bone formation in rats (Mosley et al. 1997), and similarly, the intensity of impacts during a 12 month intervention in humans was the most significant predictor of change in bone geometry.
(explaining up to 36% change) (Vainionpää et al. 2007). The latter study demonstrated that although bone circumference increased overall in exercisers compared to controls, CSMI correlated most strongly with impacts >1.1g while cortical thickness and bone circumference correlated with impacts >3.9g. These findings suggest that even low-impact exercise can initiate a positive redistribution of bone mass, while a higher threshold is perhaps needed to increase bone mass. The 2.5% increment in bone strength measured in the most active exercisers was also significantly higher than that observed in the least active exercisers, thus indicating that the number of impacts is also an important determinant of bone geometric adaptation. It can be argued that these changes in bone geometry observed in longitudinal studies are small, but if exercise is continued for several years the cumulative influence on bone may greatly enhance ultimate fatigue resistance (Warden et al. 2005).

From their results of an exercise intervention in growing girls, Petit and colleagues (Petit et al. 2002) brought up a very interesting issue. They proposed that bending can be improved by increasing bone diameter but, unless CSA also increases, there would be a reduction in areal BMD. Since a high-impact activity like jumping increases axial compression compared with normal activity, and because axial compression is uniformly distributed through the bone cross-section rather than being concentrated on the periosteal surface; bone formation on the endosteal surface seems more likely. This could explain why exercise effects on bone with areal BMD as the outcome measure (as with DXA) shows greater response to impact forces. They consequently hypothesise that some types of exercise could actually improve bone strength through relevant structural adaptation and that high-impact exercise is only critical to increase BMD, which is the parameter of bone most commonly measured. Several cross-sectional studies would agree with this proposition and assert that, like bone material changes, bone structural adaptations are loading-specific (Faulkner et al. 2003, Heinonen et al. 2001, Nikander et al. 2005), as a mechanically competent bone structure should evolve in relation to the magnitude and modality of customary loading (Nikander et al. 2006). The association of thicker cortices with impact loading at weight-bearing sites with similar CSA (Nikander et al. 2006) is also in accordance with the optimum shape of tubular bones in terms of minimal weight and rigidity (Currey 1984). As with exercise-induced increases in bone mass, there is no direct evidence that increased mechanical loading affects anti-fracture efficacy, but in long bones, positive alterations in CSMI result in a mechanically stiffer structure that can withstand a greater fracture load (Currey 2002).
Regardless, these cross-sectional and intervention studies clearly demonstrate that exercise-induced mechanical loading can activate a modelling response to influence bone geometry, independently of material properties. This response could be attributed to the dynamic loads from muscle force during exercise as opposed to the static load imposed by weight-bearing, because bone geometric strength has been found to be more strongly associated with lean mass than fat mass (Petit et al. 2005). However, this observation was made in overweight children, so would need to be confirmed in adult women of healthy weight.

2.2.12 Current recommendations

Evidence from both animal and human studies clearly indicate that if strains are dynamic, high in magnitude, high in rate, and of abnormal distribution, considerable bone formation can be achieved at the skeletal site coming under strain after a remarkably short duration of loading. Selection of exercises for a training regime therefore needs to be specifically based on these principles. In the UK, the Department of Health propose that “a total of at least 60 minutes of moderate-intensity physical activity each day is needed, and at least twice a week this should include activities to improve bone health (activities that produce high physical stresses on the bones), muscle strength and flexibility” (Department of Health 2004). This exercise prescription for bone health is too vague and if the findings in animal models can be transferred to humans it could be advised that brief but more frequent weekly exercise sessions are most effective in improving bone health. Animal models are not necessarily accurate for predicting bone response in humans, but they allow well-controlled manipulations in vivo to study how the physical and mechanical properties of bone adapt to mechanical loading and which characteristics of strain are most effective for osteogenesis. Of course it cannot be confirmed that human bone responds in exactly the same way as animal bone since invasive procedures cannot be carried out on humans, so cross-sectional observations of different human populations and longitudinal, intervention studies must instead be relied on to distinguish the loading characteristics for optimal bone formation in humans.

It is also important to consider the target population because outcomes from exercise studies involving athletes have certain implications in that they relate to relatively extreme conditions that are beyond the scope and capacity of ordinary, non-athletic people. High impacts are undoubtedly effective in strengthening the bones in young, healthy adults, but this kind of activity also has the potential to compromise the loaded cartilage tissue, especially at the ankle and knee (Beck and Snow 2003). As a
result, such exercise types may not be viable for older adults who have more fragile joints and a diminished sense of balance, or individuals with current or previous injuries. Consequently, different exercise recommendations are likely to be needed for different populations.

2.2.13 Summary

The following dimensions of physical activity are recognised as important to bone health: (1) type of activity with respect to the forces applied to the skeletal sites of interest, (2) rate of force applied, and (3) frequency of exposure to the activity (Turner 1998). Many more studies have addressed the first two elements, whereas the last is less well-defined. Existing knowledge tells us that rapid repetition of single load cycles appears to cause desensitisation to subsequent loading, whilst once a saturating number of cycles have been applied, bone is not stimulated any further within the same bout of loading. However, inserting a rest period of 1-4 hours seems to allow resensitisation of the mechanoreceptor system to induce additional effects. Along with the type, duration, and intensity; frequency of exercise is an important aspect of exercise prescription for optimal bone health and therefore warrants greater investigation than has been conducted so far.
2.3 Other predictors of bone mass and their interaction with exercise

It was mentioned at the start that there exists a host of factors that contribute to an individual's skeletal health. These include non-controllable influences, such as ethnicity and sex, and environmental influences that can be controlled, such as diet and exercise. The discussion so far has focused on exercise, but it is clear that exercise-induced mechanical loading is not an independent predictor of bone mass because a certain dose of loading would then have the same influence on bone irrespective of these other determinants. It is evident that their effects on bone cannot be separated, but rather they interact with one another to produce varied responses in bone. Gene-environment interactions are present when genetic factors regulate bone's response to exercise, whereas one environmental factor (e.g. calcium intake) controlling the expression of another (in this case, bone's response to exercise) is an example of an environment-environment interaction (Khan et al. 2001a).

2.3.1 Sex and age

Bone loss occurs with ageing in both men and women but while men experience trabecular thinning, the thinning in women can progress to very deep resorption cavities at certain sites that result in a loss of connections between the trabecular plates. Compared to men, women also attain a lower peak BMD and at about the age of 50 years there is a rapid decline in their BMD (Figure 2.7) due to an imbalance in the rate of bone resorption to bone formation from their loss of ovarian oestrogen production during the menopause (Borer 2005). Over their lifetimes, women lose about 30-50% of their total bone mass (Riggs et al. 1981), with reductions in spinal BMD of 2-5% per year for up to 8 years after menopause compared to about 0.4% per year in premenopausal women (Wolman and Reeve 1998). It is thought that after the menopause, the set points of minimum effective strain increase, thus transmitting a message of disuse to the bone even if normal mechanical utilisation continues (Saxon and Turner 2005). Older women therefore need greater mechanical force in order to conserve existing bone mineral. Declines in the number and vigour of osteocyte populations, levels of circulating growth factors, and production of bone matrix proteins may all be responsible for the age-related attenuation of bone's adaptive response to strain (Beck et al. 2001).
Animal studies have demonstrated that bone has an age-dependent response to mechanical loading. Following an 8-week period of unilateral daily loading of a physiologically normal level of strain, bone cross-sectional area in 1 year-old turkey ulnae increased 30.2% compared to their contralateral control ulnae, whereas the areal properties of the 3 year-old turkeys remained essentially unchanged (-3.3%) (Rubin et al. 1992). A physical signal that is clearly osteogenic in the young adult skeleton is perhaps hardly acknowledged in older bone tissue. Whether this represents a deterioration of older bone cells’ ability to perceive these physical signals or a failure of their capacity to respond is not clear. It may also be linked to the role of oestrogen in amplifying the osteogenic response to a single period of loading and its absence in raising the modelling threshold of bone strain in post-menopausal women (Lanyon and Skerry 2001). The aetiology of postmenopausal bone loss may thus be considered as an oestrogen-related failure of bone’s ability to conserve structurally adequate levels of bone mass.

Exercise Intervention studies in humans have also shown that bone’s osteogenic response to loading is age-dependent. Although a large proportion of bone mineral
increase in growing girls is attributable to growth itself, a 9-month high-impact exercise programme (60mins aerobics and step training 3 times per week) that resulted in additional bone gain in exercising premenarcheal girls, but not in exercising postmenarcheal girls (Heinonen et al. 2000) supports the hypothesis that growing bone has the strongest response to mechanical loading. Nonetheless, it is clear that exercise continues to benefit the skeleton through the other decades of life. Figure 2.8 displays a selection of RCTs that involved young, adult women and showed positive changes in BMD from brief, high-impact exercises (mainly jumping and skipping).

Figure 2.8: Percentage BMD changes per year observed in randomised controlled intervention trials of high-impact exercise in premenopausal women

*Significantly greater increase in the training group compared to the control group (p<0.05)
*Values estimated from Figure 2 in Heinonen et al. (1996) because exact data was not provided.

Postmenopausal skeletal tissue appears to respond differently to exercise from that of younger, premenopausal women. Comparison of pQCT measurements between tennis players who started young and those who started later in life suggest that mechanical loading after bone maturation does not stimulate the same cortical expansion seen in young players (Nara-Ashizawa et al. 2002). Post-menopause, mechanical loading may serve more to prevent bone loss rather than produce large increases in bone mineral, as some studies examining the effects of exercise in postmenopausal women found the training group to maintain BMD while the control group continued losing the BMD.
that is expected during this stage of life (Engelke et al. 2006). Because of the great variation in hormone status and nutrient intake between individual postmenopausal women, the effects of exercise in this population of women are inconclusive. Some authors indicate that exercise prevents bone loss in postmenopausal women regardless of whether or not they use HRT (hormone replacement therapy) (Maddalozzo et al. 2006), while others argue that a combination of exercise and HRT is required to increase postmenopausal BMD (Kohrt et al. 1995). These disparate findings may be explained by the different stages of the menopause the participants are in. Women in the former study had a mean age of 52 years, whereas those in the latter study were 60-72 years of age, so perhaps the skeletons of early postmenopausal women are more responsive to exercise.

The relatively inconsistent evidence that physical activity prevents bone loss or increases bone mineral after menopause may also be a consequence of the low intensity of exercise in training studies (Wallace and Cumming 2000). The majority of exercise studies in older women use low rather than high impact types of activities (primarily walking) as an intervention (Kelley and Kelley 2006), which may not generate sufficient strain on bone to stimulate increased bone formation. Furthermore, changes in neuromuscular performance tend to be greater than changes in BMD following exercise intervention in postmenopausal women and a more pronounced effect is often observed than in premenopausal women. Increases in muscle strength and balance in postmenopausal women have been recorded to be up to twice the magnitude of changes observed in premenopausal women following an exercise intervention (Bassey et al. 1998), which strongly implies that in older women the importance of exercise in fracture prevention could be from improved muscle function and hence reduced risk of falling, as opposed to actual improvements in bone strength.

2.3.2 Oestrogen status

Overlapping with the influence of age on bone is circulating hormone levels. It is clear that adequate oestrogen levels are a prerequisite for BMD to increase in response to strain application. Oestrogen acts directly on bone cells in a receptor mediated manner, but also indirectly via effects on other hormones and growth factors that influence BMD (Liu and Lebrun 2006). It has been proposed that the pathway through which bone senses mechanical strain and adjusts its level of remodelling accordingly is oestrogen-dependent so that an inadequate level of oestrogen increases the MES threshold, thus impairing the transmission of mechanical loading into a signal for bone
formation (Frost 1999). Cross-sectional observations support this theory, as higher BMD is observed in exercising postmenopausal women taking HRT compared to those who do not (Saxon and Turner 2005), but results from intervention studies are not always as compelling. Some studies have found the combined effect of exercise and HRT to be greater than either intervention alone (Kohrt et al. 1995, Milliken et al. 2003), whereas others did not detect this difference (Bassey et al. 1998, Maddalozzo et al. 2006). However, regardless of the strength of effect, there is no evidence to suggest that taking HRT negatively interacts with bone.

In premenopausal women, the detrimental effects of oestrogen deficiency are often highlighted in endurance athletes. There appears to be a continuum whereby the lowest BMD values are found in amenorrheic young athletes, moderate values in those with oligomenorrhea, and finally no or very little indication of low bone mass in athletes with normal menstrual function (Drinkwater et al. 1984). Even though their skeleton undergoes sufficient loading, the low body fat that is associated with endurance sports results in diminished ovarian oestrogen production (Reid et al. 1992). The pattern of high training volume, low body fat, menstrual irregularities, and low BMD is recognised clinically as The Female Athlete Triad (Otis et al. 1997). However, it would seem that the impact forces involved in gymnastics are still high enough to exceed the raised MES threshold and override the negative effects derived from a lack of oestrogen, because exceptionally high BMD values are measured in gymnasts despite the prevalence of menstrual disruption in this population (Robinson et al. 1995).

2.3.3 Oral contraceptives

While HRT augments low endogenous levels of oestrogen, oral contraceptives (OC) may replace or suppress higher endogenous production. OC are widely used not only by athletes with menstrual dysfunction, but by non-athletes too. The literature covering the effects of OC on BMD present conflicting results, as individual studies demonstrate both a positive (Recker et al. 1992) and negative (Shoepe and Snow 2005) effect of OC on BMD. A systematic review by Liu and Lebrun concludes that the evidence for a positive effect of OC on BMD is "good" in perimenopausal women, "fair" in oligo/amenorrhoeic premenopausal women, and "limited" in both anorexic and healthy premenopausal women (Liu and Lebrun, 2006). As always when comparing different studies, divergent results are attributed to differences in study design, inadequate sample sizes, the method and anatomical site of BMD measurement, heterogeneity in study populations, and in this case, the type and dose of the OC.
Examination of the effect of oestrogen dose on bone loss in postmenopausal women suggests there is a dose-response effect with net bone loss occurring at <15μg ethinyloestradiol per day, net bone gain occurring at >25μg/day, and no bone gain or loss taking place between 15 and 25μg/day (Horsman et al. 1983); thus implying that the doses used in the majority of studies that administer around 20 μg ethinyloestradiol per day may have been insufficient to have any effect on BMD. Somewhat surprisingly, intervention studies have shown the combination of exercise and OC to suppress the normal increase in BMD observed in young women (Burr et al. 2000) or to actually cause a decrease in their spinal BMD (Weaver et al. 2001). Other authors have proposed that it is the duration of OC use that determines its interaction with exercise, with short-term OC use and long-term exercise having a beneficial effect on BMD, whilst long-term OC use even along with long-term exercise having no effect (Hartard et al. 1997). It is clear that the interaction of OC with exercise requires further investigation and although it must be recognised that there is individual variation, reviewers assert that the overall advantages of OC for athletes outweigh the disadvantages (Bennell et al. 1999), especially if treating menstrual disruption (Tudor-Locke and McColl 2000) because shorter life-time oestrogen exposure has been identified as a risk factor that predicts vertebral and non-vertebral fractures (Finigan et al. 2008).

2.3.4 Diet

**Calcium intake**

One of the functions of the human skeleton is to store calcium; hence any depletion of that reserve will result in compromised bone structure, for the body must be provided with the necessary materials for bone formation to take place. Variations in calcium nutrition early in life may account for as much as a 5-10% difference in peak adult bone mass, which translates into an approximate 25-50% difference in hip fracture risk later in life (Heaney et al. 2000). Calcium intake is consistently shown to positively correlate with bone mass (Cumming 1990) and slightly reduce fracture risk (Cumming and Nevitt 1997), although the strength of relationship between calcium and bone appears to depend upon oestrogen status and consequently age. Increased dietary calcium consumption has a modest benefit on child or young adult bone health (Lanou et al. 2005), whilst during the post-menopausal period, calcium serves to prevent the rate of bone loss rather than produce a net gain (Mazess and Barden 1991). Differences between studies in calcium’s effect on bone may be related to baseline intake, with individuals with higher intakes less likely to show a response to supplementation. Compared to the site-specific effects of exercise, calcium also seems
to confer a more systemic effect on skeletal sites, even if they are unloaded. In a large cross-sectional study of young and old women, high calcium intake was positively associated with a structurally strong radius, whereas it was exercise and not calcium intake that was associated with the loaded tibia (Uusi-Rasi et al. 2002).

Reduced calcium bioavailability has been shown to limit mice’s osteogenic response to exercise training (Lanyon et al. 1986) and a bout of aerobic exercise is known to induce an acute rise in intestinal calcium absorption (Zittermann et al. 2002). Whether or not calcium and exercise interact synergistically in humans is considered “one of the most important questions in the area of lifestyle-related bone health research” (Murphy and Carroll 2003). Calcium has been described as a “threshold nutrient”, meaning the beneficial effects of exercise cannot be realised when intake is below the threshold amount, but when above it, bone gain remains constant regardless of intake (Murphy and Carroll 2003). Several authors have identified this threshold as being 1000mg/d (Beck and Snow 2003, Kelley 1998, Specker 1996), an amount that was calculated to be associated with a 24% reduction in hip fracture risk (Cumming and Nevitt 1997). In light of such findings, it appears that calcium and exercise have a permissive effect on each other, so that in the absence of one, the other cannot exert its influence on BMD. However, the interactive effect of calcium and exercise again appears to be age-, or perhaps, oestrogen-dependent. Calcium intake is positively correlated with BMD change (Maurer et al. 2005) and exercise combined with even only 800 mg calcium per day has been found to produce greater BMD change in women not on HRT than those using HRT (Cussler et al. 2005). On the other hand, daily calcium supplementation of 1500 mg was not shown to additionally benefit a two-year aerobic and weight training exercise intervention in young women (Friedlander et al. 1995), thus implying that calcium has a more pronounced effect combined with exercise when another environmental factor is lacking, e.g. in a situation of low oestrogen levels. Alternatively, as suggested earlier, failure to observe a response in bone could be related to high baseline calcium levels in the study population. Nevertheless, as separate influences, the magnitude of effect of calcium supplementation seems to be similar to the effect of exercise on BMD, but together, it would seem that adequate levels of calcium allows full expression of bone’s response to exercise.

Other nutrients

Vitamin D is derived exogenously and (mainly) endogenously from exposing the skin to ultraviolet sunlight. It enhances intestinal absorption of calcium and phosphorus,
and its deficiency results in negative calcium balance that stimulates parathyroid secretion. This subsequently increases bone remodelling and diminishes BMD (Reid 1996). Positive associations have been established between Vitamin D intake and BMD in pre-, peri-, and postmenopausal women, and there is evidence that vitamin D together with calcium supplementation may reduce fracture rates in elderly populations (New 2002a). Mutations affecting genes involved in vitamin D metabolism or vitamin D receptor functions are associated with impaired mineralisation of bone matrix and calcium metabolism and absorption (Dawson-Hughes et al. 1995, Ferrari et al. 1998); a clear demonstration of how nutrients can interact with genes as well as one another, hence altering each of their mutual requirements.

Evidence presenting a positive link between the consumption of alkali-forming foods (in particular fruit and vegetables) and indices of bone health continue to emerge, providing evidence of the importance of the acid-base content of diet on the skeleton (New 2002b). The ratio of protein (acidic) to potassium (alkali) has consequently been identified as a predictor of calcium excretion so that excessive protein intake can lead to higher bone resorption, though animal protein is more detrimental than vegetable protein (Sellmeyer et al. 2001). In contrast, experimental and clinical intervention studies as well as large prospective epidemiologic observations indicate that relatively high protein intakes, including those from animal sources, are associated with increased bone mineral mass and reduced incidence of osteoporotic fractures, thus leading to the opposing claim that dietary proteins are as essential as calcium and vitamin D for bone health and osteoporosis prevention (Bonjour, 2005).

Additional nutrients that facilitate bone accretion and protect against mineral loss include magnesium, phosphorus, vitamins B12, K, A, and E, as well as the plant group of phytoestrogens (Borer 2005). Currently, calcium is the only nutrient whose intake has been assessed with the effects of exercise on bone, but it would seem that overall, even though these other nutrients do not have a controlling influence on bone adaptation, they are very likely to have a permissive one (Skerry 2006).

2.3.5 Body mass

Body mass has been defined as the largest single determinant of the variability in adult total BMD (Heaney et al. 2000). A strong, positive relationship between body mass and BMD is consistent with the tenets of Wolff's Law in that a high body mass applies a greater daily gravitational load on the skeleton (Beck et al. 2001, Rubin et al. 1999). Elderly women with a BMI below 22 kg/m² were found to have significantly
reduced BMD and BMC compared with their counterparts who had BMI values within the range of 22-30 kg/m² (Coin et al. 2001). As well as influencing BMD, body mass has also been cited as protective against fracture, as it was shown in women of a mean age of 72 years that a 20% increase in body mass since the age of 25 is associated with a 40% reduction in fracture risk (Cummings et al. 1995). Body mass does not appear to control bone's response to exercise, because an exercise intervention conducted by Vainionpää et al. resulted in a significantly greater increase in BMD in the exercise group compared to the control group in spite of the fact that the exercisers lost weight and the controls gained weight (Vainionpää et al. 2005). However, it is possible that the degrees of weight change in the exercisers and controls (-1.1% vs. 1.1%, respectively) was not considerable enough to affect BMD. Besides, the additional gravitational force from the high-impact exercise may have magnified the decreased body mass of the exercisers and the strain on their bones would have exceeded the increased body mass of the controls who did not experience any extra mechanical loading. On the other hand, not all weight reduction studies demonstrate a decline in bone mass. Nakata and colleagues (2008) reported no change in bone mineral properties in overweight, premenopausal women following a successful 14-week weight loss intervention, and lumbar spine BMC continued to increase during long-term weight loss in obese adolescents even after adjustment for growth-related changes (Stettler et al., 2007).

2.3.6 Body composition

The two primary components of body composition that contribute to total body mass are fat mass and lean mass. The mineral, fat, and lean contents of the human body are allometrically and functionally associated (Nuti et al. 1994), but fat mass and lean mass are recognised to have separate influences on BMD (Reid et al. 1995) and which component exerts the strongest influence is an issue of debate.

Fat mass

Apart from the contribution to skeletal loading by the contribution of fat mass to total body mass, the mechanism underlying the relationship between greater fat mass and higher BMD is believed to relate to the conversion of adrenal androgens in adipocytes to oestrogen, which is a significant contributor to bone mass (Reid et al. 1992). Data taken from long-distance female runners and anorexia sufferers - populations who both have low levels of body fat - suggest that low body fat could be a precursor of oestrogen deficiency (Dunkwater et al. 1984), although an alternative argument to
CHAPTER TWO

this critical fat hypothesis is that hormonal disruption originates from energy deficiency (Zanker and Cooke 2004). The association between fat mass and bone may be sex and age-dependent, but findings are inconclusive. Higher fat mass in adolescence is associated with early menarche and increased skeletal maturity, which may have lasting effects on bone mass in adulthood (Frisch 1991). Some studies have shown fat mass to contribute positively to BMD only in postmenopausal women and older men (Cul et al. 2007), whilst others highlight fat mass as an independent determinant of whole body BMD in premenopausal women and not in men (Reid et al. 1992). Body fat can be protective against fracture simply because increased fatness results in greater soft tissue absorption of energy in falls, but an excess amount of fat can of course lead to obesity, which predisposes the body to a host of other diseases (Hardman and Stensel 2003). Fortunately, a threshold of 20kg fat mass has been identified, beyond which its influence on bone is minimal (Ferretti et al. 1998). On the other hand, in spite of dietary-induced weight loss leading to bone loss, exercise-induced reductions in fatness do not (Stewart et al. 2005). This dissociation of fat mass and BMD observed in exercisers may be explained by the effects of exercise on these two variables, since exercise tends to increase BMD while having the opposite effect on adiposity (Reid et al. 1995).

Lean mass

Bone is loaded mechanically both by forces transmitted from ground impact forces and by muscular forces pulling on bones (Rittweger et al. 2000). Skeletal muscle is the primary component of lean mass so it is presumed that the relationship between lean mass and BMD stems from muscular contraction and the subsequent pull on bone that results in bone-forming strains. Although relatively small compared to mechanical loading produced from ground impacts, mechanical strains induced by muscle contractions are often sustained for extended periods of time and therefore may characterise a bone's loading history (Frost 2000). Exercise increases lean mass and hence the muscular tensions generated on bones (Vicente-Rodriguez 2006). In premenopausal women, when combining all bone and lean tissue measures, the most significant correlation has been shown to exist between lean mass and BMD (Chilibeck et al. 2000, Shaw et al. 1993), and lean mass reflected by muscle strength is proposed to account for 15-20% of the total variance in their BMD (Snow-Harter et al. 1990). However, observations of greater lean mass but similar BMD in swimmers compared to controls (Fehling et al. 1995), and increases in muscle strength but not BMD following exercise interventions (Bassey and Ramsdale 1994) weakens the supposed effect of lean mass on bone.
The mixed results of whether it is total lean mass or total fat mass that exerts the greatest influence on BMD are most likely due to differences in methodology and/or subject selection. Lean mass has been shown to more strongly correlate with BMD than fat mass (Snow-Harter et al. 1992), with a 15% increment in lean mass resulting in a 10% increment in femoral neck BMD (Seeman et al. 1996); but when fat and lean mass are expressed as a percentage of body weight or when the variable BMD/height is created as a surrogate for volumetric BMD, it turns out that the primary relationship is between fat mass and BMD (Reid et al. 1995). Also, BMD appears to be most strongly determined by fat mass in sedentary women, whilst in exercising women proportion of lean mass is most highly correlated with BMD (Reid et al. 1995). Exercise therefore has a major impact on these relationships. Considerably less is known about the contribution of these exercise-related components of body composition to bone geometry.

2.3.7 Previous and current physical activity

Data from prospective studies support the notion that physical activity in youth promotes the achievement of optimal peak bone mass, thus greatly influencing lifelong skeletal adequacy (Bass 2000, MacKelvie and Khan 2002). Ulrich et al. studied the relationship between BMD and physical activity during specific time periods of life, and it appeared that physical activity during the three earliest stages (childhood, teens, and young adulthood) was most strongly associated with current BMD (Ulrich et al. 1999). Their results also indicated that the level of lifetime weight-bearing exercise (which included large amounts of occupational, household, and child-rearing activities) is a stronger predictor of total and peripheral BMD than levels of total exercise (which included non-weight-bearing exercise). In female racquet sports players, Kontulainen et al. demonstrated the BMC of the playing arm to be approximately twice as much as the non-playing arm if the individual had started training before or during menarche rather than afterwards, and furthermore, the amount of exercise-induced bone gain was 1.3-2.2 times greater in the young starters (mean age 10.5 ±2.2 years) than the old starters (mean age 26.4 ±8.0 years) (Kontulainen et al. 2003). Similarly, Helnonen et al.’s 9-month exercise intervention on pre- and postmenarcheal girls showed that there was significantly greater bone gain in the exercising premenarcheal girls (Helnonen et al. 2000). Although a large proportion of the BMD increase could be attributed to growth, starting physical activity prior to the pubertal growth spurt has been seen to stimulate both bone and skeletal muscle hypertrophy to a greater degree.
than observed with normal growth in non-physically active children (Vicente-Rodriguez 2006).

Specific examination of exercised rats indicates that brief exercise during growth results in lifelong changes in bone quantity, structure, quality, and mechanical properties; for even after almost 2 years of detraining, the previously trained limb had significantly greater ultimate force, indicating enhanced bone strength (Warden et al. 2007). As well as experiencing greater bone accrual, it seems that residual benefits of exercising at a young age are maintained into adulthood even if training has since ceased. Former gymnasts continue to have greater proximal femur BMD than controls, despite their reduced exercise level, which may help postpone or prevent osteoporosis later in life (Bass et al. 1998, Kudlac et al. 2004); and the same trends have been observed in female racquet sports players (Kontulainen et al. 2001) and male footballers (Uzunca et al. 2005). As mentioned, although it would seem preferable to start exercising at a younger age, any previous exercise-induced bone gain seems to be well maintained regardless of starting age and/or amount of exercise-induced bone gain (Kontulainen et al. 2001). The lack of a detraining effect on bone may be due to the fact that former players still kept up activity levels that were sufficient enough to preserve the exercise-induced bone gain. It would appear that the amount of training required to maintain exercise-induced alterations can be less than that required to achieve additional bone and, as evident in some studies, the amount can be as little as once per week (Kontulainen et al. 2001). Although it has been noted for some previously active individuals to lose bone mass when they stopped training, their BMD values are still considerably higher than their peers who never trained (Nordström et al. 2005). This has positive implications for more athletic people but could be due to selection bias. The critical issue is whether controlled interventions in sedentary individuals would result in similar benefits and ultimately translate into a reduction in the risk of sustaining a fracture. For even if the ideal bone-promoting exercise prescription was defined, the challenge of motivating people to follow a life-long exercise regime would still exist.

2.3.8 Genetics

Although osteoporosis is multifactorial, bone mechanosensitivity has a significant genetic component (Robling et al. 2002). Evidence for a genetic contribution to BMD comes from twin and family studies that show, depending on the site examined, between 50% and 85% of BMD variance is genetically determined (Ralston 2002). Since low BMD is an important risk factor for fracture (Cummings et al. 1995), the
majority of genetic studies have used BMD as a major phenotype to identify genes underlying susceptibility to osteoporotic fracture (Khan et al. 2001a). However, the correlation between BMD and risk of fracture is suggested to be very weakly determined by genetics (Deng et al. 2002). Genetic epidemiological studies show that a parental history of fracture is a significant risk factor for osteoporotic fracture independent of BMD (Kanis et al. 2004), with a maternal history of hip fracture doubling the risk of hip fracture (Cummings et al. 1995) possibly owing to greater cortical instability (Looker and Beck 2004). Consequently, more studies are now focussing on identifying genes that directly control susceptibility to osteoporotic fracture. The predominant ones recognised so far are the vitamin D receptor, oestrogen receptor, and type I collagen genes (Lei et al. 2007). Vitamin D receptor plays an important role in calcium homeostasis by regulating bone cell growth, intestinal calcium absorption, and parathyroid secretion; oestrogen receptor prevents bone loss, whilst type I collagen is the most abundant protein in bone. Any mutations in these genes could therefore result in a detrimental effect on bone. There are other candidate genes that have a relationship with risk of osteoporotic fracture, such as the parathyroid hormone receptor gene, apolipoprotein E gene, and growth factor genes, but compared to the aforementioned three, far fewer studies have concentrated on these genes, so concrete conclusions have not yet been made on their associations with fracture risk (Lei et al. 2007).

Genes do not act in isolation but rather interact with an uncertain number of other genes (gene-gene interactions), as well as environmental and physical factors (gene-environment interactions) that all influence their overall expression. The observed increased risk of vertebral fractures from the interaction between vitamin D receptor and oestrogen receptor mutations (Colin et al. 2003) is an example of a significant gene-gene interaction; while a gene-environment interaction would be present if genetic factors regulated bone’s response to exercise, meaning some individuals respond either more or less to identical loading. This possibility that athletes are genetically disposed to having high BMD might explain the substantial differences regularly observed between athletes and controls in cross-sectional studies compared to the differences between exercising subjects and controls in intervention studies conducted in the general population. An individual’s choice of lifestyle could also be determined by genetic factors. Another interaction involving gene expression occurs when factors related to exercise share common genes with determinants of bone mass, e.g. more than 50% of the covariance between BMD and muscle mass is supposed to be determined by genes regulating body size (Seeman et al. 1996).
2.3.9 Predicting fracture

Fracture is the most serious clinical consequence of osteoporosis. Osteoporotic fracture is associated with BMD, bone size and structure, bone loss, and propensity to fall (Ralston 2002). The greatest weakness of all interventions that aim to increase BMD or enhance bone structural properties is the relative insignificance of their outcome measures. Bone mass and bone geometry contribute to overall bone strength, and bone strength is one determinant of fracture risk, which is the clinical importance of these investigations. However, no RCTs of physical activity with anti-fracture efficacy as an end-point have been published and is unlikely to ever be published, because it would be too difficult to achieve high enough compliance to an exercise programme for a sufficiently long period to measure fracture occurrence that most likely will take place in the later years of life. This is especially true for interventions in young populations who are not at risk of fracture for perhaps another 20-30 years. Therefore, clinical and public health recommendations concerning exercise for prevention of osteoporotic fractures are based on trials with intermediate endpoints (bone density and geometry measures) that observational epidemiological studies have highlighted as predictors of osteoporotic fracture (Melton et al. 2005, Rivadeneira et al. 2007).
2.4 Development of an exercise intervention

2.4.1 Cross-sectional studies

A large body of cross-sectional studies demonstrate that many athlete groups have higher bone mass than non-athletic individuals. This is observed in all populations: men (Lorentzon et al. 2005), premenopausal women (Torstveit and Sundgot-Borgen 2005), postmenopausal women (Nurzenski et al. 2007), and children (Nanyan et al. 2005). However, the biggest limitation of observational studies is that they cannot eliminate the possibility that people choosing to exercise are systematically different from those who do not. Indeed, the skeletal status (as well as muscle mass and overall health) of the self-selected exercisers may already be above average before the start of the intervention, thus making it easier to gain bone during a period of intensive training and subsequently sustain it with moderate exercise thereafter. Their diets and other lifestyle habits may also contribute to their success in maintaining a high BMD, in addition to the likelihood that they have been participating in regular physical activity since childhood, endowing such long-term exercisers a greater BMD than those who did not start exercising until adulthood (Karlsson 2003, Nelson and Bouxsein 2001). However, assessment of bone-effecting exercise is unreliable, as most studies do not measure the actual loading on the skeleton. Assessing past exercise is equally as difficult and causes misclassification due to the limited ability of participants to recall complex patterns of physical activity over a lifetime. Reliance on subject recall of current and previous physical activity can create inaccurate assumptions and is another weakness of this type of study.

2.4.2 Randomised controlled trials

The strongest evidence that a change in BMD is caused by exposure to exercise comes from RCTs in which individuals are randomly assigned to an intervention group and then tracked with repeated measurements over time. A recent meta-analysis of carefully selected RCTs revealed positive effects of exercise on the lumbar spine and femoral neck in pre- and postmenopausal women (Wallace and Cumming 2000). Based on yearly estimated changes in BMD, a pooled measure of effect of 1.5% at the spine and 0.7% at the femoral neck was calculated from impact exercise in premenopausal women, which were comparable to the respective 1.3% and 0.5% effects derived in postmenopausal women. Compared to the results of cross-sectional studies, these exercise-induced increases in BMD are much smaller and less consistent.
(Table 2.1), thereby suggesting that exercise may serve more to prevent age-related bone loss rather than to considerably increase it. The lack of conviction and consistency between RCTs is largely caused by the heterogeneity of the trials. The extent of variation in the study populations (e.g. pre- or postmenopausal women), the type, length, and intensity of the exercise programmes, and the duration of the follow-up periods can all make meaningful statistical statistical pooling unfeasible.

Table 2.1: Summary of overall treatment effects from meta-analyses of randomised controlled trials

<table>
<thead>
<tr>
<th>Type of intervention</th>
<th>Skeletal site</th>
<th>Premenopausal women</th>
<th>Postmenopausal women</th>
</tr>
</thead>
<tbody>
<tr>
<td>Strength training</td>
<td>Lumbar spine</td>
<td>1.0%&lt;sup&gt;1&lt;/sup&gt;, 1.2%&lt;sup&gt;3&lt;/sup&gt;</td>
<td>NS&lt;sup&gt;2&lt;/sup&gt;, 1.0%&lt;sup&gt;4&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>Femoral neck</td>
<td>NS&lt;sup&gt;5&lt;/sup&gt;, Not reported&lt;sup&gt;2&lt;/sup&gt;</td>
<td>NS&lt;sup&gt;2&lt;/sup&gt;, 1.4%&lt;sup&gt;3&lt;/sup&gt;, NS&lt;sup&gt;4&lt;/sup&gt;</td>
</tr>
<tr>
<td>Aerobic (impact) exercise</td>
<td>Lumbar spine</td>
<td>1.5%&lt;sup&gt;2&lt;/sup&gt;</td>
<td>1.0%&lt;sup&gt;2&lt;/sup&gt;, 1.6%&lt;sup&gt;3&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>Femoral neck</td>
<td>0.9%&lt;sup&gt;3&lt;/sup&gt;</td>
<td>0.9%&lt;sup&gt;2&lt;/sup&gt;,&lt;sup&gt;3&lt;/sup&gt;</td>
</tr>
<tr>
<td>Aerobic exercise + strength training</td>
<td>Lumbar spine</td>
<td>0.9%&lt;sup&gt;4&lt;/sup&gt;</td>
<td>0.8%&lt;sup&gt;2&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>Femoral neck</td>
<td>0.9%&lt;sup&gt;4&lt;/sup&gt;</td>
<td>0.9%&lt;sup&gt;2&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

NS = no significant change

<sup>1</sup>Martyn-St James and Carroll 2006,  <sup>2</sup>Wolff et al. 1999,  <sup>3</sup>Wallace and Cumming 2000,  
<sup>4</sup>Kelley and Kelley 2006.

Reviewers have highlighted a number of limitations to some of the earlier RCTs concerning exercise and bone (Ernst 1998). Firstly, the exercise programmes were sometimes too general rather than specific to the hip or spine, which are the key sites that should be targeted. Secondly, considering the physiological limits of bone formation and remodelling, the duration of the protocols were sometimes too short to observe significant effects of a lifestyle intervention like exercise. Thirdly, most studies use BMD as their primary outcome measure, which is a suboptimal surrogate for bone fracture rates, and lastly, many trials had small sample sizes that are associated with type II error. These and other methodological issues must be considered when designing an exercise intervention and are discussed in more detail below.

2.4.3 Methodological considerations

The exercise programme

Wolff's Law is often not considered when designing exercise interventions. With increasing loading, exercise becomes an increasingly less efficient mechanism to stimulate bone gain, meaning that progressive overload of the skeleton is required in
order for it to continue to positively adapt. Exercise interventions with little or no supervision also risk becoming less rigorous (Sheth 1999).

Considering the time required for progression and adaptation, many training programmes are of inadequate length for measurable changes in BMD to take place. One complete cycle of activation, resorption, and formation of bone lasts three to four months, so the exercise intervention must be continued through several cycles in order to detect a meaningful change in BMD (Chilibeck et al. 1995).

**Randomisation**

Random assignment of the participants to either the control or experimental group is essential otherwise the experiment can lead to biased and erroneous conclusions. The strong confounding influence of non-random allocation of subjects to treatment groups is brought to attention by Wolff and colleagues who noted that the overall treatment effect discovered in their meta-analysis was almost double the size for nonrandomised trials than for randomised trials (Wolff et al. 1999). The pooled measure of effects of the highest quality studies (RCTs) was a modest but clinically relevant effect of 0.9% per year, whereas the overall effect of non-randomised trials was twice as high.

**Attrition and adherence**

Relatively high attrition rates are not unusual for exercise intervention trials. Previously conducted RCTs between 6 and 36 months duration involving premenopausal women experienced drop out rates between 14% (Heinonen et al. 1996b) and 47% (Friedlander et al. 1995). Intervention studies of longer duration enable clearer observations to be made, yet they provide greater chance of participants dropping out.

Adherence rate is the percentage of prescribed exercise sessions that were actually completed out of the total prescribed sessions. It is obviously an important factor to record because the main effecter of interest on outcome measures is the actual exercise done. Adherence rates of past RCTs vary from 56% (Sinaki et al. 1996) to 97% (Snow-Harter et al. 1992) and it appears that the studies reporting the largest effects of exercise on BMD are those that achieved the highest compliance (>80%) to the exercise programme (Wallace and Cumming 2000, Wolff et al. 1999).
Measurement issues

A certain amount of measurement error is inevitable and this refers to the accuracy of a measurement (the closeness with which the measurement is to the true value) and the reliability of a measurement (the extent to which the same measurement is obtained either on the same occasion by the same observer, on multiple occasions by the same observer, or on the same occasion by different observers).

The type of exercise performed must be specific to the target bones. Side-to-side comparisons of racquet sport players clearly demonstrate that gains in bone mass occur only at sites that come under mechanical strain (Haapasalo et al. 1998), and jumping significantly increases BMD in the hip and lower limbs but not in the upper limbs (Bassey et al. 1998, Vainionpää et al. 2005). On the other hand, by measuring a non-weight-bearing bone in some studies has revealed evidence of the possibility of a systemic, cross-over effect of exercise (Snow-Harter et al. 1992, Vuori et al. 1994).

It must be noted that most investigations do not include occupational physical activity or housework when providing some kind of quantitative measure of exercise, and subjects and researchers alike tend to define activity levels primarily on the basis of structured exercise sessions. However, occupational and household activity contribute to the strong association that has been found between lifetime total weight-bearing physical activity and total body BMD (Ulrich et al. 1999), and something like child-rearing represents a significant component of many women's lifetime activity. Therefore, there is much variance across studies depending on the criteria used to classify physical activity.

The methods by which changes in bone are measured vary between studies. Variations include the skeletal site measured, measurement tools, precision error, and the property of bone measured (e.g. bone mineral content, volumetric density, cortical wall thickness, etc.). It has been confirmed in rats that even marginal changes in bone mass detected by DXA can significantly improve bone strength by favourably altering bone geometry (Robling et al. 2002). If these findings are extended to human populations, they suggest that measurements of bone mass are not the best parameter for assessing the effectiveness of exercise to improve bone strength, yet most studies rely on DXA measurements that omit bone shape and size. This is especially true for studies carried out on premenopausal women who have yet to reach their peak bone mass. Before skeletal maturity, the effects of exercise on young bone may be mediated by changes in bone size and shape rather than in bone.
density, hence it is recommended that BMC (bone mineral content) instead of BMD is used as an outcome measure in children (Ashizawa et al. 1999, Haapasalo et al. 1996).

Results from animal models suggest that the anabolic effect of osteogenic loading in cortical bone is not as clearly observed as in trabecular bone (Rubin et al. 2001), of which the calcaneus, hip, and epiphyses of long bones are mostly comprised. Other results from human trials have found that exercise-induced changes in cortical bone are predominantly in bone geometry and not density, whereas at trabecular sites the reverse is true – that being a change in density rather than geometry (Ward et al. 2005). Limb dominance must also be taken into account when selecting which skeletal site(s) to measure, for BMD is noted to be higher in an individual’s dominant limb (Taffe et al. 1994). In summary, according to these site-specific, side-specific and apparent bone-type-specific findings, caution must be taken when interpreting data from the literature, whereby measurements are normally taken from only one-side of the body.

**Statistical analysis and interpretation**

The power of a study is its probability to detect a real difference of a certain magnitude, but it must be remembered that this is estimated from other published data, which can cause a build-up of inaccuracy. Finding statistical significance means the result only has a 5% likelihood of being a consequence of chance, but besides the strength of the association, statistical significance depends on the number of people in the study. With small sample sizes there is a high chance of a false negative result, i.e. not finding a statistically significant difference between groups when in fact one does exist (Chilibeck et al. 1995). Moreover, a statistically significant difference may not necessarily be of practical importance. Confidence intervals, on the other hand, give a range of plausible population values for the parameter being estimated that are found to be consistent with the data. They are more informative than simply testing for statistical significance as a very wide interval indicates that more data should be collected before anything very definite can be assumed about the parameter (Kelsey and Sowers 2001). However, many studies fail to consider magnitudes of associations and their confidence limits in addition to $p$ values. If a result is statistically significant in one study and not in another, but the magnitudes of the association are similar, this is evidence for consistency between studies, not inconsistency.
On more general terms, decisions on the likelihood of causality are partly judgemental and the problem with all scientific research is that data can be interpreted with bias in order for the desired results to be obtained (Wallace and Cumming 2000). Such publication bias means that it is impossible for the declared outcomes to be verified by the reader because articles do not publish raw data. Therefore, designing studies based on previous ones by different authors will always require deliberation.

2.4.4 Longitudinal, unilateral studies

Although RCTs reduce the limitations inherent in cross-sectional studies, differences in genetic and environmental determinants of BMD between individuals (e.g. calcium intake, baseline activity level, oestrogen level etc.) can still introduce variance and, along with some of the aforementioned weaknesses in design, the training programmes employed may not produce the maximum osteogenic response in the skeletal sites being measured. In addition, RCTs often struggle to recruit large numbers of participants. These considerations lead to the idea that a specific unilateral exercise intervention would be a favorable method of assessing the effects of exercise on bone. The major advantage of a unilateral training programme is that the participant has their own perfectly matched control limb, hence it can be confirmed that any differences between the trained and control limb have been caused by the exercise intervention and not any other factor. This makes for a more tightly controlled study and the paired design reduces the required sample size and eliminates many of the confounding factors that normally weaken results.

The studies listed in Table 2.2 represent the extremely few RCTs that have used a unilateral study design. The lack of exercise effect seen in the premenopausal women may be explained by their actual lower-than-prescribed training frequencies (2.8 times per week in Heinonen et al.'s study (1996a) and 3.9 times per week in Vuori et al.'s (1994)), the fact that the young participants had only recently completed longitudinal growth (up to 25 years of age) and may still be accumulating bone, or because loading may have been inadequately different in magnitude and distribution to the habitual loading of the already active subjects. The study by Kerr et al. did observe a training effect, which may be explained by the high compliance rate of their participants (82%) and the likelihood that the exercise intervention was a greater stimulus on the ageing bones of the sedentary women (Kerr et al. 1996). Therefore, providing the exercise intervention is designed specifically for the population being examined, a unilateral training programme could serve as a useful way to isolate the effects of mechanical loading on bone.
Table 2.2: Summary of unilateral randomised controlled trials

<table>
<thead>
<tr>
<th>Study</th>
<th>Mean age</th>
<th>Intervention</th>
<th>Duration of exercise programme</th>
<th>Prescribed weekly frequency</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heinonen et al. (1996a)</td>
<td>24.8</td>
<td>Strength training of the left upper limb</td>
<td>1 year</td>
<td>5 times</td>
<td>No differences at any measured bone site.</td>
</tr>
<tr>
<td>Vuori et al. (1994)</td>
<td>21.5</td>
<td>Strength training of the left lower limb</td>
<td>1 year</td>
<td>5 times</td>
<td>No differences at any measured bone site.</td>
</tr>
<tr>
<td>Kerr et al. (1996)</td>
<td>57</td>
<td>Strength or endurance strength training of either the left or right upper and lower limb</td>
<td>1 year</td>
<td>3 times</td>
<td>Significant BMD increase (1.7-2.4%) for the strength group at the trochanter, Ward's triangle, and forearm of the trained side.</td>
</tr>
</tbody>
</table>

2.4.5 Research rationale – Defining the optimal exercise prescription for bone health

As discussed, there is scarce information regarding the optimum exercise frequency to increase bone mass. Even if it were feasible to compare different exercise programmes across studies, the minority of RCTs that have investigated the effects of exercise on BMD have not covered a wide range of exercise frequencies. It is necessary to establish this aspect of exercise prescription because as well as recommending certain types of exercise that are good for the skeleton and how long to exercise for, people also need to know how many times a week to do the exercise, especially since physical inactivity is becoming a bigger problem worldwide. It is clear that there is a need for one single RCT that compares the effects of different exercise frequencies on bone. Considering a high frequency of training will have to be undertaken so that it can be compared to a lower frequency, an exercise model that non-athletic individuals will adhere to in the long-term needs to be designed. Important aspects would therefore include ease, convenience, and brevity, at the same time as being an effective osteogenic stimulus.

If evidence demonstrates that brief, rapid-onset, high-intensity, unusually-distributed strains produce a maximal osteogenic response, it follows that low-repetition, high-impact jumping would be an ideal type of activity to stimulate bone formation. Jumping is an efficient activity because one jump produces two rapid reversals of strain (take-off and landing), and it is also a feasible activity, since no special
equipment is required so it can be conveniently fitted into daily living. Indeed, jumping has been found to produce ground reaction forces (GRF) and muscle actions that provide large stimuli for bone. Jumping modest heights translate into GRF ranging between 2 and 5 times body weight (Bassey et al. 1998, McKay et al. 2005), which, as demonstrated with implanted hip prostheses, are then almost trebled when converted into internal compressive forces on the hip (Bassey et al. 1997). The studies in Table 2.3 emphasise the practical application of jumping to enhance and maintain peak BMD in young adult women. Certainly, high-impact exercise represents loading patterns that differ considerably from those of everyday activities. It seems that including high-impact activities in exercise programmes elicits the overload necessary to stimulate bone formation. The study by Bassey and Ramsdale was the first to report significant gains at the hip and the first to extend the cross-sectional and longitudinal findings in gymnasts to a "normal" group of young women (Bassey and Ramsdale 1994).

Table 2.3: Summary of randomised controlled trials in premenopausal women that involved jumping

<table>
<thead>
<tr>
<th>Study</th>
<th>Mean age</th>
<th>Exercise intervention</th>
<th>Frequency</th>
<th>Duration</th>
<th>Significant BMD increase in exercisers compared with controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bassey &amp; Ramsdale (1994)</td>
<td>32</td>
<td>50 vertical jumps</td>
<td>Daily</td>
<td>6 months</td>
<td>Trochanter – 3.4%</td>
</tr>
<tr>
<td>Bassey et al. (1998)</td>
<td>38</td>
<td>50 vertical jumps</td>
<td>6 d/week</td>
<td>5 months</td>
<td>Trochanter – 2.9%</td>
</tr>
<tr>
<td>Heinonen et al. (1996)</td>
<td>39</td>
<td>20mins multi-directional jump training</td>
<td>3 d/week</td>
<td>18 months</td>
<td>Femoral neck – 1.6% Lumbar spine – 2.4%</td>
</tr>
<tr>
<td>Kato et al. (2006)</td>
<td>21</td>
<td>10 vertical jumps</td>
<td>3 d/week</td>
<td>6 months</td>
<td>Femoral neck – 2.6% Lumbar spine – 2.4%</td>
</tr>
<tr>
<td>Vainionpää et al. (2005)</td>
<td>38</td>
<td>10mins jumping, skipping, stepping</td>
<td>Daily</td>
<td>12 months</td>
<td>Femoral neck – 1.1% Total hip – 0.1%</td>
</tr>
<tr>
<td>Winters &amp; Snow (2000)</td>
<td>40</td>
<td>100 vertical jumps</td>
<td>3 d/week</td>
<td>12 months</td>
<td>Trochanter – 2.7%</td>
</tr>
</tbody>
</table>

Considering the strengths of a unilateral exercise design and the aforementioned effectiveness of a high-impact activity like jumping, it follows that unilateral, single-legged jumping, i.e. hopping, may stimulate an even greater bone response. Theoretically, GRFs would double if only one leg supported the weight of the whole body, as happens during hopping, as opposed to body weight being distributed on two legs, as is the case during jumping. The important feature of jumping in involving
strain distributions on the skeleton that are atypical for women who do not engage in high-impact sports (Bassey et al. 1998), thus placing unusual but effective mechanical strain on bones; advocates that hopping would be an even more unusual activity for inactive women and consequently have even greater osteogenic potential on the specific skeletal sites that come under loading.

To strengthen the rationale for the proposed exercise intervention which can only investigate short-term effects of one single factor, i.e. exercise, a pilot study first assessed if the proposed hopping exercises are feasible to perform in the long-term. A cross-sectional study then examined the potential contribution of muscle/lean mass, strength, and impact forces to bone density and structure, which would provide evidence that the intervention may be effective in stimulating a positive adaptive response in bone. Although such analyses cannot infer causal effects, they are able to identify associations that potentially exist as a result of long-term interactions. Therefore, being able to advocate whether it was the influence of muscle mass/strength, the high ground impacts generated during the exercise, or something else that more strongly contributed to any exercise-induced increases in bone would help more fully understand the changes that took place. Most studies on factors related to bone structure have been in athletic/mixed populations rather than sedentary (Helinonen et al. 2002, Nikander et al. 2006). Therefore, while the large forces associated with competitive sport may affect bone, it needs to be established if the more moderate impacts and forces associated with everyday life in sedentary people do too. For if an individual who produces high GRFs during an activity like hopping also has high bone mass and advantageous bone structure, it could be that even though they do not regularly engage in high-impact exercise, they may have superior muscle function and so be exerting higher loading on their skeleton during similar activities in daily life than someone not naturally capable of generating high GRFs.

2.4.6 Aims

Efforts should focus on first preventing fracture through a simple and inexpensive lifestyle intervention such as exercise before having to resort to treating fracture using expensive drug treatments. Therefore, the primary aim of this PhD was to refine the exercise prescription for optimum bone health, using young women as a starting point so that they know how to use exercise to efficiently maximise their peak BMD and hence prevent their future risk of osteoporotic fracture. In light of the current gaps in knowledge, the specific objective was to determine the optimum weekly frequency of
exercise that produces the greatest increase in bone mass in premenopausal women who do not already regularly participate in physical activity and so may be the population at greatest risk. My secondary aim was to identify predictors of bone density and especially bone geometry in such a population of healthy but non-athletic women.

Considering the principles discussed here, it was proposed that a brief, unilateral, high-impact exercise programme could be used as an effective model to examine bone’s response to exercise and thus successfully address the aims of my research. Until now, hopping has not been studied as an activity to enhance skeletal health, yet the unilateral and high-impact nature of the exercise design makes it a novel and potentially very efficient intervention. The major advantage is that each subject has their own perfectly-matched, “in-built” control limb, meaning that any observed differences between limbs can be confirmed to be caused by the exercise intervention. The result is a tightly controlled study, as the paired design reduces the required sample size and eliminates the confounding factors that would otherwise weaken results. In addition, hopping is a movement that the majority of healthy people can do and it is less likely to be viewed as structured exercise, which may put off some non-athletic individuals from taking up other forms of physical activity for a prolonged period of time. Piloting a shorter version of the intervention enabled the feasibility of the hopping exercises to be established and using measurements of bone, body composition, and muscle function before the start of the intervention in cross-sectional analyses highlighted relationships between bone outcome variables with the impact loading and muscle actions involved in the exercise, thus strengthening the rationale for the study.
CHAPTER THREE

General Methods

This chapter will describe and provide justification for the materials and methods that were used in the presented research. Any procedures that depart from the descriptions below are detailed in the relevant study.

3.1 Participants

Recruitment

Potential participants for all studies were recruited on the university campus and in the local community through a variety of ways. These included word-of-mouth, e-mail, advertising posters (see Appendix A), and press releases in local newspapers (see Appendix B). Interested volunteers were interviewed on the telephone to check that they met the following inclusion criteria:

Inclusion criteria

1. 18-45 years-old and premenopausal
   My target population was premenopausal women because the aim of my research was to define the optimum exercise prescription for women to attain their peak BMD before the onset of postmenopausal bone loss. Studying premenopausal women had the added advantage that they would be oestrogen-replete, which is important to ensure the best response to the exercise intervention. Older women would also be more likely to have degenerative or other medical conditions (e.g. osteoarthritis) that may put them at risk of injury whilst performing high-impact exercise. Even though most women generally do not experience menopause until their sixth decade of life, the cut-off age was set at 45 years because hormonal changes are reported to start 4-9 years before the cessation of menses (Landgren et al. 2004). Studies among perimenopausal women, where ovarian aging is associated with a shortening of menstrual cycles, noticed BMD of the whole body, spine, and femoral neck began to decline about two years before last menses (Recker et al. 2000).
2. **BMI between 18.5 and 30 kg/m²**
   An individual’s BMI provides an indication of their body mass relative to their height and this ratio has been found to be positively associated with BMD (Ulrich et al. 1999). Besides body composition changes, other factors occurring in malnutrition, such as the likelihood of having insufficient minerals for bone remodelling, could be involved in the association between underweight and osteoporosis (Coin et al. 2001). Alternatively, being too heavy is equally as undesirable if undertaking exercise (especially high-impact exercise like jumping) represents too challenging or dangerous a task. Therefore, women accepted onto the present study had to have a BMI that fell within the International Classification of adult underweight, overweight and obesity according to BMI (World Health Organisation 1995) so that they were neither excessively underweight nor obese. Any individuals who were intending to lose weight through dieting were also excluded.

3. **Eat dairy products and/or take calcium supplements**
   Considering the significant influence of calcium on bone metabolism (Specker 1996), participants who entered the study had to consume sources of calcium daily. If they represented the average 19-50 year-old British woman and included dairy and cereal products as part of a normal British diet, they were most likely to meet the recommended reference intake of 700mg calcium per day (Bender and Bender 1997). Vegans were not excluded if they took calcium supplements.

4. **Not currently or recently (previous 12 months) doing high-impact, weight-bearing exercise > 1 hour per week**
   In order to encourage as large an osteogenic response as possible, my study recruited women who did not currently engage in regular high-impact exercise. The exercise intervention would otherwise have no effect on a skeleton that was already habituated to regular mechanical loading.

5. **Not currently or recently (previous 12 months) pregnant or lactating**
   Changes occur in a variety of factors during pregnancy and lactation, such as depleted skeletal stores of calcium, which negatively affect BMD (Kovacs and Fuleihan 2006). Both pregnancy and lactation have been associated with a BMD loss of up to 5% (Karlsson et al. 2005), thus the confounding effects of calcium and hormonal changes during these times were limited by excluding such women from taking part in the study.
6. Have 10-13 menstrual cycles per year unless on continuously administered contraception (oral contraceptive usage permitted)
Since a low level of circulating endogenous oestrogen represents a powerful confounding factor in exercise interventions, participants in the current study had to be regularly menstruating (10-13 cycles per year) to ensure that bone’s response to the exercise would not be dampened by a hormonal deficiency. Even though the interactive effects of oral contraceptives and exercise on bone are not fully understood, oral contraceptive users were accepted onto the study because it was decided that it was more important to know that all participants were not oestrogen-deplete.

7. No recent (previous 12 months) or current medical or surgical problems likely to affect bone metabolism or provide contraindications to high-impact exercise
It was necessary to exclude individuals who had any kind of condition that would predispose them to a higher risk of injury. For example, activities that are associated with high strain rates or impact loading are associated with a risk for osteoarthritis (McAlindon et al. 1999).

8. No previous or existing lower limb or back problems that could be provoked by undertaking regular high-impact exercise
Likewise, considering the nature of the proposed exercise programme (i.e. hopping), it was necessary to only recruit individuals who would not be at risk of aggravating parts of the body that would come under strain, i.e. the ankles, knees, hips, or back.

3.2 Determination of reliability

Table 3.1: Physical characteristics of participants used in the “test-retest” study

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean (SD) n=10</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>32.5 (8.3)</td>
</tr>
<tr>
<td>Body mass (kg)</td>
<td>64.6 (12.1)</td>
</tr>
<tr>
<td>Height (m)</td>
<td>1.60 (0.10)</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>23.7 (3.9)</td>
</tr>
<tr>
<td>Body fat percentage (%)</td>
<td>28.9 (7.6)</td>
</tr>
</tbody>
</table>
Ten women not involved in the study but who met the same inclusion criteria volunteered to undergo two assessments on separate days during the same week. Their physical characteristics are described in Table 3.1. Exactly the same procedures as those employed in the main study were performed by the same operator.

Short-term precision was evaluated as described by Glüer et al. (1995). The root-mean-square averages of standard deviation of repeated measurements (SD) was used to calculate coefficient of variation (CV) as follows:

\[
CV(\%) = \frac{SD}{mean} \times 100
\]

The CVs calculated for each measurement outcome are provided in the relevant descriptive text.

**Familiarisation effects**

Table 3.2 compares the mean scores obtained in each of the two testing occasions, which do not show evidence of a familiarisation effect having taken place. Knee extensor strength increased significantly, but only in the left leg. If participants had experienced a learning effect from their first testing session, then it is expected that both legs would have improved. The strength of statistical significance was also relatively weak. Although there were significant differences in one of the limbs for the measurement of peak GRF and maximum hop height, the changes demonstrate a deterioration, rather than an improvement, in performance.

**Table 3.2: Means (SD) and \( p \) values of first and second trials for test-retest of functional measures**

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Leg</th>
<th>Trial 1</th>
<th>Trial 2</th>
<th>( p ) value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sway velocity (mm/s)</td>
<td>L</td>
<td>24.0 (8.5)</td>
<td>24.4 (6.9)</td>
<td>0.81</td>
</tr>
<tr>
<td></td>
<td>R</td>
<td>24.6 (8.6)</td>
<td>24.1 (5.3)</td>
<td>0.83</td>
</tr>
<tr>
<td>Knee extensor strength (N)</td>
<td>L</td>
<td>295.3 (88.3)</td>
<td>318.9 (81.4)</td>
<td>0.046*</td>
</tr>
<tr>
<td></td>
<td>R</td>
<td>306.1 (77.5)</td>
<td>325.7 (97.1)</td>
<td>0.10</td>
</tr>
<tr>
<td>Peak ground reaction force (kg)</td>
<td>L</td>
<td>184.6 (47.5)</td>
<td>173.4 (43.5)</td>
<td>0.40</td>
</tr>
<tr>
<td></td>
<td>R</td>
<td>193.4 (30.1)</td>
<td>161.0 (29.2)</td>
<td>0.005**</td>
</tr>
<tr>
<td>Maximum hop height (cm)</td>
<td>L</td>
<td>12.9 (3.1)</td>
<td>11.4 (2.9)</td>
<td>0.008**</td>
</tr>
<tr>
<td></td>
<td>R</td>
<td>12.6 (3.2)</td>
<td>11.9 (3.2)</td>
<td>0.22</td>
</tr>
</tbody>
</table>

*Significant difference between values obtained in the two trials \((p<0.05)\)
*Significant difference between values obtained in the two trials \((p<0.01)\)
3.3 Measurement of bone strength

Fracture is the clinical outcome of osteoporosis and fracturing depends on fall risk and bone strength. Bone strength is the product of both intrinsic material properties (mass, areal density, and volumetric density) and structural properties (size, shape, cross-sectional area, and cortical thickness). The most commonly used imaging methods of determining bone status and predicting future fracture risk are quantitative ultrasound (QUS), dual-energy X-ray absorptiometry (DXA), and more recently, peripheral quantified computerised tomography (pQCT). Each technique produces a different measurement of bone and has its advantages and limitations.

3.3.1 Quantitative Ultrasound

Rationale

Quantitative ultrasound (QUS) consists of sound waves of frequencies that are above the audible range (>20,000 Hz), which are produced by applying an alternating field to a piezo-electric crystal situated in a transducer. The transducer is applied to the skin via either water or gel (depending on which ultrasound machine is being used). QUS is the most low-cost, non-invasive, radiation-free, portable, and simple method of assessing bone. It has the extra advantage of providing information on bone elasticity, an indication of architectural change as well as density; in addition to the amount of bone mineral present (Khan et al. 2001b). The two outcome measurements of QUS are broadband ultrasonic attenuation (BUA) and speed of sound (SOS). BUA represents the change in attenuation with ultrasound frequency as it travels through bone; a greater change being a sign of denser bone, whereas SOS expresses the time taken for the ultrasound to pass through the bone; a faster speed signifying denser bone. SOS most accurately measures trabecular bone (Toyras et al. 2002), whereas BUA appears to be the more precise determinant in longitudinal studies (Zochling et al. 2004), but increased physical activity is associated with an increase in both parameters at the calcaneus (Mentzel et al. 2005), a skeletal site commonly measured with this technique.

The reservations of QUS are, firstly, it is estimated that around 10% of patients will have a false positive result for osteoporosis (as is the same for DXA); secondly, only peripheral skeletal sites can be assessed; and thirdly, no definitive morphological differences have been found to be associated with QUS (Moyad 2003). Nevertheless, as long as measurements are performed by the same individual with the same
equipment, QUS is a practical technique that provides a safe and cost-effective means of gauging bone status during long-term intervention studies, since its use in a research setting is to monitor change within an individual rather than to make an accurate diagnosis of osteoporosis or to predict fracture risk.

Procedure

Three skeletal sites were measured by two lab-based ultrasound machines. SOS was assessed in the tibia and radius by the gel-coupled Sunlight Omnisense 7000 (Sunlight Medical Ltd., Tel Aviv, Israel), whilst SOS and BUA were determined in the calcaneus by the water-coupled DTU-One Ultrasound Bone Scanner (version 2.02, Osteometer MediTech, Hørsholm, Denmark). SOS of the tibia and radius were measured because the former would come under mechanical loading during high-impact exercise, and the latter served as a non-weight-bearing control site. The calcaneus is the most widely used site in ultrasound assessment of bone as it has two almost parallel sides, is surrounded by a layer of very thin tissue, consists mainly (90%) of trabecular bone (which has a more rapid response rate to mechanical loading than cortical bone), and is also a weight-bearing bone (Murphy et al. 2006). Ultrasound measurements at the calcaneus have been shown to correlate strongly with femoral strength (Bouxsein et al. 1999) and, most importantly, calcaneal BMD is an independent predictor of hip BMD (Graafmans et al. 1996) and fracture risk in postmenopausal women (Bouxsein et al. 1999, Cummings et al. 1995).

Considering the unilateral nature of the training intervention, measurements were taken at the selected skeletal sites on both sides of the body. A quality assurance test using a phantom at room temperature was performed before each testing session at approximately the same time of day. CVs were 6%, 0.9%, 4.9%, and 7.5% for calcaneus BUA, calcaneus SOS, radius SOS, and tibia SOS, respectively.

3.3.2 (Peripheral) Quantitative Computed Tomography

QCT is a bone densitometry technique that takes a cross-sectional image of bone, meaning it can determine volumetric density and can differentiate between cortical and trabecular bone. Its high sensitivity and ability to distinguish architectural properties such as cortical thickness makes it a superior method of presenting a more complete picture of bone strength compared to DXA and QUS (Moyad 2003). Still, QCT has its drawbacks, the major one being its high dose of radiation (200 mrem is emitted for assessment of the spine compared to 1.6 mrem from DXA). Along with
Increased cost and lower availability, subjecting patients to such high radiation renders the technique less appropriate for the repeat measurements required in assessing the effects of an intervention.

Smaller purpose-built, high-resolution scanners that X-ray only the peripheral skeleton have subsequently been developed in order to minimise radiation exposure. Peripheral QCT can be specifically performed on lower limbs of the tibia and radius, thereby making it an especially useful measuring technique in exercise and bone health research. Increasingly more exercise studies are using pQCT and some have revealed that improvements in the mechanical characteristics of bone in response to exercise is actually related to negative changes in volumetric BMD and positive adaptations in periosteal area, cortical area, and cortical thickness (Liu and Tokuyama 2005).

3.3.3 Dual Energy X-Ray Absorptiometry (DXA)

*Measuring BMD and BMC by DXA: Rationale*

DXA is a calculation of the attenuation of a photon X-ray beam at two sites - the region of interest (bone and soft tissue) and the baseline region (soft tissue only). It is considered the “gold standard” method for the non-invasive measurement of bone mass (Lewiecki et al. 2004) and it has been proposed that it can predict approximately 80-90% of the variance in breaking strength (Beck 2003). The technique has good short-term precision, which is demonstrated by its *in vivo* precision of 0.5-1.5% for the lumbar spine and 1-2% for the femur (Khan et al. 2001b), although its long-term reliability is poorer (Hangartner 2007).

Another reason DXA is the most commonly used method to measure BMD and BMC is due to its availability of reference data. The WHO developed the reference ranges for osteoporosis diagnosis using DXA, thus making its measurements the most accurate for identifying the disease. However, the WHO did not specify how many skeletal sites to measure or which region(s) of interest within a site should be selected. Inconsistencies in the way bone densitometry is performed and how results are interpreted could have adverse effects on the exchange of scientific information (Watts 2004). Furthermore, the International Society for Clinical Densitometry asserts that the WHO classification should not be applied to healthy premenopausal women (Lewiecki et al. 2004).
The greatest limitation of DXA is that it offers a two-dimensional estimate of bone's three-dimensional structure, meaning it measures mass per unit area \((g/cm^2)\) instead of mass per unit volume \((g/cm^3)\). A more precise term for DXA-derived BMD is therefore areal density, a difference that leads to an overestimation of volumetric BMD in larger people with bigger bones who have more bone mineral but not necessarily a higher density; while the BMD of smaller individuals would be underestimated (Carter et al. 1992). The technique cannot accurately measure the internal architecture of bone, the ratio of cortical to trabecular bone, bone shape, size, or distribution around its central axis; variables which are known to affect bone strength and to change with age (Faulkner et al. 2006). This is problematic when determining exercise effects on bone because there is evidence to show that exercise may significantly improve bone strength through site-specific alterations in structural parameters, sometimes in the absence of detectable changes in BMD (Haapasalo et al. 2000, Heinonen et al. 2002). Despite DXA’s inherent limitations, its usefulness in research is that the measurement is fairly rapid, of moderate cost, and has a low radiation exposure compared to other X-rays (Moyad 2003), thus conferring high patient acceptability and safety of repeat measurements.

Measuring BMD and BMC by DXA: Procedure

BMD and BMC of the spine, dual hip, and dual tibia were measured at the start and at the end of the study using the Lunar Prodigy Advance DXA machine (GE Healthcare, Madison, WI, U.S.A.). The spine and hip were chosen due to their clinical relevance in assessing fracture risk, and the tibia was an appropriate site to monitor change in BMD due to the specificity of mechanical loading from the proposed hopping exercises. Standardised positioning protocol was carefully employed and the manufacturer’s lumbar spine phantom was scanned on each testing day to maintain quality control and to correct for any instrument drift. The two scans (baseline and post-intervention) for each participant were performed by the same operator. Reliability of bone measurements are displayed in Table 3.3.

Lumbar vertebrae 1-4 (Figure 3.1, opposite), total hip, the femoral neck, upper neck, lower neck, Ward’s triangle, trochanter, and femoral shaft (Figure 3.2, opposite) were measured. These regions of interest were determined automatically by Lunar’s enCORE 2006 software (version 10.10). In the tibia, three regions of interest were highlighted. Figure 3.3 on the next page shows how 5 boxes were drawn on the scan image. Boxes 1 and 2 served positional purposes and boxes 3, 4, and 5 were the regions of interest. All boxes were a set width of 4.5cm. Box 1 was drawn from
directly underneath the cortical bone at the epiphysis, (an anatomical landmark that was easy to visually locate because it is the boundary between distinct shades of white and dark on the scan), and the box was extended to half the length of the participant's tibia length (which was measured prior to the scan and was a measurement from the inferior aspect of the patella to the lateral malleolus of the ankle). Box 2 extended from the same starting position as box 1, but only went to half its length, i.e. a quarter of the tibia length, Box 3 extended 1cm down from the top of boxes 1 and 2 and represented the proximal epiphysis of the tibia, box 4 extended 1cm up from the bottom of box 2 and represented the proximal tibia, and box 5 extended 1cm up from the bottom of box 1 and represented the midshaft tibia.

*Measuring bone geometry by DXA: Rationale*

Bone is normally loaded in bending and axial compression (Burr 1997). Axial stress (the force applied to bone per unit area) on bone is proportional to the total bone surface area in the cross-section [cross-sectional area (CSA)] after excluding soft tissue space, whereas bending strength depends on this amount of surface area and how far it is distributed from the bone cross-section’s centre of mass [cross-sectional moment of inertia (CSMI)]. The two methods by which bones have been proposed to cope with the mechanical demands caused by increased loading are reshaping of the bone (i.e. increased CSA by periosteal expansion) and redistribution of bone mineral further from the bone’s centre (i.e. increased CSMI) (Adami et al. 1999); adaptations which cause an increase in bone bending and torsional strength that may (Kaptoge et al. 2003a, Petit et al. 2002) or may not (Adami et al. 1999, Jarvinen et al. 1999) occur along with bone densitometric changes. Femoral neck width is a dimension of bone width and reflects periosteal expansion that has a negative effect on BMD, but positive effect on bending strength (section modulus) (Beck et al. 2001).

Femoral strength index (FSI) is an estimation of the ability of the femur to withstand a fall and is calculated as the ratio of compressive yield strength of the femoral neck to the expected compressive stress of a fall, taking into consideration the patient’s BMD, femur geometry, age, height, and weight (Yoshikawa et al. 1994). Compressive stress is calculated by an empirical equation developed by Robinovitch et al. (1991, cited in Crabtree et al. 2002) that relates fall force to body weight and height. This stress gives a compressive force parallel to the neck axis and a bending force perpendicular to the neck axis, the latter of which produces a bending moment. The compressive force and bending moment are then combined to calculate total compressive stress at the femoral neck’s weakest point. Using empirically defined, age-dependent values for
Figure 3.3: Example DXA image of the right tibia, showing the positioning of regions of interest

- Box 1: 4.5 cm
- ½ Box 1
- ½ tibia length
- Border of epiphysis
- Box 3: Tibia proximal epiphysis
- Box 4: Proximal tibia
- Box 5: Midshaft tibia
Figure 3.1: Example DXA image of the lumbar spine

Figure 3.2: Example DXA image of the dual hip, highlighting regions of interest
yield strength of cortical bone (Burstein et al. 1976, cited in Crabtree et al. 2002), the FSI can be deduced as the ratio of yield strength to compressive stress. The greater the FSI, it appears the lower the hip fracture risk (Faulkner et al. 2006).

Understanding bone’s response to mechanical loading is restricted by the two-dimensional skeletal outcomes that represent only one part of overall bone strength, as DXA scanners are designed to measure density, not structure. DXA can only accurately measure CSMI for bending in one direction due to the axial asymmetry of bone cross-sections. This means bones are stronger when bent in certain directions than in others so if a bone is rotated between sequential scans, a different CSMI value would be given that corresponded to bending in slightly different directions (Beck 2003). Therefore, conclusions regarding bone geometry that are based on BMD measurements may be spurious if positioning is not consistent between repeat measurements, especially in exercise studies when small changes are being looked for. Accordingly, DXA-derived structural outcomes are a way of expressing bone mineral mass in mechanically meaningful terms and should only be interpreted (with caution) if a more specific method of measuring the subtle but mechanically significant dimensional changes in bone (pQCT) is unavailable. If structural parameters from pQCT are taken together with the density outcomes of DXA, a relatively clear picture of bone status can be provided. Nonetheless, as long as consistent positioning is ensured, the DXA method should suffice for the present research whose aim is to monitor change over time rather than to give an accurate diagnosis of bone health.

**Measuring bone geometry by DXA: Procedure**

Recently, commercially available programmes have been developed that enable these and other bone structural variables to be measured from DXA images - the Hip Structural Analysis and the Advanced Hip Analysis. For the present study, hip structural parameters were noted using an additionally installed Advanced Hip Analysis (AHA) programme (*enCORE 2006* software, version 10.10), which measures the geometry of bone cross-sections 5 mm-thick at regions of mineral mass traversing the bone axis. The regions assessed in this study were located across the narrowest point of the femoral neck, 2 cm distal to the midpoint of the lesser trochanter. For each region the distribution of the bone mass across the bone was extracted and measured directly from the bone mass profile. Hip geometry outcome measures were the FSI, CSMI, CSA, and minimum femoral neck width. Their CVs are also listed in Table 3.3.
Table 3.3: Coefficients of variation for the bone variables measured by DXA

<table>
<thead>
<tr>
<th>Measurement</th>
<th>CV (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lumbar spine BMD</td>
<td>1.03</td>
</tr>
<tr>
<td>Lumbar spine BMC</td>
<td>0.88</td>
</tr>
<tr>
<td>Total hip BMD</td>
<td>0.97</td>
</tr>
<tr>
<td>Total hip BMC</td>
<td>0.03</td>
</tr>
<tr>
<td>Femoral neck BMD</td>
<td>1.38</td>
</tr>
<tr>
<td>Femoral neck BMC</td>
<td>0.32</td>
</tr>
<tr>
<td>Upper neck BMD</td>
<td>1.79</td>
</tr>
<tr>
<td>Upper neck BMC</td>
<td>0.26</td>
</tr>
<tr>
<td>Lower neck BMD</td>
<td>1.32</td>
</tr>
<tr>
<td>Lower neck BMC</td>
<td>0.16</td>
</tr>
<tr>
<td>Ward's triangle BMD</td>
<td>1.94</td>
</tr>
<tr>
<td>Ward's triangle BMC</td>
<td>1.53</td>
</tr>
<tr>
<td>Trochanter BMD</td>
<td>2.32</td>
</tr>
<tr>
<td>Trochanter BMC</td>
<td>1.08</td>
</tr>
<tr>
<td>Shaft BMD</td>
<td>1.20</td>
</tr>
<tr>
<td>Shaft BMC</td>
<td>1.33</td>
</tr>
<tr>
<td>Femoral strength index</td>
<td>11.51</td>
</tr>
<tr>
<td>Cross-sectional moment of inertia</td>
<td>4.37</td>
</tr>
<tr>
<td>Cross-sectional area</td>
<td>2.93</td>
</tr>
<tr>
<td>Minimum femoral neck width</td>
<td>1.42</td>
</tr>
<tr>
<td>Proximal epiphysis of tibia BMD</td>
<td>2.40</td>
</tr>
<tr>
<td>Midshaft tibia BMD</td>
<td>11.71</td>
</tr>
<tr>
<td>Proximal tibia BMD</td>
<td>20.04</td>
</tr>
</tbody>
</table>

3.4 Muscle activity and sites of bone stress during hopping

Jumping and hopping calls on mechanical leg power for both the impulse-generating capability of muscle during the push-off phase and for pre-landing muscle control in protection against the high rate of loading in landing (i.e. "absorption" of the jump). Much of the high energy and high frequency components associated with ground impact are dissipated by muscles and ligaments that are put under tension and stretched, absorbing as much as 50% of the energy (Palastanga et al. 1989). In order to protect bone from failure in tension when it is loaded, contraction of muscles attached to the bone alters the stress distribution by producing compressive stress to partially or totally neutralise the tensile stress (Frankel and Nordin 2001). Considering muscles are of course also recruited to provide the forces and moments required for the movement and balance of the body, the combination of compression and contraction result in high internal forces on the bones under loading. Hopping is biomechanically different from jumping in that only one foot is used to support the whole body and propel it upwards into the air. It is therefore necessary to identify which specific skeletal sites would experience strain during the proposed unilateral exercise intervention.
Figure 3.4a: Posterior view of the gluteus maximus, medius, and minimus muscles, showing points of origin and insertion. (Taken from Floyd 2007)
Muscle-mediated loading on bone is produced by the force of muscular contraction at the site of attachment of the tendon onto the bone. Nagano et al. carried out an insightful simulation study that investigated muscle force, work, and power output of major lower limb muscles during a maximal effort counter-movement jump (Nagano et al. 2005). As reflected by the largest mechanical work and power output, they identified the primary agonists involved in jumping to be the gluteus maximus, vastus group, gastrocnemius, soleus, and other plantar flexor muscles that are maximally activated from the latter phase of the countermovement through to the take-off (push-off) phase. On the other hand, the rectus femoris and hamstrings contributed little to work and power output, suggesting that these muscles function to transfer, rather than generate, mechanical energy. The roles of the hip abductors (gluteus medius and minimus), hip adductors (adductor longus and magnus), and external rotators in the generation of a jump are minor (despite being vigorously activated) due to their limited length change during jumping (Nagano et al. 2005), thereby indicating that they do not contribute to body segmental motions in the sagittal plane, but instead stabilise the movement of the hip joint.

The gluteus maximus that extends the hip originates from the iliac crest, sacrum, and coccyx; and one of its points of insertion is the posterior shaft of the femur (Figure 3.4a, opposite). The three vastus muscles that extend the knee originate from the femur and insert by a common tendon into the anterior tubercle of the tibia (Figure 3.4b, next page), whilst the gastrocnemius and soleus plantar flexor muscles that initiate the push-off movement have the distal femur as one of their sites of origin and join to form the Achilles tendon that inserts into the posterior calcaneus (Figure 3.4c, opposite page 61). When supporting the body on one leg as required during a hop, the gluteus medius muscle (Figure 3.4a) contracts to shift the pelvis over the supporting leg. This muscle also produces tensile stress on the lower neck and compressive stress on the upper neck in order to resist the bending moments in the femoral head that are applied during locomotion (Tyldesley and Grieve 2002). It originates from the iliac crest and inserts into the greater trochanter. In light of the positions of points of attachment between muscle and bone of the aforementioned agonists involved in jumping/hopping, the femur, the proximal end of the tibia, and calcaneus were relevant skeletal sites to measure during the current study.

Muscles that were not mentioned in Nagano’s study but also come into play are the back and abdominal muscles, which are essential for maximum force production because they stabilise the trunk and maintain the neutral upright position. The ability
Figure 3.4b: Anterior view of the three vastus muscles, showing points of origin and insertion. (Taken from Floyd 2007)
of the quadriceps to generate useful force is limited by the strength/activation of these fixator muscles (Rutherford and Jones 1986). Bassey et al. observed greater activity in the erector spinae than the vastus lateralis during jogging compared to jumping, which was proposed to be due to the greater stabilising activity of the back muscles needed for the alternating weight-bearing leg action of jogging (Bassey et al. 1997). It is therefore possible that these back extensor muscles are also recruited more during hopping, a locomotive action that is likened to the single leg supporting role of jogging.

3.5 Assessing muscle performance

The strength of a muscle depends on a combination of central factors, which include motivation, motoneuron excitability, and the coordination of other muscles required to stabilise the limb; and peripheral factors, which involve the intrinsic strength of the muscle, e.g. the size and arrangements of fibres. Muscle hypertrophy is generally not observed until about the eighth week of exercise training in previously untrained individuals, up to which time neural factors dominate strength development (Moritani and deVries 1979). Increases are attributed primarily to the increased muscle activation of the trained agonist muscles via either an increase in the number of active motor units or an increase in their voluntary firing frequency. However, it is also suggested that an improvement in agonist/antagonist muscle coordination could play a role in increased power production (Kyröläinen et al. 2005); that is, reduced co-activation of the antagonist muscles that subsequently enhances the net force production of the agonists (Hakkinen et al. 2000), as well as an optimisation of joint control by the central nervous system (Gabriel et al. 2006). Tests specific to the actual motion of the exercise training would provide the most direct evidence of changes in functional muscle strength. Since maximal vertical jump performance is a well-documented measure of human power (Bosco et al. 1983, Harman et al. 1990), it was hypothesised that a similar vertical hop test could track performance over time and subsequently determine the efficacy of the unilateral exercise intervention on lower limb muscle function.

Rationale: Ground reaction forces

A maximal vertical jump involves launching the body into the air by the rapid extension of the legs pushing against the ground to overcome inertia when accelerating the body upward (Kreighbaum and Barthels 1990). The landing from a jump that follows results in a sharp rise in the force on the ground as the body
Figure 3.4c: Posterior view of the gastrocnemius and soleus muscles, showing points of origin and insertion. (Taken from Floyd 2007)
decelerates rapidly from a downward velocity, which also causes the ground to exert force on the body. These forces from the ground acting on the body during takeoff and landing are referred to as ground reaction forces (GRFs) and may provide a surrogate measure for the strain experienced by bone, thereby providing an indication of the kinds of activities that will provoke a positive bone response (Bassey et al. 1997).

Research into vertical jumping combine kinematic data with force platform data to analyse net joint torque and muscular action at the ankle, knee, and hip joints; which, depending on the size of the jump, are estimated to contribute 20%, 40%, and 40%, respectively, to the generation of power (Fukashiro 1987). As for muscular action, jumping works on a stretch-shortening basis: eccentric muscle action first loads a spring system, then there is a concentric phase when stored elastic energy is utilised to produce force against the ground, which moves the body’s centre of gravity via reaction forces. The power generated by a jump is therefore a combination of stored energy and muscle contraction. Measuring the vertical force between the feet and the ground gives the force applied in order to lower the body in preparation for take-off, to accelerate the body upwards off the ground, and to support the body under the action of gravity. These GRFs indicate that jumping is fast and strenuous (up to 5 times body weight) compared to normal daily locomotive activities, such as walking (1-2 times body weight) or jogging (2-3 times body weight) (Aura and Vittasalo 1989).

Instead of relying on GRFs, some authors have attempted to measure the actual in vivo forces on bone in order to more accurately quantify the stress experienced by bone. Bassey and colleagues (Bassey et al. 1997) measured compressive axial forces in a hip implant of the upper half of the femur, which they compared to GRFs and EMG activity during walking, jogging, and hopping. During a jump they recorded implant forces up to three times greater than GRFs, a finding attributed to the contraction of the large extensor muscles of the knee (a source of power for take-off and of protective braking force upon landing), which are attached across the femur and thus apply compressive force to its shaft and tendons. Bergmann et al. (1993) tested hip joint force moments using total hip prostheses, but during walking and running. These internal forces also tended to be higher than the GRFs measured in other studies. For example, peak forces reached 5.8 times body weight when measured in their hip prostheses, compared to the magnitude of 3.5-5 times body weight that were measured in terms of GRFs by Aura and Vittasalo (Aura and Vittasalo 1989). It is clear that implant forces result from a combination of gravitational force and muscle tension and although it can be argued that the response to loading of a metal implant may not be identical to that of bone, and that surgery may have altered the way in which
Figure 3.5a: Force-displacement curve and the work during the jump.\[ W_{\text{GRF}} - W_{\text{BW}} = \frac{1}{2} \text{(body mass x takeoff velocity)}^2 \] where \( W_{\text{GRF}} \): work done on the body by the ground reaction force; \( W_{\text{BW}} \): work done on the body by gravity. (Taken from Lara et al. 2006)

![Diagram of force-displacement curve and work]

Figure 3.5b: Force-time curve and the resulting impulses.\[ I_A - I_{\text{ND}} = \text{body mass x takeoff velocity} \] where \( I_{\text{ND}} \): negative downward impulse; \( I_B \): braking impulse; \( I_A \): acceleration impulse; \( I_{\text{NU}} \): negative upward impulse. (Taken from Lara et al. 2006)

![Diagram of force-time curve and impulses]
muscle forces are transmitted to the skeleton, available data confirm that internal forces are high and that the more measurable GRFs can reflect the intensity of actual loading on bone. These data, together with the high reliability estimate obtained for peak vertical GRF (Cordova and Armstrong 1996) imply that directly measuring GRFs may provide a valid method for quantifying lower limb functional strength.

Rationale: Hop height

One of the most largely used parameters to characterise jumping performance is jump height (Bosco et al. 1983). The height of a jump may be calculated (1) from the flight time of the jump, (2) by applying the impulse-momentum theorem to the force-time curve, or (3) by applying the work-energy theorem to the force-displacement curve. All methods use data obtained from a force plate and rely on knowledge of the velocity of the jumper’s centre of mass at the instant of takeoff, which is related to flight height by applying the law of conservation of mechanical energy to the flight phase of the jump.

The work-energy method is based on the theory that the integral of a force over work (i.e. displacement) produces a change in the kinetic energy of a body. The total work done during a jump comes from the GRF, which is calculated from the area under the force-displacement curve by numerical integration; and from gravity (i.e. body weight), which is read from the GRF curve (Figure 3.5a, opposite). This method is very sensitive to correct selection of the Instant before the jump where the body is stationary and the GRF equals body weight, but it is often the least reliable of the three methods, due to the double integration calculation that results in compounding of error (Linthorne 2001).

The impulse-momentum method is based on the theory that the integral of a force over time (i.e. impulse) produces a change in the momentum of a body. The GRF impulse is calculated from the area under the force-time curve also by numerical integration, and the body weight impulse is again read from the GRF curve (Figure 3.5b, opposite). For this method, precise selection of takeoff time is not as important in calculating impulse as it is for work, as long as the body is stationary before the start of the jump. Although measurement and computational errors that can lead to systematic and random errors still exist, jump height determined by impulse is agreed to be valid and reliable (Harman et al. 1990, Hatze 1998, Kibele 1998), and the most accurate technique to calculate flight height compared to the work-energy and flight time methods (Linthorne 2001).
The flight time method uses sampling frequency of the force plate and the resultant force-time curve to calculate the time spent by the body’s centre of mass in the airborne phase of the jump. This method is accurate only if the position of the centre of mass at the instant of landing is the same as at the instant of takeoff, which it usually is not. Lara et al. (2006) found the position of centre of mass of subjects to be an average of 4 cm lower at landing compared to at takeoff, a difference most likely attributed to the almost full extension of the ankle and knee joints at takeoff, but their slight flexion during landing, as well as changes in shoulder position and the degree of back flexion. For this reason, despite being the simplest method to compute, flight height calculated using the flight time method is usually a couple of centimetres greater than the true value as calculated using the impulse-momentum method (Kibele 1998). However, use of the flight time method is reliable in assessing vertical jump performance if no other accurate instruments are available (García-López 2005), and from the comparison of the relative differences of individual subjects’ jump heights with regard to different measuring techniques, Baca (1999) inferred that using flight time is better suited to compare trials of the same subject than to compare different subjects or to calculate the exact jump height value. Although it was interesting to know how high subjects were hopping, the main aim of calculating hop height in the present study was to track changes over the course of the exercise intervention. In consideration of this, in addition to the fact that impulse would have had to be calculated manually from force-time curves since specialist commercial software was not available, it was decided that a straightforward formula devised and validated by Bosco et al. (1983, see below) would be adopted. Bearing in mind the effect of body position on the resulting flight time, when instructions were given to participants it was stressed that they endeavour to maintain the same hopping technique throughout the study.

Formula:

\[
\text{Height (m) } = 1.226 \times (\text{flight time (s)})^2
\]

where flight time was the number of seconds when there was no force on the plate, i.e. a value of \( \leq 0 \) kg.

**Equipment**

In the present study, the available force plate was raised above the ground so for safety reasons a specially constructed triangular wooden border was fitted around its perimeter, making the surface of the force plate lie flush with the border, thus increasing the available area to hop/jump on. The plate had strain gauge transducers (*Tede-Huntly type 355 load cells*) attached at each corner to give an electrical output
that is proportional to the force on the plate. Amplification was based on TechniMeasure type 300 strain gauge modules, total plate reaction was calculated by the sum of the three sensor signals, while centre of gravity was determined by simple ratiometric geometry and mechanical logic. Data acquisition and file storage was accomplished with a Strawberry Tree Datashuttle pod under a DasyLab VI control programme. Data of the vertical component of the GRFs were sampled at a rate of 50 Hz and then processed with software developed in-house using Microsoft Excel. Estimated within-subject CVs were 7.3% for measurement of peak GRF and 8.7% for maximal hop height.

Procedures

Peak GRF and maximum hop height were recorded when participants performed one single vertical hop using a countermovement style. A countermovement technique (see Figure 3.6) was employed for all jumping and hopping tests because it is proposed as the most "natural" technique and requires the least amount of practice by participants (Harman et al. 1990). Each leg was tested separately so that comparisons during the course of the intervention could be made in order to identify effects from the training programme. Participants placed one leg in the middle of the force plate with their contralateral knee flexed at 90° to prevent the foot from touching the plate. They began each hop from an upright position. The protocol allowed arm swing. They were instructed to: "hop up into the air as high as you can. When you land, make sure your other foot doesn't touch the ground". The technique was demonstrated to each participant before they had one practice hop. Once ready, the data-logger was started and they performed three maximal attempts with approximately 30s rest between trials. The test value for peak GRF was taken as the highest loading on the force plate recorded by the data-logger out of the three trials and this value was expressed as force in terms of multiples of body mass. Maximum height was calculated from the longest time interval in the air.

Submaximal GRF and submaximal hop height were obtained for each participant in an attempt to determine the typical GRFs and heights that were being produced when doing the training individually at home. This was important in order to quantify the actual intervention that bone is adapting to. The same countermovement style was used but instead of doing one maximal hop, participants completed 10 vertical hops in succession (the equivalent to one set of hops of the prescribed home exercise session). During the first testing occasion, they were told to, "Hop up and down 10 times at a consistent height and consistent speed". On the second and third visits to
the lab during the study, their instruction was to "perform 10 vertical hops in a similar way to how you have been doing it at home". The mean of peak GRF (i.e. during the landing phase) for the 10 hops was subsequently calculated and was reported as the test score. Hopping height was calculated using the same formula above, but the mean time in the air for all 10 hops was used.

Figure 3.6: Demonstration of the countermovement technique used during the jumping and hopping performance tests (taken from Harman et al. 1990).

3.6 Maximal isometric knee extension strength test (IKES)

Isometric knee extension tests provide one way of evaluating lower limb force (Marcora and Miller 2000, McBride et al. 2007), so maximal voluntary isometric force of the quadriceps femoris group of muscles was measured separately for the right and left limb in order to assess whether the hopping exercises have an effect on maximal force development of the knee extensors that are used during the hopping movement. The subject sat on the chair of a custom-built knee extension rig in an upright position with their hip, knee, and ankle flexed at 90° and a restraint around their ankle that was linked to a strain gauge. The subject was told to push their leg out against the resistance as hard as possible until they felt that they could push no harder. Specifically, they were instructed not to kick their leg out in a rapid jerking motion, but rather to build the tension up to maximum over a period of a few seconds. They relaxed tension after this point and rested for 30s before repeating the test again. Peak force (N) was recorded for each maximal effort and the best score was used in
further analysis. The estimated within-subject CV over two separate trials for this test was 6.5%.

3.7 Static postural sway test

In addition to strengthening muscles, improving balance leads to a reduction in overall risk of falls and fractures (Borer 2005, Chan et al. 2003, Kohrt et al. 2004). Balance training was demonstrated to prevent functional decline and bone fragility in elderly women (Karinkanta et al. 2007) and body sway is recognised as an extraskeletal risk factor for hip fractures in this population (Korpelainen et al. 2006). Jumping exercise has previously been found to improve dynamic balance and postural sway (Uusl-Rasi et al. 2003), so it could be hypothesised that single-legged jump training, i.e. hopping, would improve balance even more. Static balance was assessed using the force plate by recording movement of the subject’s centre of pressure for 30s. The participant stood on the platform with their feet shoulder-width apart and was then instructed to lift one foot so that the knee was flexed at 90° and touching the balancing leg. They were instructed to "look directly ahead, and stand as still as possible". A data-logger (DASYLab version 7.0, Omega Engineering Inc., Connecticut) linked to the force plate produced a diagrammatic representation of sway and recorded pressure from the sway of their centre of gravity at a sampling rate of 20 Hz. Maximal mediolateral and anteroposterior amplitudes were determined and sway velocity subsequently calculated. The test was repeated individually for each leg. Its' estimated within-subject CV over two separate trials was 14.7%.

3.8 Anthropometry

To measure body mass and stature, standardised procedures as detailed by Gordon et al. (Gordon et al. 1988) were followed.

3.8.1 Stature

After removing shoes, height was measured using a portable suitcase-mounted stadiometer (Holtain, Pembrokeshire). The participant stood barefoot with arms hanging by their side and their heels, buttocks, scapulae, and the posterior aspect of their cranium touching the wall. Their head was positioned in the Frankfort Horizontal Plane with eyes looking straight ahead, and their heels were kept together on the floor with weight evenly distributed on both feet. The participant was asked to inhale deeply while maintaining a fully erect position. The movable headboard of the stadiometer
was lowered onto the most superior point on the head with sufficient pressure to compress the hair. The reading was taken to the nearest 0.1cm.

3.8.2 Body mass and body mass index

Measurement of body mass was made to the nearest 0.1kg using digital scales (*Tanita*, Tokyo) after removing shoes and outer layers of clothing. Participants were requested not to have eaten a meal 4 hours prior to testing and were encouraged to void before being weighed in order to reduce the short-term fluctuations caused by hydration and abdominal contents (Durnin 1961).

Body Mass Index (BMI) is a simple index of weight-for-height that is commonly used to classify underweight, overweight and obesity in adults (World Health Organisation website). It is calculated by dividing the weight in kilograms by the square of the height in metres (kg/m²). BMI is limited as a measure of body fatness due to the increasing evidence that the associations between BMI, percentage of body fat, and body fat distribution differ across populations and amongst individuals of varying build (World Health Organisation 1995). For example, an individual with a high proportion of lean tissue may be classed as overweight for their height despite having a low fat content, so individuals with the same BMI can have a different body fat percentage. Consequently, body composition was measured in the present study to complement BMI readings.

3.9 Body composition

A variety of methods to assess body composition have been developed, none of which are perfectly free from error. Each has its advantages and limitations, and they are all based on certain assumptions that are not necessarily valid in all populations.

3.9.1 Hydrodensitometry

This method is based on measuring body volume and density from water displacement and involves immersing the subject underwater in a tank. Although considered the “gold-standard” of body composition analysis (Heyward and Wagner 2004), the method is very technical and time-consuming. It also requires considerable subject cooperation because the subject must perform a maximal exhalation while completely submerged in water, which may be difficult and uncomfortable for some.
3.9.2 Air displacement plethysmography

Similar to hydrodensitometry, this method measures body volume and density but uses air displacement instead of water displacement. A large, egg-shaped fibreglass chamber called the Bod Pod estimates body volume by pressure-volume relationships between two chambers. The accuracy of the method is comparable to hydrodensitometry and has been ranked highly in terms of cost, time, maintenance, ease of use, and subject acceptability (Fields et al. 2002).

3.9.3 Dual energy X-ray absorptiometry

The principle of DXA technology is based on the attenuation, or weakening, of two different X-ray energies as they pass through fat, lean tissue, and bone, which have different densities and chemical compositions. The major sources of error are the assumptions made about soft-tissue composition, differences in instrumentation among manufacturers, software versions, and subject factors (body size and hydration status). However, the reproducibility for measuring percentage body fat by DXA is only about 1% body fat, as there is minimal error from technical skill (Lohman 1996).

3.9.4 Skinfold method

The skinfold is a measure of the thickness of two layers of skin and the underlying subcutaneous fat. The method involves using a calliper device to “pinch” the skin at various predetermined body sites and entering the values into a specific regression equation that converts them into a body density and then percentage body fat reading. The skinfold test is easy to administer at a low cost, making it suitable in field and clinical settings as well as large-scale epidemiological studies, but the accuracy of measurements depend greatly upon technician skill. Even two highly trained operators can deduce significantly different outcomes when measuring the same subject and a prediction error\(^1\) of ±3.5% is generally accepted (Heyward and Wagner 2004). The type of calliper used introduces error in this method, as does the hydration level of the subject (e.g. an accumulation of extracellular water can increase skinfold thickness) and their degree of muscularity (which makes it difficult to separate the subcutaneous tissue from the muscle underneath). Also of concern is the compression of fat by the calliper due to variances in fat density and selecting the most appropriate equation for

\(^1\) A measure of the predictive inaccuracy of a prediction equation in estimating reference measures of body composition. Also called the standard error of estimate, it reflects the degree of deviation of the individual data points around the line of best fit and is mathematically calculated using an equation developed by Jackson (1989).
the age, sex, ethnicity, levels of body fatness and physical activity of the subject, as there are over 100 population-specific equations to predict body density from various combinations of skinfolds. Moreover, this method cannot be used to assess obese individuals because their skinfold thickness exceeds the maximum aperture of the calliper.

3.9.5 Bioelectrical impedance analysis

Bioelectrical impedance analysis (BIA) involves the measurement of the opposition of a conductor (the human body) to the flow of an alternating current. The impedance of a conductor is related to its length and cross-sectional area, and this relationship between impedance and volume is applied to the body by assuming that it is made up of cylinders with a uniform cross-sectional area and constant resistivity of tissues. Water conducts electricity much better than fat and because lean tissue is comprised of approximately 70-75% water whilst only 5-10% of adipose is water, lean tissue and fat tissue have very different resistance (impedance) values when a high-frequency electrical current is passed through the body via electrodes attached to the hand and foot, as occurs with BIA. The resulting impedance value reflects the degree of resistance to the flow of current in the body and, together with details of the subject’s age, sex, height, and weight, specific regression equations are used to calculate body composition (BODYSTAT Ltd 2000).

Rationale

Since BIA depends on the body’s water content, factors influencing hydration affects impedance. Low fluid levels increase the impedance measurement resulting in an artificially higher body fat percentage (Kyle et al. 2004), whereas ingesting 1.2-1.8 litres of water can increase impedance by about 15% (Khaled et al. 1988). The positioning of the electrodes and changes in temperature also influence impedance. It has been observed that displacement of electrodes by 1 cm can produce a 2% variation in body fat (Lohman 1992) and increases in skin temperature decrease impedance (Caton et al. 1988), thus resulting in falsely low body fat values. The device itself presents further inaccuracies, as there is no standardisation of BIA analysers so different devices may not produce the same resistance measure. However, numerous articles have validated the accuracy of BIA measurements when compared to the standard underwater hydrostatic weighing technique (BODYSTAT Ltd 2000). Although prediction error is between 3 and 4% body fat (Houtkooper et al. 1996), which is similar to the skinfold method, it was chosen for the present study.
because the technique is rapid, non-invasive, and non-intrusive, thus making it more acceptable as well as comfortable for subjects. Human skill is not a major source of error with the BIA method (Lohman 1992) and serial measurements of body composition using BIA are agreed to be valid in healthy subjects with a BMI between 16 and 34 kg/m² and normal hydration (Kyle et al. 2004). As long as the same operator takes all pre- and post-intervention measurements using the same device and consistent protocol, it was an appropriate method to track the trend in body composition changes over the course of the present study.

Procedure

The hydration status of the participants was controlled as much as possible by requesting them to avoid strenuous exercise, alcohol, and caffeine intake during the preceding 24 hours, and to have fasted for at least 4 hours (Deurenberg et al. 1988). A hand-held bioimpedance meter (Bodystat 1500, Bodystat Ltd., Douglas, Isle of Man) that supplies current at 50 Hz to four electrodes were attached to the hand, wrist, foot, and ankle. The area of skin where the electrodes were to be placed was cleansed with alcohol prior to their application to ensure that good electrical contact was made. The participant lay supine on a mat with their limbs slightly abducted so that there was no contact between the legs or between the arms and trunk, as contact would "short-circuit" the electrical path, thus affecting the impedance value. The distal electrodes (red colour) were placed at the base of the second/third metacarpal-phalangeal joints of the hand and foot, and the voltage drop due to impedance was detected by the proximal electrodes (black colour) on the dorsal surface of the wrist (so that the upper border of the electrode bisects the line between the styloid processes of the ulna and radius) and the dorsal surface of the ankle (so that the upper border of the electrode bisects the line between the medial and lateral malleoli). Placement of the electrodes is illustrated in Figure 3.7. Values of fat mass (kg), fat-free mass (kg), and body fat percentage (%) were produced by the meter after inputting the subject’s age, height, and body mass.
3.10 Assessment of potential confounders

Matching in the study design, controlling in the analyses, and recording through questionnaires are valid ways of being aware of and adjusting for potential confounders (Kelsey and Sowers 2001). A lifestyle questionnaire (see Appendix C) was designed to provide a general indication of the genetic and lifestyle factors detailed below that could exert different degrees of influence on the bone status of the participants and their subsequent response to the exercise intervention. The questionnaire was piloted on individuals who were not part of the study and the appropriate modifications were made.

3.10.1 Menstrual patterns

As discussed in Chapter 2, it is well established that oestrogen exerts a beneficial effect on bone (Turner et al. 1994) by enhancing the effects of mechanical stimulation on the skeleton through a modulation of bone remodeling (Frost 1999). Hence, it is clear that the full osteogenic benefit of exercise on bone is apparent only in oestrogen-replete women (Dnnkwater 1994). Assuming that regular menstruation is an indication of a healthy hormonal profile in a young woman, and since regular menstruation was listed in inclusion criteria, menstrual patterns of participants were therefore assessed through the lifestyle questionnaire. Age at menarche was also noted because a later menarcheal age is indicated to be a risk factor for lower BMD and more rapid rate of bone loss, which is first of all due to a shorter gynaecological age and secondly, events that precipitate earlier menarche (i.e. weight gain) may be associated with events that produce greater BMD (Sowers 2001).
3.10.2 Previous and current physical activity

Training history is not one of the present study's main variables but, along with current physical activity levels, it will be recorded because it could influence the magnitude of change observed in each individual, which is the major outcome of interest. If a high baseline BMD value in one participant is the result of exercise during puberty, then a smaller increase would be expected over the course of the intervention compared to someone who had a less active childhood and hence a lower starting BMD value at baseline. As explained earlier, strain due to loading will stimulate an osteogenic response until the bone is strong enough to bear the load, but if the bone is already strong enough at baseline, the exercise will not produce effective new strains (Frost 1997). Household, child-rearing and occupational activities were also included because although generally of lower intensity and impact than intentional exercise, non-exercise physical activities often incorporate relatively high degrees of weight-bearing, e.g. carrying children (Ulrich et al. 1999).

3.10.3 Family history

The impact of genetics on the efficacy of exercise in preventing osteoporosis is not well-understood, but considering the evidence for the genetic influence on peak BMD and rates of change in BMD over time (Brown et al. 2005), family history of osteoporosis was noted in the present study to allow examination of any differences between groups.

3.10.4 Previous fractures

Studies of bed rest and weightlessness show that bones respond to prolonged skeletal unloading by detrimentally altering the balance in bone turnover via a rapid and sustained increase in bone resorption and a more subtle decrease in bone formation (Smith et al. 2005, Zerwekh et al. 1998). Previous fractures were recorded so that anyone who has had a period of prolonged immobilisation and possible bone loss in the past could be detected. It would be particularly important to consider excluding these individuals for the current study, because this factor could contribute to asymmetry between limbs.
3.10.5 Smoking status and alcohol intake

The diagnosis of osteoporosis is based on the measurement of BMD, but there are a number of clinical risk factors that provide information on fracture risk over and above that given by BMD, one of which is smoking. Existing literature establishes that there is an association between cigarette smoking and low BMD (Demirbag et al. 2006, Mazess and Barden 1991, Yoshimura 2005), and even though the risk ratios are lower than for current smoking, past smokers are at a significantly increased risk of osteoporosis compared to individuals with no smoking history (Kanis et al. 2005).

The effects of alcohol on bone are not as clear as those of smoking. Chronic consumption of excessive alcohol increases the incidence of falling and also delays the bone healing process compared with non-alcoholics (Chakkalakal 2005). Yet there is mounting epidemiological evidence indicating that individuals who have a moderate intake of alcohol have a higher BMD than abstainers (Jugdaohsingh et al. 2006, Wosje and Kalkwarf 2007), and it is thought that alcohol may have a dose-dependent toxic effect on osteoblast activity (Chakkalakal 2005). The mechanism behind smoking and low BMD could also be the result of a direct toxic effect on bone cells (Jesudason and Need 2002), but there are other potential causes since smoking and drinking are associated with other lifestyle factors that affect bone, such as low nutrient levels (e.g. calcium and vitamin D) and low levels of physical activity (Tudor-Locke and McColl 2000).

Again, it was important to record smoking status and alcohol consumption because these two factors could potentially explain baseline BMD and its subsequent rate of increase over the course of the intervention.

3.10.6 Diet

Dietary assessment involved a food frequency questionnaire (FFQ) for calcium intake (adapted from Magkos et al. 2006) (see Appendix D) that asked participants to define how often and how much of specific calcium-rich food items they habitually (during the previous year) consumed. FFQs are easy to administer and are the method of choice for investigations relating diet to disease when longer-term patterns of intake are more important than intake during a few specific days (Willett 1990). However, compared to the relatively precise intake measurements obtained from a short diet diary, information derived from a FFQ is more crude, thus is used to classify individuals into levels of daily intake rather than to calculate actual daily intakes.
(Bodner et al. 1998). A second FFQ was administered to participants that was a more general dietary survey (see Appendix E), for there is increasingly more evidence about the way in which nutrients interact with one another and thereby alter their mutual requirements. For example, urinary calcium excretion is strongly influenced by sodium, potassium, and the acid/alkaline residue of the diet (Heaney et al. 2000, New 2001), meaning excessive intakes of certain nutrients could negatively affect calcium absorption in the body. Establishing relationships between diet and BMD was not one of the current study’s main objectives, but the information was collected to identify any differences between groups or changes over time in diet that may confound findings.

3.11 Statistical analysis

To describe the population, basic descriptive statistics including means, standard deviations (SD), and percent changes in variables were calculated. Differences between groups at baseline were detected with an independent samples t-test. Various statistical tests were employed for different purposes and are detailed in each study chapter. Principal analyses were paired t-tests, repeated measures analysis of variance, correlations, and linear regression. All tests were two-tailed and differences were considered statistically significant at the 5% probability level ($p<0.05$). Data were analysed using the SPSS statistical package (SPSS 14.0 for Windows, SPSS, Chicago, Illinois, USA).
Assessing the effectiveness and feasibility of high-impact, unilateral exercises as a model to study skeletal and neuromuscular responses to exercise: A pilot study

4.1 Introduction

There is consensus that exercise can maintain bone health in adulthood and prevent its decline during ageing (Kohrt et al. 2004). Research has further established that bone responds to strain that is dynamic rather than static, shorter rather than longer in duration, and novel rather than typical (Turner 1998). Therefore, it seems that physical activity for bone health should focus on variables other than those deemed important for the cardiovascular system, e.g. force magnitude and the rate of force development, rather than exercise bouts of longer duration and prolonged elevation of heart rate.

As described in earlier chapters, brief but regular bouts of jumping can significantly increase BMD (Bassey et al. 1998, Kato et al. 2006). The models for these studies were animal studies that have produced large osteogenic responses from few cycles of mechanical strain (Umemura et al. 1997). Although it is not possible to assess bone strain in vivo in humans, direct measures have been obtained from patients with instrumented hip protheses, which suggest that compressive forces in the hip during jumping are about twice as high as the GRFs (Bassey et al. 1997). An important feature of jumping in addition to its capacity to generate high magnitude strains, is that it involves strain distributions on the skeleton that are atypical for women who do not engage in high-impact sports (Bassey et al. 1998); thereby placing unusual but effective mechanical strain on bones. To reiterate the rationale of the present research, in light of the osteogenic characteristics of jumping, it follows that hopping could be an even more effective activity for women not used to high-impact exercise. The benefit of hopping providing a contralateral untrained limb also offers a very strong study design because effects of confounding factors are substantially reduced.

So far there have been no studies that have considered hopping as an activity to increase BMD, thus it is unknown whether it would be practical to use as an exercise intervention. Therefore, the aim of the pilot study was to investigate the effectiveness and feasibility of hopping exercises as a long-term exercise intervention to study bone’s response to mechanical loading. Primary objectives were to compare the GRFs produced in hopping with those in jumping and to assess compliance rates and subject-acceptability to the hopping exercises in a short-term intervention. Secondary
objectives were to evaluate if hopping exercises induce a physiological and/or neuromuscular response that may be consistent with increased bone loading. These included body mass, leg circumference, balance, leg strength, and hopping height. It was also important to detect any evidence of asymmetry that could deter participants.

4.2 Methods

Design

The study was a RCT including a training experimental group and a non-training control group. The training protocol consisted of brief, unilateral, high-impact exercise that was performed 5 days per week for a period of 6 weeks. Control subjects continued their normal lifestyle. Both groups were measured at baseline and post-intervention.

Participants

A total of 13 healthy females between the ages of 18 and 45 participated in the study. As detailed in chapter 3, exclusion criteria included being younger than 18 years or older than 45 years, having a BMI below 18.5kg/m² or above 30kg/m², current or recent (previous 12 months) participation in high-impact, weight-bearing exercise for more than 1h/week, current or recent (previous 12 months) medical or surgical problems likely to affect bone metabolism, history of lower limb or back problems, low calcium intake (i.e. avoiding dairy products unless taking calcium supplements), and having less than 10 or more than 13 menstrual cycles per year (oral contraception use was permitted). Women were also excluded for pregnancy, recent childbirth (previous 12 months), or current or recent (previous 6 months) lactation. From a sealed container, they were instructed to draw out a card that designated them into either the control group or the exercise group. They then withdrew another piece of paper from a second container that assigned their right leg or left leg to be their hopping leg. Exercisers were to do the hopping exercises only on this leg for the duration of the intervention and for controls it was a way to randomly name each leg as the “trained leg” or the “control leg”. Before giving their consent all recruits were fully informed about the study as well as any possible health risks. The study design and procedures were approved by Loughborough University’s Ethical Advisory Committee.
Anthropometry

Body mass was measured to the nearest 0.1 kg using electronic scales and standing height was measured to the nearest mm from a wall-mounted stadiometer. BMI was then calculated by the following equation: weight (kg) / height\(^2\) (m)

The circumference of the thigh midway between the iliac crest and patella and the circumference of the calf midway between the patella and calcaneus were measured to the nearest mm using a tape measure so that any considerable asymmetry in leg circumference in the trained leg could be detected.

Maximal isometric strength

Maximal isometric knee extensor force was measured separately for the right and left limb using a dynamometer as described in Chapter 3.

Ground reaction forces and jump/hop height

In addition to measuring GRFs and hop height in the maximal hop test and submaximal hopping test described in Chapter 3, the pilot study included a maximal vertical jump test during which the subject performed one stationary countermovement jump, again with arm swing. This enabled the GRFs produced during jumping, an activity known to increase hip BMD, to be compared to the GRFs involved with the proposed hopping exercises.

Bone measurements

Quantitative ultrasound techniques were used to measure BUA and SOS from three skeletal sites on both sides of the body. The calcaneus was assessed by the water-coupled Osteometer DTU-One Instrument (version 2.02, Osteometer MediTech, Hørsholm, Denmark) whilst the tibia and radius were assessed by the gel-coupled Omnisense 7000S (Sunlight Medical Ltd., Tel Aviv, Israel). Both were calibrated with a phantom at the beginning of each new day of measurement.

Questionnaires

The lifestyle questionnaire described in Chapter 3 was completed by all participants and the evaluation form by the exercisers.
The exercise programme

Participants remained in their normal clothes and removed their shoes. They were instructed to perform the hopping exercises on a hard, even, non-slippery floor. Each session began with a warm-up of walking on-the-spot, knee flexes, and hip and ankle rotations to mobilise the muscles and joints of the legs and lower back. The exercise session consisted of a total of 50 single-legged hops, divided into 5 sets of 10 and separated by a recovery period of approximately 15s. Each set of 10 hops were performed in a variety of different directions. Sets 1 and 5 consisted of vertical hopping; set 2, anteroposterior hopping; set 3, mediolateral hopping; and set 4, twisting hops that alternated medial rotation of the leg and lateral rotation of the torso and vice-versa. Participants were encouraged to hop as high as possible but at a height that they could maintain consistently for each set. They chose where and on which 5 days of the week to do the training and they were given individual training logs on which to record their completed hops during the 6 weeks.

Statistical analysis

Changes in variables at the end of the training were expressed as percentages of baseline values. Differences between groups at baseline were detected with an independent samples t-test and changes within each group were also estimated by a paired samples t-test. A repeated measures ANOVA detected whether differences in response between legs differed between groups.

4.3 Results

The physical characteristics of the participants are given in Table 4.1. Their mean height and weight are comparable to British women of these age groups (Office for National Statistics 2004). Table 4.2 displays mean values of tested variables at baseline, which did not significantly differ between the two groups.

Table 4.1: Physical characteristics of participants at baseline, mean (SD)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Training group (n=7)</th>
<th>Control group (n=6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>36.2 (7.4)</td>
<td>29.5 (9.2)</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>1.66 (0.08)</td>
<td>1.68 (0.10)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>67.3 (12.6)</td>
<td>63.3 (9.6)</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>24.2 (3.1)</td>
<td>22.4 (2.5)</td>
</tr>
</tbody>
</table>

No significant differences between groups (p>0.05)
Feasibility – osteogenic potential of hopping

One of the aims of the study was to assess the osteogenic potential of the hopping training. This can be achieved by comparing our measurements of GRF with those reported in studies that have reported considerable improvements in properties of bone. Since the principal determinant of habitual loading and loading during the hopping exercises experienced by each subject is their body mass, landing forces are expressed in multiples of body mass. Peak landing force recorded during a maximal hop varied between 2.7(1.5) and 4.1(0.8) times body mass in this sample of untrained young women. These values are comparable to the peak landing force experienced during a maximal jump in the training group (3.3(2.1) times body mass), and exceed those recorded in the control group (5.0(0.9) times body mass). If the landing force during a jump is halved by assuming body mass is evenly distributed on two legs, then the landing force on one leg during a hop is even greater than that experienced by one leg during a jump.

Table 4.2: Tested variables of participants at baseline, mean (SD)

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Training group (n=7)</th>
<th>Control group (n=6)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Trained leg</td>
<td>Control leg</td>
</tr>
<tr>
<td>Thigh circumference (m)</td>
<td>0.55 (0.47)</td>
<td>0.55 (0.61)</td>
</tr>
<tr>
<td>Calf circumference (m)</td>
<td>0.36 (0.24)</td>
<td>0.38 (0.24)</td>
</tr>
<tr>
<td>Calcaneus BUA (dB/MHz)</td>
<td>43.1 (8.3)</td>
<td>45.6 (9.5)</td>
</tr>
<tr>
<td>Calcaneus SOS (m/s)</td>
<td>1564 (8.2)</td>
<td>1565 (5.9)</td>
</tr>
<tr>
<td>Tibia SOS (m/s)</td>
<td>4049 (188)</td>
<td>4067 (155)</td>
</tr>
<tr>
<td>Radius SOS (m/s)</td>
<td>4255 (109)</td>
<td>4251 (108)</td>
</tr>
<tr>
<td>Sway speed (mm/s²)</td>
<td>25.1 (7.2)</td>
<td>28.1 (10.4)</td>
</tr>
<tr>
<td>Maximum isometric knee extension force (N)</td>
<td>393.4 (76.5)</td>
<td>465.0 (54.0)</td>
</tr>
<tr>
<td>Mean of peak landing GRF from 10 hops (xBM)</td>
<td>2.39 (0.31)</td>
<td>2.28 (0.44)</td>
</tr>
<tr>
<td>Peak landing GRF from a maximal hop (xBM)</td>
<td>2.73 (1.50)</td>
<td>3.02 (0.74)</td>
</tr>
<tr>
<td>Peak landing GRF from a maximal jump (xBM)</td>
<td>3.33 (2.13)</td>
<td>5.04 (0.86)</td>
</tr>
<tr>
<td>Mean of peak hop height from 10 hops (cm)</td>
<td>6.2 (1.9)</td>
<td>7.2 (1.6)</td>
</tr>
<tr>
<td>Peak hop height from a maximal hop (cm)</td>
<td>10.4 (2.3)</td>
<td>11.1 (2.0)</td>
</tr>
<tr>
<td>Peak jump height from a maximal jump (cm)</td>
<td>24.1 (4.1)</td>
<td>22.2 (2.8)</td>
</tr>
</tbody>
</table>

xBM = force in multiples of body mass
No significant differences within groups or between groups (p>0.05)
Feasibility - programme adherence

All 13 subjects completed the study and compliance in the training group, defined as the percentage of completed training sessions out of the prescribed sessions per week, was 97%. One participant missed five days of hopping because she was ill for a week, and another forgot to hop on one day whilst on holiday. The positive feedback received from the hoppers indicates the high subject-acceptability of the training programme (Table 4.3). As one commented, "the hopping didn’t take long and wasn’t difficult to do". All subjects reported that they enjoyed taking part and said they would continue the exercise long-term if it would reduce their risk of developing osteoporosis. A couple of women made a specific note that they thought their balance had improved over time. The only barrier highlighted was that "sometimes it was difficult to remember". No injuries were reported and 2 participants experienced muscle soreness but this was only a transient discomfort at the start of the intervention.

### Table 4.3: Frequencies of responses to the training intervention

<table>
<thead>
<tr>
<th>Comment</th>
<th>Number of responses</th>
</tr>
</thead>
<tbody>
<tr>
<td>I enjoyed taking part in this study</td>
<td>7</td>
</tr>
<tr>
<td>Doing the hopping exercises was boring</td>
<td>1</td>
</tr>
<tr>
<td>I found the hopping exercises easy to do</td>
<td>6</td>
</tr>
<tr>
<td>I experienced muscle soreness</td>
<td>2</td>
</tr>
<tr>
<td>I experienced injury</td>
<td>0</td>
</tr>
<tr>
<td>I easily fit the exercise into my regular routine</td>
<td>6</td>
</tr>
<tr>
<td>The hopping exercise was too time-consuming</td>
<td>0</td>
</tr>
<tr>
<td>It was easy to remember to do the hopping</td>
<td>3</td>
</tr>
<tr>
<td>I feel fitter than I did beforehand</td>
<td>1</td>
</tr>
<tr>
<td>I would carry on long-term if it reduces my risk of developing osteoporosis</td>
<td>6</td>
</tr>
</tbody>
</table>

Effectiveness - changes incurred from hopping

Table 4.4 displays changes in each leg that took place during the hopping exercises intervention. Apart from a significant decrease in calcaneus SOS in all legs, there were no changes in other bone parameters that suggested the short-term training programme had an effect on bone. There were, however, neuromuscular changes over the course of the intervention, which were demonstrated by the greater improvements in maximal (Figure 4.1) and submaximal hopping performance in the exercisers compared to the controls, although improvements were observed in both the trained
and untrained limbs. There was a significant reduction in BMI in both exercisers and controls and the decrease in body mass in each group almost reached significance (p=0.05). Despite these changes in each leg, when tested by a RMANOVA, the changes in the trained leg were not significantly different from those in the control leg within each group, and neither were there differences in response between groups.

Table 4.4: Changes in tested variables at the end of the 6-week intervention expressed as a percentage of the baseline value, mean (95% CI)

<table>
<thead>
<tr>
<th></th>
<th>Hopping group (n=7)</th>
<th>Control group (n=6)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Trained leg</td>
<td>Control leg</td>
</tr>
<tr>
<td>Body weight (%)</td>
<td>-1.9* (-3.8 to -0.1)</td>
<td>1.4 (0 to 2.8)</td>
</tr>
<tr>
<td>BMI (%)</td>
<td>-1.9* (-3.8 to -0.1)</td>
<td>1.4* (0 to 2.8)</td>
</tr>
<tr>
<td>Thigh circumference (%)</td>
<td>-1.1 (-4.5 to 2.4)</td>
<td>-0.6 (-4.0 to 2.9)</td>
</tr>
<tr>
<td>Calf circumference (%)</td>
<td>-0.4 (-1.7 to 1.0)</td>
<td>-0.8 (-2.4 to 0.9)</td>
</tr>
<tr>
<td>Calcaneus BUA (%)</td>
<td>3.0 (-11.9 to 17.9)</td>
<td>-4.2 (-14.8 to 6.5)</td>
</tr>
<tr>
<td>Calcaneus SOS (%)</td>
<td>-2.0*** (-3.1 to -0.9)</td>
<td>-1.9* (-3.2 to -0.6)</td>
</tr>
<tr>
<td>Tibia SOS (%)</td>
<td>1.4 (-1.5 to 4.4)</td>
<td>0.7 (-1.8 to 3.2)</td>
</tr>
<tr>
<td>Radius SOS (%)</td>
<td>0.1 (-1.7 to 1.8)</td>
<td>1.8 (-0.8 to 4.4)</td>
</tr>
<tr>
<td>Average sway velocity (%)</td>
<td>-11.1 (-26.4 to 4.2)</td>
<td>12.2 (-34.3 to 9.9)</td>
</tr>
<tr>
<td>Maximal isometric knee extension strength (%)</td>
<td>13.1 (-8.0 to 26.9)</td>
<td>9.9 (-11.8 to 31.7)</td>
</tr>
<tr>
<td>Mean of peak landing GRF from 10 hops (%)</td>
<td>5.8 (-1.0 to 12.6)</td>
<td>13.8 (-9.7 to 37.3)</td>
</tr>
<tr>
<td>Mean of peak hop height from 10 hops (%)</td>
<td>43.3*** (29.7 to 56.9)</td>
<td>48.5*** (36.0 to 61.1)</td>
</tr>
<tr>
<td>Peak landing GRF from a maximal hop (%)</td>
<td>-2.2 (-23.0 to 18.7)</td>
<td>-0.1 (-35.6 to 35.4)</td>
</tr>
<tr>
<td>Peak hop height from a maximal hop (%)</td>
<td>22.4* (3.2 to 41.5)</td>
<td>16.2* (4.4 to 28.1)</td>
</tr>
<tr>
<td>Peak landing GRF from a maximal jump (%)</td>
<td>4.2 (-31.0 to 39.4)</td>
<td>-5.7 (-21.0 to 9.7)</td>
</tr>
<tr>
<td>Peak jump height from a maximal jump (%)</td>
<td>2.9 (-9.3 to 15.2)</td>
<td>4.0 (-1.2 to 9.3)</td>
</tr>
</tbody>
</table>

*Significantly different from zero (p<0.05)
**Significantly different from zero (p<0.01)
***Significantly different from zero (p<0.001)
Figure 4.1: Comparison of the changes within legs in maximal hop height between the exercisers and controls, mean (95% CI)

4.4 Discussion

One of the principal aims of this pilot study was to assess the osteogenic potential of hopping, which is an activity that has not yet been studied in terms of exercise for bone health; with the intention to use such a unilateral activity in a long-term intervention. We demonstrated that the GRFs acting on one leg during submaximal hopping exceeds the GRFs acting on one leg during a maximal jump when assuming symmetrical distribution of body weight on each foot. The values we recorded are also greater than those measured previously by Bassey et al. (Bassey et al. 1998), who reported a significant increase in BMD at the trochanter following a jumping programme that involved a peak GRF of 3 times body weight. Moreover, the women in the latter study had to jump almost 9cm to produce this impact force, whereas in the current study a hopping height between 5cm and 7cm corresponded to a landing force of approximately 2 times body mass (which is all applied on one leg). These comparisons indicate that our unilateral exercise design is sufficient in intensity to potentially produce significant gains in BMD and that the required height of the hops is achievable for healthy premenopausal women.

For such exercise to provoke skeletal adaptation more time would be needed, thus the second major aim of the study was to determine the feasibility of the hopping exercises as an activity that people could and would adopt in the long-term. This short-term study observed a 0% drop out rate and 97% of the prescribed sessions
were completed by exercisers. Although it can be argued that the number of subjects was small and the intervention relatively short, the fact that none of the women dropped out and that the only reason for missed sessions was illness, are strong indicators that the training programme was extremely well-received. The positive comments made on the evaluation forms are also evidence of high subject-acceptability. The high adherence rate may be due to the low demands of the programme, because unlike many previous exercise studies, participants were not required to spend time travelling to a specific location to perform the training in a group under supervision (Friedlander et al. 1995, Gleeson et al. 1990, Heinonen et al. 1998, Vainionpää et al. 2005). Instead they were free to decide where and when to do their hopping, thereby making it a much easier activity to fit into daily routine.

Although a lifestyle-intervention approach would ultimately prescribe hopping on both legs, the lack of change in leg circumference shows that this type of unilateral training is not associated with asymmetrical leg circumference. This is in line with existing evidence that prolonged power training causes an increase in muscle force production without muscle fibre hypertrophy (Hakkinen et al. 2000). Alternatively, it could be that the short-term exercise intervention was not long enough to observe changes in muscle hypertrophy, since neural factors play a more dominant role than hypertrophic factors in the course of strength development up to 6 weeks of training (Montan and deVries 1979), which is when this study ended. Neither do the hopping exercises seem to have a negative impact on postural balance; rather, there was a reduction in average sway velocity in both legs, although not significant. There were no reports of injury or discomfort indicating an absence of adverse effects in this small sample. Overall, the intervention did not seem to have undesirable side effects that may limit the feasibility, acceptability, or safety of a longer-term intervention.

The phantom measurements did not display a notable instrument drift, so the decrease in calcaneus SOS may have been due to chance (especially in such a small sample size) or a seasonal effect, but probably not a true biological effect caused by the hopping exercises since the same trend was observed in the controls. It is also unlikely that such dramatic changes took place in the bone after such a short period of time, because unlike the more rapid adaptations in neuromuscular function, changes in bone take up to 4 months to be biologically meaningful enough to be detected (Chilibeck et al. 1995).

It is questionable as to whether the exercise programme per se caused the reduction in BMI in the hoppers because oxygen consumption during submaximal jumping is
23.7-33.0 ml/kg/min (Kyrolainen et al. 2004) or 119-157 kcal, an inadequate amount of energy expenditure to appreciably influence energy balance during the brief-lasting bout of hopping exercises. It may be that women who undertook the training made other lifestyle changes (e.g. diet) that resulted in weight loss and hence a lower BMI value. Reductions in body mass may have affected findings, since weight loss is strongly associated with bone loss in men and women alike (Ensrud et al. 2005, Stewart et al. 2005), but mean weight loss was less than 1kg; a minimal amount to negatively influence bone adaptation over such a short time. More considerable weight loss could have provoked bone loss through reduced loading during habitual activities, reduced intake of nutrients such as calcium, and/or a weakened osteogenic effect of the hopping as a lower gravitational impact from body mass reduces mechanical loading on the supporting bones.

There were no differences in response between limbs indicative of a local skeletal response, but the sample size was possibly too small to detect significant changes in these variables. However, the exercise appeared to provoke neuromuscular adaptation because exercisers could hop significantly higher during both the 10 hops test and the single maximal hop test at the end compared to the start of the study, whereas the same improvements were not observed in the controls. Additionally, although not significant, an increase in IKES in both legs and a decrease in postural sway speed in the trained leg were evident. The improvements in maximal hopping performance were not limited to the allocated hopping leg, as although not as large, the control leg also showed a significant improvement in maximal hop height. It is likely that there was a central effect in that balance and/or coordination had improved, thus improving performance when hopping on either leg. Local neuromuscular effects on both trained and control legs may also be possible. Reports of contralateral limb exercise training producing a "cross-education" or "cross-over" effect has existed since the end of the 19th century (Gabriel et al. 2006). Eight weeks of unilateral, isometric training has been known to increase the strength of the contralateral limb by as much as 25% (Moritani and deVries 1979), but even though considerable evidence of a cross-over effect during training of one limb has since followed (Zhou 2000), the mechanism remains unclear. One possibility is that the intermuscular coordination of the stabilisers, synergists, and antagonists involved in the movement is learnt during the early phase of training and subsequently applied to the untrained, contralateral side (Rutherford and Jones 1986). The possibility of a cross-over effect in unilateral exercise studies needs to be further examined.
4.5 Conclusions

Unilateral high-impact exercise is feasible and acceptable and so may be useful for studying musculoskeletal adaptation. Hopping exercises provide greater peak GRF than jumping, which can increase BMD, so hopping may be effective in increasing bone mass, although this study was too short to detect skeletal response. Whilst exercisers showed significant increases in hop height consistent with neuromuscular adaptation (although this did not differ significantly from controls so cannot eliminate a familiarisation effect), no significant local muscular effects were observed. Nevertheless, factors such as improved coordination and stability are equally important for fracture prevention in that they reduce the risk of falling. Overall, this pilot study has demonstrated that the proposed unilateral exercise programme provides an effective model to accurately study the effects of exercise on bone adaptation and that it would be feasible for healthy women to perform in the long-term.
Using a high-impact, unilateral exercise programme to determine the optimum exercise frequency for optimal bone health

5.1 Introduction

Both human and animal studies have investigated the characteristics of mechanical loading for optimal bone formation. It has been demonstrated that strain from mechanical loading needs to be of a high magnitude (Nikander et al. 2006, Robinson et al. 1995, Rubin and Lanyon 1985), a high rate (Heikkinen et al. 2006, Mosley and Lanyon 1998) of unusual strain distributions (Heinonen et al. 1995, Lanyon 1996, Milgrom et al. 2001), and not necessarily of long duration (Snow 1996, Srinivasan et al. 2002, Umemura et al. 1997). It seems that mechanical loading is not only more osteogenic if short rest intervals are inserted between cycles, but also if each bout of loading is separated by several hours (LaMothe and Zernicke 2004, Robling et al. 2001). However, the optimum frequency of loading bouts, i.e. the number of times per week that bone needs to undergo mechanical loading, has yet to be defined. Along with the type, duration, and intensity, frequency of exercise is an important aspect of exercise prescription and warrants investigation.

Findings of the recent pilot study demonstrated that unilateral jumping, i.e. hopping, produces greater GRFs per leg than was recorded in previous jumping studies that significantly increased hip BMD (Bassey et al. 1998, Kato et al. 2006), thereby strongly suggesting that hopping exercises could potentially be an even more effective activity to increase BMD at relevant skeletal sites. The benefits of having a contralateral untrained limb; in that effects of confounders are reduced and a large sample size is not required, have been emphasised many times before.

Consequently, the aim of this study was two-fold: First, to investigate the long-term effectiveness and feasibility of hopping exercises to increase BMD in premenopausal women, and second, to establish the weekly frequency of exercise for optimum gains in BMD.
5.2 Methods

Design

The study was a home-based, RCT conducted in premenopausal women who were randomly divided in blocks of 12 into 3 exercise groups and 1 control group. The exercisers performed a total of 50 hops either 2 (G2), 4 (G4), or 7 (G7) days per week, for a period of 6 months. The controls continued their normal lifestyle but came into the laboratory for the same measurements at the same times as the intervention groups. Measurements were made of BMD and hip geometry at baseline and post-intervention; while anthropometry, body composition, neuromuscular function, hopping performance, ground reaction forces, and lifestyle characteristics were assessed at baseline, mid-way, and post-intervention. Participants were requested to maintain their usual diet and lifestyle throughout the study. The study was approved by Loughborough University’s Ethical Advisory Committee and all participants provided written, informed consent. They were free to withdraw from the study at any time without explanation.

It was necessary to organise the study into 2 cohorts to aid recruitment by allowing two separate intakes and to make it more feasible for the study to be conducted by one person. The actual intervention lasted 6 months, but the process of recruitment, preparation, testing, and following-up individuals who were unavailable at the exact 6-month time point demanded a considerably longer time. Once the intervention started, it was then important to keep in regular contact with participants to sustain their interest in the relatively long, unsupervised, home-based programme. Following each testing time point (i.e. at 0, 3, and 6 months) time was taken to analyse data and produce a newsletter for each individual that included preliminary results and their DXA reports (at baseline and post-intervention). Consequently, two 6-month interventions were carried out exactly 12 months apart. This served to reduce any seasonal effect - variation that may be introduced by a decrease in total body and regional BMC in the winter and their increase in the summer (Rico et al. 1994).

Calculation of sample size

Three criteria usually need to be specified to determine the appropriate sample size: the level of precision, the level of confidence or risk, and the degree of variability in the attributes being measured (Miaoulis and Michener 1976). However, it was not possible to calculate accurately the required sample size for my study from established equations because no other unilateral exercise study has recorded significant effects.
on bone. One practical approach is to use the same sample size as those of similarly conducted studies. The risk of this is that the procedures employed in published studies are often not reviewed so it is possible to repeat errors that were made in determining the sample size for other studies. Nonetheless, a review of the relevant literature can provide guidance about "typical" sample sizes that have been used. Table 5.1 lists the most similar studies conducted to date, with details of their sample size and results.

Table 5.1: Review of sample sizes in studies of similar exercise intervention and duration (effects of the intervention were only included in the table if the changes in exercisers' BMD significantly differed from those which occurred in the control group)

<table>
<thead>
<tr>
<th>Study</th>
<th>Intervention</th>
<th>Sample size</th>
<th>Increases in BMD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bassey and Ramsdale (1994)</td>
<td>Weekly high-impact exercise session + 50 jumps daily for 6 months</td>
<td>14 exercisers 13 controls</td>
<td>3.2% at trochanter</td>
</tr>
<tr>
<td>Bassey et al. (1998)</td>
<td>50 jumps 6 d/week for 5 months</td>
<td>30 exercisers 25 controls</td>
<td>2.9% at trochanter</td>
</tr>
<tr>
<td>Kato et al. (2006)</td>
<td>10 maximum jumps 3 d/week for 6 months</td>
<td>18 exercisers 18 controls</td>
<td>2.4% at lumbar spine 2.6% at femoral neck</td>
</tr>
<tr>
<td>Valinionpaa et al., (2005)</td>
<td>Variety of high-impact exercises 3 d/week for 12 months</td>
<td>39 exercisers 41 controls</td>
<td>1.0% at trochanter 1.0% at femoral neck 2.6% at Ward's triangle</td>
</tr>
</tbody>
</table>

In view of the above treatment effects and sample sizes of most similar studies, we anticipated that a 6-month high-impact exercise intervention could increase hip BMD by approximately 2%. Based on 80% power to detect a significant difference ($\rho=0.05$, two-sided) with an assumed standard deviation of 2%, 16 women in each group (64 in total) were required. This number was calculated using the following formula:

$[7.9 \times 2 \text{ (SD of change)}^2] / \text{BMD change}^2$

An important difference between my proposed study and the ones highlighted in Table 5.1 is the use of a unilateral exercise intervention. Since exercisers will have a control limb to compare their trained limb to, as well as a group of participants acting as controls, the required sample size for the proposed study was considerably reduced. To compensate for drop outs, we planned to enrol at least 20 participants per group, but it was decided that an end number of 12 participants in each intervention group would adequately address my research questions.

Participants
Women in good health and able to perform brief, high-intensity exercise were recruited on the university campus and in the local community as described in Chapter 3. To be eligible to take part, participants had to be 18-45 years-old, have a BMI between 18.5 and 30kg/m$^2$, do less than 1hr/week of high-impact weight-bearing exercise, consume dairy products or calcium supplements daily, have 10-13 menstrual cycles per year, be able to perform high-Impact exercise safely (i.e. no medical, lower limb or back conditions), not to be currently pregnant or lactating, and not to have given birth in the previous year.

For the first intake, 59 women were initially interested and the 51 who were eligible to enter the study were randomised equally between the 4 groups. For the second intake, 38 women were recruited and all met inclusion criteria. After evaluating the end numbers in each group following completion of the first study, participants in the second cohort were randomised unequally to protect the number of lost exercisers in certain groups. The sample size of the two cohorts combined at each stage of the study is traced in Figure 5.1 in the Results section.

**Anthropometry and body composition**

In addition to previously described stature and body mass measurements, body composition was assessed using the BIA method (*Bodystat 1500*). As detailed previously, subjects were requested to avoid strenuous exercise, alcohol, and caffeine intake during the preceding 24 hours, as well as food and water for 4 hours beforehand, in order to control hydration status. Body fat percentage and fat-free mass were noted.

**Maximal knee extension strength**

The maximal force that could be exerted during an isometric knee extension test was determined for each leg separately, as detailed in Chapter 3.

**Maximal and submaximal ground reaction forces and hop height**

GRFs and hop height during submaximal hopping and a single maximal hop were recorded for each leg using a force plate, replicating the methods described in Chapter 3.
Postural sway

Velocity of sway during a static, single-leg balance test was assessed for each leg with the force plate. Specific details are covered in Chapter 3.

Bone measurements

As explained in Chapter 3, BMD at the lumbar spine, left and right proximal femurs, and left and right tibiae were assessed using DXA, as were FSI, CSMI, CSA, and minimum femoral neck width – parameters that represent hip structure. The two cohorts had their scans taken by two different machines. Cohort 1 had their bone measurements taken at the University of Derby, whereas cohort 2 were measured at Loughborough University. All scans for the same subject were performed on the same instrument (Lunar Prodigy Advance) by the same operator.

As in the pilot study, BUA and SOS of the calcaneus and SOS of the tibia and radius were measured by ultrasound techniques (DTU-One Ultrasound Bone Scanner and Sunlight Omnisense 7000) on both sides of the body.

Questionnaires

In addition to the lifestyle questionnaire and dietary food frequency questionnaires explained in Chapter 3, exercisers completed an additional evaluation form mid-way during the intervention as well as at the end. This served to acquire feedback concerning the acceptability and feasibility of the exercise programme by seeking graded responses to a variety of comments that included occasions of injury or experience of discomfort, subjective perceptions of improvement in hopping performance, balance, and strength; and attitudes towards commitment and enjoyment of participation (see Appendix F).

The exercise programme

Each training session consisted of several minutes of gentle warm up and mobilisation exercises followed by 5 sets of 10 hops, which provided 100 strain reversals from take-off and landing. Repetitions were performed in succession with approximately 15s walking on-the-spot between sets. Hops were performed without shoes on to prevent a potential cushioning effect on strain magnitude and in a variety of orientations to ensure high strain distribution: vertically up and down, with
anteroposterior movement, with mediolateral movement, and twisting hops (i.e. incorporating rotation). Progression in the proposed study could be achieved in more than one way. Since force is a product of mass and acceleration, either increasing acceleration by jumping higher, or increasing the strain rate by jumping faster would introduce a progressively more osteogenic stimulus. Thus, exercise intensity increased naturally by encouraging participants to continue to hop as high as they could each time (but at a height that they could maintain consistently for the whole set) and to gradually increase the speed at which they hopped as they became familiar and more confident with the routine. Participants chose where and on which days of the week to do the exercises, but they were recommended to allocate a regular time and location where possible. Individual training logs (see Appendix G) were given to the exercisers on which they recorded the days of the week when they did the training and the number of hops completed on each occasion. They were encouraged to make any comments on their log, especially the occurrence and extent of adverse effects. Exercisers received two training logs: the first was given when they came to the laboratory for the baseline tests and returned when they came in for the mid-way tests, which was when they received the second to register their training for the last 3 months. This log was then collected during their final visit for the post-study measurements.

Statistical analysis

To describe the population, basic descriptive statistics including means, standard deviations (±1SD), and percent changes in variables were calculated. Differences between groups at baseline were detected with a one-way ANOVA. Paired t-tests assessed whether changes occurred within each leg in the control group and each exercise group. The overall effects of the intervention were examined using repeated measures ANOVA to determine whether the changes/response differed between the trained leg and control leg. A one-way ANOVA was employed again to assess differences in response to the intervention (i.e. the change in the trained leg minus the change in the control leg) between the groups of differing weekly frequencies, and a Bonferroni post hoc test controlled for multiple comparisons.
Figure 5.1: Diagram showing the flow of participants through each stage of the study

Assessed for eligibility ($n=93$)

Enrollment

Excluded ($n=8$)
Did not meet inclusion criteria

Randomised Allocation

Allocated to intervention Group 0 ($n=20$)
Discontinued intervention ($n=1$)
Changed circumstance ($n=1$)
Analysed ($n=16$)
Excluded from analysis due to losing >5kg body mass ($n=3$)

Allocated to intervention Group 2 ($n=21$)
Discontinued intervention ($n=5$)
Changed circumstance ($n=2$)
Kept forgetting ($n=1$)
Moved away ($n=1$)
Sprained leg ($n=1$)
Analysed ($n=16$)

Allocated to intervention Group 4 ($n=22$)
Discontinued intervention ($n=9$)
Changed circumstance ($n=2$)
Personal reasons ($n=1$)
Kept forgetting ($n=1$)
Too busy ($n=1$)
Discomfort during exercise ($n=1$)
Aggravated old back complaint ($n=1$)
Sustained injury unrelated to the exercise ($n=2$)
Analysed ($n=13$)

Allocated to intervention Group 7 ($n=22$)
Discontinued intervention ($n=6$)
No time ($n=1$)
Discomfort during exercise ($n=4$)
Recurring knee problem ($n=1$)
Analysed ($n=16$)
5.3 Results

Baseline characteristics, attrition, and compliance

Body mass change has been associated with loss of BMD in the femoral neck and lumbar spine (Macdonald et al. 2005); therefore the data of 3 controls who lost more than 5kg during the study were excluded in analysis so as not to confound results. Table 5.2 summarises characteristics of the remaining participants at baseline. There was one vegan who took a daily calcium supplement. Apart from reported daily number of cereal/bread servings, groups did not differ significantly. Participants were of a comparable height but lower body mass and BMI than those recorded for women aged between 19 and 44 years in The National Diet and Nutrition Survey (163cm, 67.3kg and 25.6kg/m², respectively) (Office for National Statistics 2004).

Table 5.2: Baseline characteristics of participants included in analysis (n=61), mean (SD)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group 0 (n=16)</th>
<th>Group 2 (n=16)</th>
<th>Group 4 (n=13)</th>
<th>Group 7 (n=16)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>33.0 (9.2)</td>
<td>30.7 (7.4)</td>
<td>32.2 (10.0)</td>
<td>34.6 (7.9)</td>
</tr>
<tr>
<td>Body mass (kg)</td>
<td>60.8 (7.5)</td>
<td>58.1 (7.9)</td>
<td>60.3 (10.3)</td>
<td>60.7 (10.2)</td>
</tr>
<tr>
<td>Height (m)</td>
<td>1.62 (0.06)</td>
<td>1.64 (0.05)</td>
<td>1.64 (0.07)</td>
<td>1.63 (0.08)</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>23.1 (2.7)</td>
<td>21.7 (3.0)</td>
<td>22.4 (3.3)</td>
<td>22.9 (3.2)</td>
</tr>
<tr>
<td>Body fat (%)</td>
<td>29.1 (4.3)</td>
<td>26.1 (6.5)</td>
<td>27.8 (6.2)</td>
<td>30.1 (6.1)</td>
</tr>
<tr>
<td>Age at menarche (yrs)</td>
<td>13.6 (2.2)</td>
<td>13.9 (2.5)</td>
<td>13.0 (1.7)</td>
<td>13.2 (1.2)</td>
</tr>
<tr>
<td>No. of dairy servings per day</td>
<td>3.0 (1.4)</td>
<td>2.4 (1.0)</td>
<td>2.7 (1.8)</td>
<td>2.7 (1.2)</td>
</tr>
<tr>
<td>No. of cereal/bread servings per day *</td>
<td>2.0 (1.4)</td>
<td>1.3 (0.6)</td>
<td>2.8 (2.2)</td>
<td>2.9 (1.8)</td>
</tr>
<tr>
<td>Weekly alcohol intake (units)</td>
<td>5.7 (7.3)</td>
<td>3.9 (3.5)</td>
<td>3.5 (3.2)</td>
<td>4.2 (3.8)</td>
</tr>
<tr>
<td>Proportion of smokers (%)</td>
<td>6</td>
<td>6</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Current physical activity duration (min/week)</td>
<td>142 (118)</td>
<td>126 (108)</td>
<td>186 (175)</td>
<td>183 (155)</td>
</tr>
<tr>
<td>Proportion of regular participants in</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>extracurricular sports/exercise during</td>
<td>50</td>
<td>69</td>
<td>61</td>
<td>62</td>
</tr>
<tr>
<td>childhood/adolescence (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Significant difference between groups (p<0.05)

The flow diagram in Figure 5.1 opposite displays the progression of participants during the study from both cohorts combined. Overall drop out rates for controls, G2, G4, and G7 were 0%, 27%, 44%, and 36%, respectively. When examining the two separate intakes, 22 participants in cohort 1 (43%) did not complete the intervention, while only 6 in cohort 2 discontinued (16%). Reasons for withdrawing from the study are detailed in Figure 5.1.
It is worth noting that the complaints of discomfort during exercise in the individuals who withdrew from the study occurred during the early stages of the intervention (5/6th week), yet when the responses on feedback forms were examined at the end of the study, a number of exercisers who completed the whole 6-month intervention had reported muscle soreness too: 3 women in G2, 5 in G4, and 6 in G7. "Slight foot strain midway (6 weeks) but went away after 2 days", "a little (muscle soreness) at the beginning of the study", "knee felt bit sore but only at the start", "muscles were sore in early days of hopping but improved with time", "left foot felt a little painful in the first few weeks but then ok", "stiff ankle some mornings, but didn't last more than a few minutes" are examples of comments that were made. Obviously, the exercisers who remained in the study had similar experiences to those who decided to drop out, thereby implying a possible difference in attitude/motivation. Injuries did occur that were related to the hopping exercises, but they were either an aggravation of previous problems (covered by exclusion criteria that participants denied or had forgotten at enrolment), or they were a result of not following the protocol correctly. For example, the participant in G2 who sprained her leg admitted that she "probably didn't warm up enough". The exercisers remaining in the study achieved compliance rates to the exercise programme of 84% (range 65-100%), 90% (74-100%), and 86% (65-97%) for G2, G4, and G7, respectively. Compliance to the training was the same in each cohort: 88.9% (65-105%) in cohort 1 and 88.7% (72-100%) in cohort 2.

Effects of the hopping intervention on body composition and neuromuscular function

Table 5.3 displays baseline values of body composition measurements and their subsequent change during the study. Body mass did not significantly change in any group (p=0.59-0.71). Neither were there changes in body composition, specifically body fat percentage and fat-free mass (p=0.08-1.00).
Table 5.3: Body composition before (baseline) and after (post-intervention) a 6-month hopping exercises intervention according to exercise frequency, mean (SD)

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Group</th>
<th>Baseline</th>
<th>Post-intervention</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body mass (kg)</td>
<td>0</td>
<td>60.9 (7.5)</td>
<td>60.5 (7.6)</td>
<td>0.59</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>58.1 (7.9)</td>
<td>57.8 (8.5)</td>
<td>0.57</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>60.3 (10.3)</td>
<td>60.1 (10.8)</td>
<td>0.71</td>
</tr>
<tr>
<td></td>
<td>7</td>
<td>60.7 (10.2)</td>
<td>60.4 (9.9)</td>
<td>0.60</td>
</tr>
<tr>
<td>Body mass index</td>
<td>0</td>
<td>23.1 (2.7)</td>
<td>23.1 (2.8)</td>
<td>0.90</td>
</tr>
<tr>
<td>(kg/m²)</td>
<td>2</td>
<td>21.7 (3.0)</td>
<td>21.6 (3.2)</td>
<td>0.58</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>22.4 (3.3)</td>
<td>22.4 (3.4)</td>
<td>0.87</td>
</tr>
<tr>
<td></td>
<td>7</td>
<td>22.9 (3.2)</td>
<td>22.9 (3.1)</td>
<td>0.81</td>
</tr>
<tr>
<td>Body fat percentage (%)</td>
<td>0</td>
<td>29.3 (4.3)</td>
<td>29.0 (4.7)</td>
<td>0.33</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>26.1 (6.5)</td>
<td>25.3 (6.8)</td>
<td>0.74</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>27.7 (6.0)</td>
<td>27.7 (6.1)</td>
<td>0.13</td>
</tr>
<tr>
<td></td>
<td>7</td>
<td>30.1 (6.0)</td>
<td>29.8 (6.7)</td>
<td>0.93</td>
</tr>
<tr>
<td>Fat-free mass (kg)</td>
<td>0</td>
<td>42.9 (5.1)</td>
<td>42.8 (4.9)</td>
<td>0.25</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>42.6 (4.0)</td>
<td>42.9 (4.4)</td>
<td>0.73</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>43.2 (5.1)</td>
<td>43.0 (5.0)</td>
<td>0.18</td>
</tr>
<tr>
<td></td>
<td>7</td>
<td>42.2 (6.8)</td>
<td>42.2 (6.7)</td>
<td>0.63</td>
</tr>
</tbody>
</table>

Table 5.4 presents some significant changes in neuromuscular function. The difference in response between legs in submaximal hopping performance (reflected by hop height) was significant in all exercise groups (p=0.003-0.03) and these differences were also significant between groups (p=0.005). No changes took place in the controls (p=0.32). Similarly, there were significant differences in response between legs in maximal hopping performance, but only in G4 and G7 (p=0.04 and 0.02); whereas none was detected in the control group in either parameter (p=0.32 and 0.28 for submaximal and maximal hop height, respectively) (Figure 5.2).

Speed of sway whilst standing on the trained leg decreased significantly in the exercisers’ trained leg (27.5±8.2 to 24.6±7.3 mm/s, p=0.01), but not in their control leg (28.1±13.8 to 27.3±18.4 mm/s, p=0.81). Maximal knee extension strength of the trained leg was greater when measured at the end of the study compared to the start in G2 (36.6±7.8 from 32.4±6.2 kg, p=0.01) and G7 (31.4±6.3 from 28.6±5.4 kg, p=0.01) as well as in the controls (35.3±9.5 from 31.8±8.1 kg, p=0.04). A positive change also occurred in G7’s control leg (30.5±7.2 from 28.6±6.4 kg, p=0.03).
Table 5.4: Neuromuscular measurements before (baseline) and after (post-intervention) a 6-month hopping exercises intervention according to exercise frequency, mean (SD)

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Group</th>
<th>Trained leg</th>
<th>Post-Intervention</th>
<th>Control leg</th>
<th>Post-intervention</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Baseline</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Knee extensor strength (N)</td>
<td>0</td>
<td>312.0 (79.5)</td>
<td>348.3 (93.2)*</td>
<td>324.7 (81.4)</td>
<td>351.2 (91.2)</td>
<td>0.34</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>317.8 (80.4)</td>
<td>359.0 (78.5)**</td>
<td>327.7 (81.4)</td>
<td>347.3 (91.2)</td>
<td>0.29</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>316.9 (80.4)</td>
<td>335.5 (58.2)</td>
<td>299.2 (63.8)</td>
<td>302.1 (51.0)</td>
<td>0.56</td>
</tr>
<tr>
<td></td>
<td>7</td>
<td>280.6 (53.0)</td>
<td>308.0 (61.8)*</td>
<td>280.6 (62.8)</td>
<td>299.2 (70.6)*</td>
<td>0.37</td>
</tr>
<tr>
<td>Postural sway</td>
<td>2</td>
<td>28.1 (9.9)</td>
<td>23.8 (8.1)</td>
<td>24.5 (4.8)</td>
<td>25.7 (11.0)</td>
<td>0.04*</td>
</tr>
<tr>
<td>speed (mm/s)</td>
<td>4</td>
<td>26.7 (7.5)</td>
<td>24.8 (6.1)</td>
<td>24.9 (5.4)</td>
<td>23.3 (7.5)</td>
<td>0.87</td>
</tr>
<tr>
<td></td>
<td>7</td>
<td>27.7 (7.5)</td>
<td>25.2 (7.8)</td>
<td>34.3 (21.3)</td>
<td>32.3 (28.0)</td>
<td>0.95</td>
</tr>
<tr>
<td>Mean of peak</td>
<td>0</td>
<td>2.43 (0.27)</td>
<td>2.65 (0.33)**</td>
<td>2.59 (0.28)</td>
<td>2.65 (0.34)</td>
<td>0.08</td>
</tr>
<tr>
<td>landing GRF</td>
<td>2</td>
<td>2.59 (0.44)</td>
<td>2.95 (0.42)**</td>
<td>2.37 (0.37)</td>
<td>2.77 (0.34)**</td>
<td>0.68</td>
</tr>
<tr>
<td>from 10 hops</td>
<td>4</td>
<td>2.35 (0.30)</td>
<td>2.71 (0.52)**</td>
<td>2.43 (0.34)</td>
<td>2.57 (0.31)**</td>
<td>0.047**</td>
</tr>
<tr>
<td>(oBM)</td>
<td>7</td>
<td>2.46 (0.35)</td>
<td>2.80 (0.45)**</td>
<td>2.42 (0.34)</td>
<td>2.67 (0.39)**</td>
<td>0.37</td>
</tr>
<tr>
<td>Peak landing</td>
<td>2</td>
<td>2.85 (0.63)</td>
<td>3.11 (1.70)</td>
<td>3.23 (1.57)</td>
<td>3.06 (0.74)</td>
<td>0.02*</td>
</tr>
<tr>
<td>GRF from a maximal hop (m)</td>
<td>4</td>
<td>2.73 (0.64)</td>
<td>2.94 (0.73)</td>
<td>2.88 (0.87)</td>
<td>2.68 (0.73)</td>
<td>0.12</td>
</tr>
<tr>
<td>Mean of peak</td>
<td>7</td>
<td>3.10 (1.03)</td>
<td>2.77 (0.52)</td>
<td>2.73 (0.53)</td>
<td>2.64 (0.67)</td>
<td>0.48</td>
</tr>
<tr>
<td>hop height</td>
<td>2</td>
<td>0.054 (0.019)</td>
<td>0.054 (0.010)</td>
<td>0.057 (0.018)</td>
<td>0.058 (0.014)</td>
<td>0.32</td>
</tr>
<tr>
<td>from 10 hops</td>
<td>4</td>
<td>0.059 (0.019)</td>
<td>0.080 (0.030)**</td>
<td>0.057 (0.016)</td>
<td>0.065 (0.028)</td>
<td>0.003*</td>
</tr>
<tr>
<td>(m)</td>
<td>7</td>
<td>0.045 (0.022)</td>
<td>0.073 (0.034)*</td>
<td>0.046 (0.022)</td>
<td>0.051 (0.025)</td>
<td>0.02*</td>
</tr>
<tr>
<td>Peak hop height from a maximal hop (m)</td>
<td>2</td>
<td>0.120 (0.024)</td>
<td>0.118 (0.017)</td>
<td>0.135 (0.048)</td>
<td>0.123 (0.028)</td>
<td>0.28</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>0.128 (0.038)</td>
<td>0.148 (0.039)*</td>
<td>0.122 (0.033)</td>
<td>0.133 (0.034)</td>
<td>0.25</td>
</tr>
<tr>
<td></td>
<td>7</td>
<td>0.104 (0.031)</td>
<td>0.125 (0.029)*</td>
<td>0.114 (0.043)</td>
<td>0.111 (0.033)</td>
<td>0.04*</td>
</tr>
</tbody>
</table>

*Significant change within leg (p<0.05), **Significant change within leg (p<0.01)
§ Significant difference in response between legs (p<0.05)

Figure 5.2: Changes in maximum hop height during the hopping exercises intervention, mean (95% CI)

![Graph showing changes in maximum hop height]
Table 5.5: Spine and hip BMD and BMC measurements before (baseline) and after (post-intervention) a 6-month hopping exercises intervention according to exercise frequency, mean (SD)

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Group</th>
<th>Trained leg</th>
<th>Control leg</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Baseline</td>
<td>Post-intervention</td>
<td>Baseline</td>
</tr>
<tr>
<td>Lumbar</td>
<td>0</td>
<td>1.156 (0.087)</td>
<td>1.159 (0.055)</td>
<td>0.71</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>1.187 (0.122)</td>
<td>1.187 (0.125)</td>
<td>0.94</td>
</tr>
<tr>
<td>BMD (g/cm²)</td>
<td>4</td>
<td>1.195 (0.184)</td>
<td>1.202 (0.176)</td>
<td>0.48</td>
</tr>
<tr>
<td></td>
<td>7</td>
<td>1.184 (0.141)</td>
<td>1.189 (0.137)</td>
<td>0.48</td>
</tr>
<tr>
<td>spine</td>
<td>0</td>
<td>50.597 (9.681)</td>
<td>61.111 (9.594)</td>
<td>0.43</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>59.531 (7.806)</td>
<td>60.419 (8.208)</td>
<td>0.12</td>
</tr>
<tr>
<td>BMD (g)</td>
<td>4</td>
<td>60.276 (14.008)</td>
<td>61.036 (13.163)</td>
<td>0.47</td>
</tr>
<tr>
<td></td>
<td>7</td>
<td>60.886 (10.241)</td>
<td>61.489 (10.224)</td>
<td>0.11</td>
</tr>
<tr>
<td>Femoral</td>
<td>0</td>
<td>0.055 (0.140)</td>
<td>0.053 (0.135)</td>
<td>0.01</td>
</tr>
<tr>
<td>neck</td>
<td>0</td>
<td>4.197 (0.119)</td>
<td>0.972 (0.111)</td>
<td>0.94</td>
</tr>
<tr>
<td>BMD (g/cm²)</td>
<td>4</td>
<td>1.015 (0.153)</td>
<td>1.024 (0.154)</td>
<td>0.94</td>
</tr>
<tr>
<td></td>
<td>7</td>
<td>0.972 (0.172)</td>
<td>0.991 (0.168)</td>
<td>0.008</td>
</tr>
<tr>
<td>Femoral</td>
<td>0</td>
<td>4.548 (0.689)</td>
<td>4.672 (0.535)</td>
<td>0.41</td>
</tr>
<tr>
<td>neck</td>
<td>2</td>
<td>4.449 (0.531)</td>
<td>4.965 (0.531)</td>
<td>0.28</td>
</tr>
<tr>
<td>BMD (g)</td>
<td>4</td>
<td>3.399 (0.662)</td>
<td>4.649 (0.663)</td>
<td>0.55</td>
</tr>
<tr>
<td></td>
<td>7</td>
<td>4.475 (0.634)</td>
<td>4.528 (0.633)</td>
<td>0.09</td>
</tr>
<tr>
<td>Upper</td>
<td>0</td>
<td>0.887 (0.153)</td>
<td>0.885 (0.158)</td>
<td>0.03</td>
</tr>
<tr>
<td>neck</td>
<td>2</td>
<td>0.874 (0.123)</td>
<td>0.874 (0.127)</td>
<td>0.31</td>
</tr>
<tr>
<td>BMD (g/cm²)</td>
<td>4</td>
<td>0.876 (0.150)</td>
<td>0.901 (0.151)</td>
<td>0.63</td>
</tr>
<tr>
<td></td>
<td>7</td>
<td>0.839 (0.192)</td>
<td>0.883 (0.196)</td>
<td>0.009</td>
</tr>
<tr>
<td>Upper</td>
<td>0</td>
<td>1.051 (0.332)</td>
<td>1.079 (0.325)</td>
<td>0.03</td>
</tr>
<tr>
<td>neck</td>
<td>2</td>
<td>1.058 (0.295)</td>
<td>1.083 (0.295)</td>
<td>0.03</td>
</tr>
<tr>
<td>BMD (g)</td>
<td>4</td>
<td>1.097 (0.360)</td>
<td>2.031 (0.334)</td>
<td>0.03</td>
</tr>
<tr>
<td></td>
<td>7</td>
<td>1.942 (0.415)</td>
<td>1.966 (0.453)</td>
<td>0.01</td>
</tr>
<tr>
<td>Lower</td>
<td>0</td>
<td>1.087 (0.143)</td>
<td>1.133 (0.135)</td>
<td>0.03</td>
</tr>
<tr>
<td>neck</td>
<td>2</td>
<td>1.086 (0.111)</td>
<td>1.073 (0.113)</td>
<td>0.27</td>
</tr>
<tr>
<td>BMD (g/cm²)</td>
<td>4</td>
<td>1.139 (0.174)</td>
<td>1.144 (0.172)</td>
<td>0.32</td>
</tr>
<tr>
<td></td>
<td>7</td>
<td>1.083 (0.169)</td>
<td>1.094 (0.152)</td>
<td>0.28</td>
</tr>
<tr>
<td>Lower</td>
<td>0</td>
<td>2.677 (0.300)</td>
<td>2.679 (0.296)</td>
<td>0.19</td>
</tr>
<tr>
<td>neck</td>
<td>2</td>
<td>2.683 (0.287)</td>
<td>2.528 (0.274)</td>
<td>0.97</td>
</tr>
<tr>
<td>BMD (g)</td>
<td>4</td>
<td>2.546 (0.413)</td>
<td>2.837 (0.412)</td>
<td>0.29</td>
</tr>
<tr>
<td></td>
<td>7</td>
<td>2.536 (0.444)</td>
<td>2.558 (0.419)</td>
<td>0.34</td>
</tr>
<tr>
<td>Ward's</td>
<td>0</td>
<td>0.875 (0.154)</td>
<td>0.876 (0.165)</td>
<td>0.93</td>
</tr>
<tr>
<td>triangle</td>
<td>2</td>
<td>0.879 (0.117)</td>
<td>0.875 (0.113)</td>
<td>0.75</td>
</tr>
<tr>
<td>BMD (g/cm²)</td>
<td>4</td>
<td>0.870 (0.164)</td>
<td>0.875 (0.155)</td>
<td>0.32</td>
</tr>
<tr>
<td></td>
<td>7</td>
<td>0.860 (0.217)</td>
<td>0.877 (0.227)</td>
<td>0.22</td>
</tr>
<tr>
<td>Ward's</td>
<td>0</td>
<td>2.585 (0.439)</td>
<td>2.127 (0.443)</td>
<td>0.90</td>
</tr>
<tr>
<td>triangle</td>
<td>2</td>
<td>2.559 (0.348)</td>
<td>2.077 (0.342)</td>
<td>0.35</td>
</tr>
<tr>
<td>BMD (g)</td>
<td>4</td>
<td>2.014 (0.418)</td>
<td>2.018 (0.425)</td>
<td>0.79</td>
</tr>
<tr>
<td></td>
<td>7</td>
<td>2.621 (0.553)</td>
<td>2.043 (0.603)</td>
<td>0.76</td>
</tr>
<tr>
<td>Trochanter</td>
<td>0</td>
<td>0.808 (0.133)</td>
<td>0.811 (0.130)</td>
<td>0.40</td>
</tr>
<tr>
<td>BMD (g/cm²)</td>
<td>2</td>
<td>0.797 (0.095)</td>
<td>0.802 (0.086)</td>
<td>0.44</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>0.823 (0.134)</td>
<td>0.824 (0.137)</td>
<td>0.31</td>
</tr>
<tr>
<td>Trochanter</td>
<td>0</td>
<td>3.234 (1.652)</td>
<td>0.739 (0.122)</td>
<td>0.12</td>
</tr>
<tr>
<td>BMD (g)</td>
<td>2</td>
<td>2.223 (1.688)</td>
<td>2.924 (1.903)</td>
<td>0.29</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>2.679 (1.602)</td>
<td>9.376 (1.965)</td>
<td>0.40</td>
</tr>
<tr>
<td></td>
<td>7</td>
<td>8.949 (2.139)</td>
<td>8.823 (2.100)</td>
<td>0.39</td>
</tr>
<tr>
<td>Shaft</td>
<td>0</td>
<td>1.213 (0.159)</td>
<td>1.214 (0.156)</td>
<td>0.29</td>
</tr>
<tr>
<td>BMD (g/cm²)</td>
<td>2</td>
<td>1.174 (0.143)</td>
<td>1.175 (0.146)</td>
<td>0.87</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>1.196 (0.187)</td>
<td>1.201 (0.184)</td>
<td>0.53</td>
</tr>
<tr>
<td>Shaft</td>
<td>0</td>
<td>15.485 (2.25)</td>
<td>15.549 (2.141)</td>
<td>0.53</td>
</tr>
<tr>
<td>BMD (g)</td>
<td>4</td>
<td>15.687 (1.816)</td>
<td>15.753 (1.873)</td>
<td>0.16</td>
</tr>
<tr>
<td></td>
<td>7</td>
<td>16.054 (2.621)</td>
<td>16.129 (2.621)</td>
<td>0.39</td>
</tr>
<tr>
<td>total</td>
<td>0</td>
<td>1.025 (0.138)</td>
<td>1.027 (0.137)</td>
<td>0.82</td>
</tr>
<tr>
<td>hip</td>
<td>2</td>
<td>0.959 (0.107)</td>
<td>0.996 (0.106)</td>
<td>0.07</td>
</tr>
<tr>
<td>BMD (g/cm²)</td>
<td>4</td>
<td>1.022 (0.154)</td>
<td>1.029 (0.153)</td>
<td>0.27</td>
</tr>
<tr>
<td>total</td>
<td>0</td>
<td>1.007 (0.185)</td>
<td>1.010 (0.187)</td>
<td>0.62</td>
</tr>
<tr>
<td>hip</td>
<td>2</td>
<td>28.375 (4.128)</td>
<td>25.625 (4.089)</td>
<td>0.39</td>
</tr>
<tr>
<td>BMD (g)</td>
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<td>30.392 (4.625)</td>
<td>30.343 (4.626)</td>
<td>0.70</td>
</tr>
<tr>
<td></td>
<td>7</td>
<td>29.489 (5.412)</td>
<td>29.473 (5.350)</td>
<td>0.18</td>
</tr>
</tbody>
</table>

* Significant change within leg (p < 0.05), ** Significant change within leg (p < 0.01)
§ Significant difference in response between legs (p < 0.05)
Effects of the hopping intervention on bone variables

Table 5.5 opposite displays changes in hip BMD and BMC variables that were measured during the study. BMD increased significantly in the exercise relative to the control limb in G7 at the femoral neck (+1.5% vs. -0.6%, respectively; \( p=0.048 \)), upper neck (+2.1% vs. -0.9%; \( p=0.01 \)), and Ward’s triangle (+2.0% vs. -0.2%; \( p=0.01 \)), but not the total hip (\( p=0.09 \)) or trochanter (\( p=0.37 \)) (Figure 5.3). The differences in response between legs at the femoral neck and upper neck were significantly different between groups (\( p=0.02 \) and \( p=0.04 \)). Even after allowing for multiple comparisons, the differences in response remained in femoral neck BMD between G7 and controls, and G7 and G2 (\( p=0.04 \) for both) (Figure 5.4). There were no changes in lumbar spine BMD (\( p>0.3 \)) or BMC at any site.

**Figure 5.3:** Differences in BMD change at selected hip sites in the trained and control limb over the course of a 6-month hopping exercises intervention according to exercise frequency, mean (95% CI). Lightly shaded bars represent the trained leg. Clear bars represent the control leg.
Figure 5.4: Differences in femoral neck BMD response to a 6-month intervention of hopping exercises according to exercise frequency, mean (95% CI)

*Significantly different response between legs between groups ($p<0.05$)
Table 5.6: Hip geometry, tibia BMD, and bone ultrasound measurements before (baseline) and after (post-Intervention) a 6-month hopping exercises intervention according to exercise frequency, mean (SD)

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Group</th>
<th>Trained leg</th>
<th>Control leg</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Baseline</td>
<td>Post-intervention</td>
<td>Baseline</td>
</tr>
<tr>
<td>Femur</td>
<td>0</td>
<td>1.65 (0.45)</td>
<td>1.65 (0.43)</td>
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<td></td>
<td></td>
<td>1.75 (0.32)</td>
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<tr>
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<td>1.72 (0.35)</td>
<td>1.67 (0.26)</td>
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<td>1.52 (0.295)</td>
<td>1.59 (0.25)</td>
<td>1.48 (0.37)</td>
</tr>
<tr>
<td>CSA (mm²)</td>
<td>2</td>
<td>8590.1 (1859.1)</td>
<td>8824.1 (1707.6)</td>
<td>8886.1 (1657.8)</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>8590.1 (1702.0)</td>
<td>8800.4 (1739.8)</td>
<td>8986.0 (1757.7)</td>
</tr>
<tr>
<td></td>
<td>7</td>
<td>8673.3 (2419.1)</td>
<td>8735.3 (2723)</td>
<td>6102.5 (1984.4)</td>
</tr>
<tr>
<td>Ulnula</td>
<td>0</td>
<td>145.9 (19.2)</td>
<td>145.5 (17.8)</td>
<td>144.9 (20.4)</td>
</tr>
<tr>
<td></td>
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<td>141.9 (18.5)</td>
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<tr>
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<td>145.9 (22.5)</td>
<td>147.2 (22.4)</td>
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<tr>
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<td>156.6 (23.3)</td>
<td>142.2 (27.8)</td>
<td>130.6 (23.5)</td>
</tr>
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<td>Medial tibia</td>
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<td>4</td>
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<td>144.0 (247.1)</td>
<td>143.1 (275.9)</td>
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<td>144.0 (247.1)</td>
<td>143.1 (275.9)</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>176.5 (263.3)</td>
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<td>173.0 (275.9)</td>
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</tr>
<tr>
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</tr>
<tr>
<td></td>
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<td>1555.0 (8.1)</td>
<td>1555.0 (8.1)</td>
</tr>
<tr>
<td>Direct</td>
<td>0</td>
<td>41094.0 (1663.3)</td>
<td>40713.0 (1264.8)</td>
<td>40986.0 (1284.0)</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>4061.5 (1254.9)</td>
<td>3982.7 (961.2)</td>
<td>4097.4 (1439.9)</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>4146.7 (1539.3)</td>
<td>4083.9 (891.7)</td>
<td>4105.3 (1758.2)</td>
</tr>
<tr>
<td></td>
<td>7</td>
<td>4065.9 (1523.1)</td>
<td>4065.9 (1303.6)</td>
<td>4061.9 (1771.1)</td>
</tr>
<tr>
<td></td>
<td>0</td>
<td>4147.2 (857.0)</td>
<td>4141.4 (847.1)</td>
<td>4154.5 (818.6)</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>4138.0 (816.1)</td>
<td>4141.0 (853.5)</td>
<td>4154.8 (1182.7)</td>
</tr>
<tr>
<td></td>
<td>4</td>
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<td>4116.9 (1179.5)</td>
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</tr>
<tr>
<td></td>
<td>7</td>
<td>4197.4 (1175.5)</td>
<td>4169.3 (818.1)</td>
<td>4179.8 (1079.0)</td>
</tr>
</tbody>
</table>

*Significant change within leg (p<0.05), **Significant change within leg (p<0.01)
§ Significant difference in response between legs (p<0.05)
Table 5.6 opposite displays hip geometry variables and ultrasound measurements of bone. There were no differences in response between legs in geometric parameters, although CSA and FSI increased in the trained limb when all exercisers were combined (2.6%; \( p=0.04 \) and 5.0%; \( p=0.02 \) in CSA and FSI, respectively), whilst CSMI increased in their control limb (1.8%; \( p=0.02 \)). There were also no significant differences in response between limbs in quantitative ultrasound parameters at the calcaneus \( (p=0.18-0.96) \) or radius \( (p=0.26-0.98) \). The exception was a consistent decrease in tibial SOS in all groups. Conversely, tibial BMD measured by DXA did not show any effects of the exercise intervention (Table 5.6). In spite of an absence of significant effects within groups, calcaneus BUA increased in the trained leg of the exercisers when they were combined as one group (4.1%, \( p=0.01 \)) (Figure 5.5).

**Figure 5.5: Calcaneus BUA in the exercisers before (baseline) and after (post-intervention) a 6-month hopping exercises intervention, mean (95% CI)**

5.4 Discussion

Performing hopping exercises 7 days per week for 6 months had a beneficial effect on BMD at the femoral neck, upper neck, and Ward's triangle, whereas training 2 or 4 days per week, or not at all, did not significantly change BMD in premenopausal women. The difference in response between legs at the femoral neck was also significantly different between groups, with a significantly greater response observed in the exercisers training everyday compared to the groups of lower weekly exercise frequency. Our observations are important because this is the first time the effects of different weekly frequencies of exercise have been compared in a RCT.
The present findings are consistent with previous studies whereby 5-6 months of brief, high-impact jumping exercises increased femoral neck BMD in premenopausal women (Bassey et al. 1998, Kato et al. 2006), although there were no significant improvements in the trochanter or lumbar spine. The trochanter is mechanically loaded by muscle forces and GRFs during countermovement jumping (Bassey et al. 1997) and it may be that the angle of compressive force is shifted slightly during single-legged hopping due to the different body position maintained. Both the femoral neck and Ward’s triangle are situated in the narrow, central section of the femur where they would experience larger strains and strain-related modelling adaptation than the cortical sections that are closer to the metaphyses (Mosley and Lanyon 1998). Also, the training programme incorporated multidirectional hops, which may have induced strain on different regions of the femur compared to previous studies that only involved vertical jumps and subsequently only one direction of force transmission through the supporting limbs. The observation of BMD changes in the upper neck but not the lower neck again may be the result of the direction of strain during multi-directional hopping as opposed to vertical jumping or, because usual locomotion loads the lower neck, this region of the hip may respond less (i.e. the exercise was a weaker osteogenic stimulus here compared to the upper neck). The difference in composition between different regions of the femur may offer another explanation of the observed changes. Since trabecular bone is more metabolically active than cortical bone (Einhorn 2001), 6 months of hopping may have only been adequate for exercise effects to become evident in the predominantly trabecular femoral neck and Ward’s triangle, as opposed to the shaft and trochanter, which have a greater proportion of cortical bone (Einhorn 2001).

In order for there to be an increase in BMD not caused by variability in positioning, either the amount of mineral must increase (i.e. more grams per cm²) or there is a change in bone dimension that would result in the same amount of bone in a smaller area. The fact that femoral neck width remained the same during the intervention implies that trabecular or endosteal adaptation took place in this region, as opposed to periosteal expansion; an occurrence in line with some exercise studies (Binkley and Specker 2004) and in contrast to others (Petit et al. 2002, Vainionpää et al. 2007). Although, the discrepancy between these studies could be due to the different subject populations, as bone’s structural adaptation is likely to be different in the rapidly-growing preschool children in Binkley and Specker’s study compared to the older, early-pubertal girls and young, adult women studied by Petit and Vainionpää, respectively. In the present results, the increase in femoral neck BMC was not significant, meaning there may have been relevant changes in both femoral neck
width and femoral neck BMC that resulted in the observed increase in BMD, but which the power of analyses was not strong enough to detect.

As for the absence of effect on lumbar spine BMD, the spine is likely to receive fewer overloads during jumping and hopping than the hip due to the attenuation of GRFs by the surrounding soft tissues that occur along the kinetic chain of the lower limb, which would prevent forces of sufficient magnitude to affect the lumbar spine (Dolan et al. 2006). Or, it could simply be that exercising twice per week is insufficient to affect bone adaptation at this site. Nevertheless, the present unilateral study was only powered to detect differences in response between hips of the exercising and control leg, so changes at the spine were not expected to be observed. Consequently, even if a response had been identified, the sample size would be too small to attribute the change as a true biological effect rather than a chance finding. Furthermore, some of these studies that report significant increases in spine BMD supplemented exercisers with calcium (Gleeson et al. 1990, Lohman et al. 1995), which, along with exercise, is associated with bones of greater mineral mass and mechanical competence (Uusi-Rasi et al. 1998). Exercisers in G2 were the only group that did not experience a significant increase in femoral neck BMD in their trained leg. It was noted that this group had a significantly lower intake of cereal servings at baseline compared to the other groups and, although not significantly different, they also reported a slightly lower number of daily dairy servings. Considering the interaction between calcium and exercise, it is possible that a lower calcium level blunted the effects of hopping in this group (Specker 1996). An interaction between the exercise intervention and the number of daily dairy servings was not evident when comparing the difference in BMD response between legs at any site, but it must be borne in mind that only a very crude indication of calcium intake could be deduced by the dietary intake method employed.

It would be expected for the tibia to come under considerable loading during a movement like hopping from both absorption of the ground reaction energy and from the pull of the tendon of the knee extensor muscles (vastus group) on its insertion point on the tibial tuberosity, yet effects were not identified in any of the measured regions at this site. Clearer bone adaptation in the femur than the tibia following a long-term programme of high-impact exercise in premenopausal women was also observed by Vainionpaa et al. (Vainionpaa et al. 2007). The authors did not suggest a reason for this, but the absence of effect in the present study could have several explanations. First, perhaps the selected regions of interest were not specific enough to the hopping exercises. It could be that the transmission of GRFs is strongest at the distal tibia with gradual abating of impact force as it travels up the bone. Measuring
BMD at the distal tibia may have been more useful, although this argument is weakened by the fact that significant changes took place in the femur. Second, measuring only bone mass rather than bone geometry at the tibia may have underestimated the effects of exercise, since evidence shows that redistribution of bone without apparent changes in bone mineral mass improves structural rigidity (Adami et al. 1999). Uusi-Rasi and colleagues demonstrated that 12 months of jumping exercises induced a thickening of bone cortex at the distal tibia as revealed by significant increases in section modulus and cortical bone to total bone area ratio (Uusi-Rasi et al. 2003). In contrast, there was no difference in bone mass at this site between the exercisers and controls. The third explanation of the absence of exercise effect at the supporting lower limb was the poorer reliability and consistency in selecting measurement areas. The selection of regions of interest on the tibia was manual, not automated, and the protocol used has not been validated. A number of the scans taken in Derby were not performed correctly (either started too high or too low) and for some participants, the positions of the boxes on their pre- and post-intervention scans were visibly non-identical. Consequently, only data that were consistent in both the pre- and post-intervention scan were included in analysis, e.g. if box 3 was included in one subject’s baseline scan but cut off in their post-intervention scan, then this region of the tibia representing the proximal epiphysis was left out of analysis. Since the degree of true change in bone mineral over such a short time is negligible (degrees of change were in the hundredths of g/cm²) and the precision of tibia BMD measurements in the study was low, especially at the midshaft and proximal tibia (CVs of 11.7% and 20%, respectively), data taken from the tibiae cannot be examined closely.

Although increasing BMD by high-impact exercise generally reports only modest gains in premenopausal women (Wallace and Cumming 2000), tests in rats show that these small changes seem to transfer to large increases in ultimate force and energy failure, especially if the bone is added to the mechanically appropriate skeletal sites (Robling et al. 2002). In the present study then, despite a lack of meaningful geometric changes, the improvements in bone mass could still optimise bone strength at the relevant bone sites. Unfortunately, it was not possible to conduct more structural measurements of bone change, such as by means of pQCT, so conclusions regarding improved bone geometry could not be made. Regardless, both DXA and pQCT have inherent in vivo inaccuracies that can cause substantial and systematic differences in measured and true BMD, thus posing a challenge to findings. When DXA-measured BMD is found to change over time, Bolotin advocates that it may be something else in the scan ROI that has changed, e.g. soft tissue composition (bone marrow and the
regional spatial distribution of fat around the body circumference) (Bolotin 2005). A relatively small change in marrow composition (increased or decreased cell numbers) in the trabecular regions of the spine and hip can induce considerable inaccuracies in BMD values that over- or under-estimate the true BMD value. The author also brings to attention that marrow undergoes marked changes in composition over relatively short periods of time, which tend to be most pronounced in axial bones (spine) and the proximal ends of appendicular bones (femur) (Bolotin 2004). These inaccuracies, as well as any changes in soft tissue composition, mean that the significant increases in the trabecular bone sites observed in the present study could be false. To counter this argument, animal studies have observed changes in dry weight and breaking strength following brief, high-impact interventions (Umemura et al. 1997), which support the view that it is the bone strength, rather than just marrow composition, that has adapted. Unfortunately, I was unable to measure changes in bone structure more accurately than by DXA, so conclusions regarding improved bone geometry could not be made with certainty.

Training twice per week was sufficient to produce improvements in the muscles but not in the bone, as maximal knee extensor strength significantly increased in this group without changes in BMD (a trend that was observed in the controls too, although this was likely a chance finding). Muscle adaptation clearly follows a different time-course than that of bone, and this is enforced by the controversial outcomes of weight-training studies that have attempted to increase BMD by increasing muscle strength (Dornemann et al. 1997, Hawkins et al. 1999, Heinonen et al. 1996a, Sinaki et al. 1996, Vuori et al. 1994). As well as being related to a reduction in the risk of falling and improved physical function (Drinkwater 1994), improvements in muscle function was most important for providing objective evidence of compliance to the exercise programme. The changes also served to confirm positive effects of the hopping exercises in the intervention groups and detect confounding changes in the control group. In the present study, representatives of muscle performance were maximal knee extensor strength and hop height. The parallel increases in knee extensor strength in both the trained and control limb could be a familiarisation effect, as noted in Chapter 3, or equally an effect of cross-education (Zhou 2000). Cross-over effects in muscle strength in alternating movements such as hopping may result from the contribution of the supporting leg to control the landing, subsequently leading to a power flow from the free leg through the hip joint (Fukashiro 1987). On the other hand, the improvement in knee extensor strength observed in the controls could be an indicator of unintentionally increased physical activity, because being involved in the study may have made them more aware of the importance of exercise for bone health.
and so lead them to subconsciously be more active. Alternatively, the trend could also be due to natural improvement by being more familiar with the testing protocol and environment (Munn et al. 2004).

GRFs were sampled to provide indirect assessment of the intensity of the loading forces produced by a set of typical hops and were found to be around 2.5 times body weight at baseline, increasing to around 2.8 times body weight post intervention in exercisers, representing an increase of 15%. During a hop these forces are transferred through one leg rather than two, so this may be equivalent to 5-6 times body weight during jumping, equivalent to a drop jump or running at 13 km/h (Valnionpää et al. 2006). It was not possible to measure internal strain in the proximal femur during hopping but Bassey et al., who measured compressive axial forces during a jump using a femoral implant, calculated that forces at the femur are 2.6-2.9 times the GRF during take-off and 1.4-1.5 times the GRF during landing (Bassey et al. 1997). Assuming that these multiples double during a hop, this might translate into peak internal forces on the loaded femur of up to 15 times body weight. Therefore, even though the hopping exercises we used in our study would be classified in the 2-4 times body weight category of "moderate intensity" according to Witzke and Snow (2000), the internal strain on the femur is clearly sufficient to promote osteogenesis. Moreover, it has been indicated that strain rate is more osteogenic than strain magnitude (Turner et al. 1995) and hopping, like jumping, produces large peak strain rates with only moderately high peak strain magnitudes (Judex and Zernicke 2000).

It has been proposed that the ability to attenuate GRF upon landing during jump training depends on skill level (Johannsen et al. 2003), i.e. trained individuals appear to attenuate impact forces more than people who are not in training, thus the women in our study who were not habituated to high-impact exercise probably received the maximum impact forces possible compared to if we had recruited trained individuals. It can, however, be argued that they started to attenuate more impact forces as they progressed during the intervention even if they continued to hop higher. Milgrom et al. used strain gauges to measure in vivo strains and strain rates and did not distinguish any differences in compression, tension, or shear strains with increasing drop jump height (Milgrom et al. 2000). Their conclusions led them to suggest that subjects were able to dissipate part of the potential energy of successively higher drop jumps by increasing the range of motion of their knee and ankle joints and not transmitting the energy to their tibia. Indeed, technique plays an influential role in hop height and the generation of GRFs (Nicol 1999).
It should be brought to attention that it would not be accurate to refer to participants in the present study as "sedentary", because although they did not regularly engage in high-impact exercise, their baseline activity levels clearly indicated that most were active individuals who walked as a mode of transport, did gardening, or participated in non- or low-impact exercise like pilates etc. Consequently, a better description of our population would be "untrained". Ultimately, participants volunteered for the study with the knowledge that they may be allocated to the group required to train everyday, thus they were obviously individuals of a certain disposition and the ones who completed the study and did not drop out were an even more select group of people. This may have introduced slight bias into the study, a possibility that is supported by the fact that all three of the women whose data were excluded from analysis because of excessive weight loss were from the control group. It could be that they volunteered for this exercise study with the intention to get fitter so even though they did not end up in an exercise group, they obviously made other lifestyle changes that resulted in their weight loss. Considering the overriding influence of body mass on BMD (Felson et al. 1993), it was decided to exclude these participants who lost 5kg or more over the 6 months in order to ensure that it was not a reduced body mass that contributed to differences in BMD change amongst groups. There were no differences in the change in body mass between controls and exercisers either before or after excluding the three controls who lost substantial weight, yet even if there were significant changes, evidence suggests that the greater gravitational force in a high-impact exercise study would override the effect on BMD from the relatively small degrees of weight change possible in a study of this duration (Vainlonpaä et al. 2005).

It is difficult to distinguish whether it was the frequency of exercise or the volume of exercise that produced the observed effects on BMD. As discussed earlier, it is possible that a certain overall amount of mechanical loading is required before there is a gain in BMD. Since all exercisers performed the same number of hops during each exercise session, the overall amount of hopping varied considerably between the different groups. Participants doing the hopping exercises everyday would have ideally completed a total of 8400 hops over the course of the study, a number that is 3.5 times greater than the 2400 hops expected of the exercisers training only twice per week. However, designing the intervention so that some participants were to have completed 175 hops in one session may have been less feasible and safe, especially considering that they were untrained individuals. It would introduce greater risk of muscle discomfort and/or injury and, considering the substantially greater effort required, potentially lower compliance to the programme. The intensity of exercise would also most likely be compromised (i.e. lower hop height and hence impact force).
Besides, evidence suggests there is a threshold number of loading cycles beyond which there is little or no additional effect. Although such a threshold has not been determined in humans, the range seems to be between 4 and 36 loading cycles in turkey ulnae (Rubin and Lanyon 1987) and 10 to 20 jumps in rats (Umemura et al. 1997). Considering intensity of exercise is a major determinant of bone response (Magkos et al. 2007, Vainionpää et al. 2007), I chose to try to standardise the intensity by having all exercisers perform the same number of hops per session, rather than risk a reduction in intensity from the fatigue of having to complete a large number of hops in one single session. There could have been differences in hopping intensity between groups, since those who did the exercises more regularly would be expected to become more proficient, but it appears that this was not the case. Changes in submaximal hopping performance did not differ between groups and the variation in submaximal hop height by the end of the intervention was relatively small, with G2 hopping a mean height of 80mm, G4 hopping 72.8mm, and G7 hopping 66.9mm.

The major limitation of this study was its duration. The skeleton is much slower to respond to physical activity than other biological systems, thus even a year may be insufficient time to assess the relationship between exercise and BMD (Sinaki et al. 1996). Bone’s full response to the training may not have been captured. The effects of training 2 days per week could become apparent after a longer period because a certain accumulation of mechanical loading may be required, especially for sites with a higher proportion of the slower-metabolising cortical bone. Therefore, it cannot be confirmed that exercising less frequently is ineffective. Rather, the present results corroborate that exercising more frequently is more effective to induce increases in BMD over a relatively short time. Conversely, high-impact exercise intervention studies that have been conducted for a longer period of time have not resulted in bone changes exceeding those reported in shorter studies. For example, femoral neck BMD increased 1.6% following an 18 month-long intervention (Heinonen et al. 1996b) and even adding additional lower limb RT to a 12-month jumping programme did not result in a marked increase in trochanter BMD (2.5% in Winters and Snow 2000) compared to studies of half the duration (2.9% in Bassey et al. 1998). Clearly, changes may become apparent in different bone sites, but the magnitude of change does not seem to be influenced by study duration. Of course, this could be the result of insufficient overload because in order for bone to positively adapt, the loading stimulus needs to continually exceed the habitual loading conditions (Lanyon 1996). Participants in the present study were instructed to always try to hop as high and as fast as they could so that they were always overloading the strain on their bones.
Obviously, it was impossible to gauge whether they did this at home but the fact that the hopping heights recorded in the laboratory at 3 and 6 months increased significantly is a strong indicator that they did progress during the study. Not only would the external GRFs be greater, but also the internal muscle contraction forces imposed on the specific load-bearing sites (Burr 1997).

The drop-out rate from the first intake may have been so much higher than the second because participants had to travel to Derby for their DXA scans. This was a very time-consuming trip because participants were organised into groups of 4-8 and taken in a taxi-van to Derby University where they had to wait for one another to be scanned. The arrangement was made more difficult by having to arrange the visit in the evening (in order to accommodate those participants in daytime employment), which was a time when traffic could be very congested. Indeed sometimes it took over an hour to get to the clinic at Derby University, making it a very long and tiring experience for the volunteers who would unsurprisingly be deterred having to do it again. On the other hand, by the time the second study took place, we had acquired our own DXA scanner, thus enabling the bone measurements to be taken at the same time as all the other tests; a visit that only took up about 45 minutes of the participant’s time, hence resulting in a positive experience of involvement in my study. Compliance in a repeated study may also be higher because people who volunteer are encouraged by the knowledge that it has been successfully completed before, especially if preliminary results are used in recruitment. Another reason to explain the low number of drop-outs during the second intervention is that I myself was probably a better investigator. I was more confident, faster at taking measurements, and the experiences from the first study enabled me to improve aspects of coordinating a successful exercise intervention; such as preparing materials, organising testing times, and interacting with participants.

5.5 Conclusions

It has been demonstrated that high-impact, unilateral exercise can be used effectively as an intervention to investigate the effects of exercise on bone. These findings indicate that the greatest changes in BMD over a 6-month period are achieved by performing osteogenic exercise everyday. The hopping exercises generated adequately high GRFs that provided effective stimuli for bone formation, particularly in the femoral neck and Ward’s triangle regions of the femur. The major strength of the study is the unilateral design of the exercise intervention. With each participant having their own “in-built” control leg, most confounders that normally weaken exercise and
bone studies were diminished, thus more strongly asserting that it was the exercises that caused the changes and not any genetic or environmental variations between individuals that exist even in the most closely matched groups in a RCT. A second attractive feature of the training programme is its feasibility, as it is brief and can be conducted at home without specialist equipment so can be more easily fit into daily living. It also produced improvements in neuromuscular function that may additionally reduce risk of falls. Critically, all complaints of discomfort were transient.

Future studies should examine whether these associations between exercise frequency and BMD change remain the same after a longer duration, and more data is needed to provide insight into geometric adaptations that underpin exercise-associated gains in BMD. Furthermore, it would be helpful to better control participants' calcium intake by a more accurate diet inventory followed by provision of the necessary supplementation to top-up any low levels. In this way, we can be sure that calcium was not limiting the effects of the exercise on bone.

The main purpose of designing the present exercise programme was to answer a scientific question, but its high subject-acceptability and effectiveness in improving skeletal status suggests that it would be useful to modify and utilise as a possible intervention for health promotion. The hopping exercises would need to be performed on both sides of the body and as they were intended for healthy premenopausal women, further modifications would be required before being applied to older, frailer individuals who would not be advised to undertake such high-impact exercise. It must also be stressed that the intervention only sought to investigate effects on bone. Despite being vigorous in nature, the exercises are too brief than the necessary minimum duration of 10mins to develop and maintain cardiovascular fitness (Pollock et al. 1998), so the public should not be misled to believe that these exercises are sufficient to maintain their general health. Furthermore, while hopping is locally effective in bones of loaded sites, there is less, if any, efficacy on the whole skeleton.

Overall, this study's most important finding is that the greatest response in hip BMD to a brief, high-impact intervention was achieved with daily exercise, thereby indicating that exercise to optimise bone health may need to be performed more frequently than both the twice weekly U.K. recommendations (Department of Health 2004) and the 3 (if vigorous-intensity physical activity) to 5 (if of moderate intensity) times per week U.S. recommendations (U.S. Department of Health and Human Services 2004).
Predictors of bone density and geometry in premenopausal women

6.1 Introduction

BMD has been found to be positively related to the mass (Block et al. 1989, Daly et al. 2004) and strength (Snow-Harter and Bouxsein et al. 1990) of muscle. The load-induced strain required to stimulate an increase in bone mass (Frost 1987) can be achieved by both gravity and muscle activity. It has been proposed that bones adapt to the increased loads imparted by larger and stronger muscles by themselves adding mass, size, and strength (Turner 2000). This biomechanical link between muscle and bone supports the concept of a “functional muscle-bone unit” (Frost and Schonau 2000), in which changes in muscle mass and strength affects bone mass, size, and strength predictably and correspondingly.

However, there is no direct evidence in humans to prove that the osteogenic stimuli created by a bigger and stronger muscle leads to a proportional increment in BMD. It could be that the close association between muscle and bone is mediated by a number of factors - common genes regulating both muscle and bone size (Seeman et al. 1996), or common influences of external or intrinsic stimuli such as nutritional or hormonal factors (Arden and Spector 1997). Moreover, it is difficult to separate the influence of muscle on BMD from the effects of exercise on BMD since physical activity can increase muscle size and strength, and physically active people more often expose their skeleton to strain induced by impact or muscular pull forces. Even if an individual did not engage in exercise, larger and stronger muscles may enable them to generate higher impact forces during infrequent, brief exertions that may influence bone, e.g. rapid stair ascent/descent. It is possible that exposure to higher impact forces consequent to actions of more powerful muscles mediates the association between muscle and bone.

Body size influences total muscle mass and overall muscle strength (and vice-versa) (Ferretti et al. 1998), hence it is possible that the positive association frequently observed between muscle strength and BMD is attributable to covariation with factors such as body mass, height, and lean mass that act independently of the influence of muscle-specific tension via increased impact and compressive forces (Duncan et al. 2002). In order to demonstrate that muscle strength in itself directly determines BMD,
it is necessary to show that the association exists independently of other body size or composition measures.

The majority of studies investigating the muscle-bone relationship have concentrated on BMD as the main outcome variable, yet this measure does not adequately adjust for bone and body size (Prentice et al. 1994). The recognised importance of bone geometry in determining overall bone strength and fracture risk (Faulkner et al. 2006) highlights the need to examine the relationship between muscle and bone structural parameters that may be contributors to bone strength, independent of BMD (Beck et al. 1993).

Therefore, the aims of this study were to determine whether bone density and geometry are associated with maximal muscle strength and/or maximum impact forces in sedentary women, and whether such associations are independent of body size and composition.

6.2 Methods

Study design

The present cross-sectional study used data that were collected during the baseline testing session of the 6-month intervention study. Therefore, testing protocol and order were identical to the sequence of measurements outlined in Chapter 5. Not all measurements were used in the current analyses, so those methods for the relevant outcome variables are briefly highlighted here.

Participants

Participants were the sedentary but healthy premenopausal women who initially enrolled on the exercise intervention study. Exclusion criteria were as previously described and the study had already been approved by the university’s Ethical Advisory Committee.

Anthropometry and body composition

Standing height without shoes was measured to the nearest 1mm using a portable suitcase-mounted stadiometer (Holtain, Pembrokeshire) and body mass was measured to the nearest 0.1 kg using digital scales (Tanita, Tokyo) after removing shoes and
outer layers of clothing. From these two values, body mass index (BMI) was calculated by dividing body mass by height squared (kg/m²).

Amounts of fat mass (FM) and fat-free mass (FFM) were assessed with a hand-held bioelectrical impedance meter (Bodystat 1500, Bodystat Ltd., Douglas, Isle of Man). Participants were requested to avoid strenuous exercise, alcohol, and caffeine intake during the preceding 24 hours, as well as food and water for 4 hours beforehand, in order to control hydration status.

*Maximal isometric knee extension strength (IKES)*

The same procedure as described in Chapter 3 was carried out.

*Maximum ground reaction forces (GRFs)*

The maximal takeoff force attainable during a jump or hop will be partly dependent upon lower limb extensor power, whilst the landing force is more a measure of the maximal impact forces to which the participant can regularly be exposed during voluntary activity. Measuring the impact forces to which an individual is exposed during everyday life would be extremely difficult, but individuals who can generate high impact forces when asked to perform a maximal hop are likely to be the ones who’s bones experience greater mechanical loading during activities that may occur briefly but regularly even in sedentary women, e.g. running up stairs and jumping over a puddle. GRFs during a maximal vertical countermovement hop was thus determined as detailed in Chapter 3 as a measure indicative of maximal impact forces that are also expected to be related to muscle function.

*BMD and bone geometry*

BMD at the lumbar spine and both hips were assessed with the Lunar Prodigy Advance DXA scanner (GE Lunar, Madison, WI.). In addition to total hip BMD, specific regions of interest were the femoral neck, Ward’s triangle, trochanter, and shaft. Hip geometry was also recorded: FSI, CSMI, and CSA. Standardised positioning protocol was used and as well as daily calibration, the manufacturer’s lumbar spine phantom was scanned prior to every testing occasion to detect any drift. All scanning and analyses were performed by the same two operators.

*Statistical analysis*
Before conducting statistical tests, values for left and right sides of the body were averaged where appropriate. Bivariate Pearson's product moment correlation coefficients were used to assess relationships between IKES, GRF, body composition and bone density and geometry variables. Partial correlations were then calculated to assess these same relationships but after controlling for height, body mass, and FFM. Lastly, height, body mass, FFM, IKES, and maximum GRFs were entered into stepwise linear regression analyses in order to identify significant predictors of bone variables.

6.3 Results

<table>
<thead>
<tr>
<th>Table 6.1: Participant characteristics (n=89)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Variable</td>
</tr>
<tr>
<td>Age (years)</td>
</tr>
<tr>
<td>Body mass (kg)</td>
</tr>
<tr>
<td>Height (m)</td>
</tr>
<tr>
<td>BMI (kg/m^2)</td>
</tr>
<tr>
<td>Fat mass (%)</td>
</tr>
<tr>
<td>Fat-free mass (kg)</td>
</tr>
<tr>
<td>Maximum knee extension strength (N)</td>
</tr>
<tr>
<td>Peak landing ground reaction force (N)</td>
</tr>
</tbody>
</table>

Table 6.1 describes the characteristics of the 89 women. Associations of bone parameters with height, body mass, FFM, and measurements of muscle function (average of left and right sides) are summarised in Table 6.2.
Figure 6.1: Graphs displaying associations between maximal knee extension strength, peak ground reaction force, and fat-free mass with hip BMD (femoral neck) and hip geometry (CSMI).
Table 6.2: Correlations ($r$) between muscle function and bone measurements

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Height</th>
<th>Body mass</th>
<th>FFM</th>
<th>IKES</th>
<th>GRF</th>
<th>IKES'</th>
<th>GRF'</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lumbar spine BMD</td>
<td>0.09</td>
<td>0.39**</td>
<td>0.25*</td>
<td>0.13</td>
<td>0.36**</td>
<td>0.09</td>
<td>0.19</td>
</tr>
<tr>
<td>Femoral neck BMD</td>
<td>0.12</td>
<td>0.43***</td>
<td>0.45***</td>
<td>0.41***</td>
<td>0.41***</td>
<td>0.29**</td>
<td>0.23*</td>
</tr>
<tr>
<td>Upper neck BMD</td>
<td>0.10</td>
<td>0.35**</td>
<td>0.41***</td>
<td>0.45***</td>
<td>0.36**</td>
<td>0.34**</td>
<td>0.22*</td>
</tr>
<tr>
<td>Lower neck BMD</td>
<td>0.14</td>
<td>0.51***</td>
<td>0.46***</td>
<td>0.31**</td>
<td>0.42***</td>
<td>0.19</td>
<td>0.18</td>
</tr>
<tr>
<td>Shaft BMD</td>
<td>0.02</td>
<td>0.42***</td>
<td>0.40***</td>
<td>0.35**</td>
<td>0.40***</td>
<td>0.23*</td>
<td>0.22*</td>
</tr>
<tr>
<td>Total hip BMD</td>
<td>0.03</td>
<td>0.41***</td>
<td>0.40***</td>
<td>0.37***</td>
<td>0.42***</td>
<td>0.25*</td>
<td>0.25*</td>
</tr>
<tr>
<td>FSI</td>
<td>0.03</td>
<td>-0.32**</td>
<td>-0.19</td>
<td>-0.01</td>
<td>-0.03</td>
<td>0.05</td>
<td>0.20</td>
</tr>
<tr>
<td>CSMI</td>
<td>0.60***</td>
<td>0.52***</td>
<td>0.67***</td>
<td>0.15</td>
<td>0.41***</td>
<td>-0.07</td>
<td>0.18</td>
</tr>
<tr>
<td>CSA</td>
<td>0.36***</td>
<td>0.55***</td>
<td>0.62***</td>
<td>0.38***</td>
<td>0.50***</td>
<td>0.24*</td>
<td>0.28*</td>
</tr>
</tbody>
</table>

*p<0.05, **p<0.01, ***p<0.001, *partial correlations with height, body mass, and FFM as covanates.

Lumbar spine BMD was weakly but positively associated with body mass and its association with GRF did not persist after inclusion of body mass. BMD at hip sites was associated with body mass, FFM, IKES and GRF. Partial correlations of IKES and GRF with hip BMD persisted after controlling for body composition variables. CSMI and CSA were most strongly associated with FFM. CSMI was not associated with IKES and GRF independently of body composition, but CSA was independently associated with both IKES and GRF. FSI was negatively associated with body mass but not significantly associated with other variables. Figure 6.1 opposite illustrates the relationships of BMD and geometry measures of the hip with neuromuscular function and impact landing measures.

Regression models for absolute values of bone mass and geometry are shown in Table 6.3. The only variables that were independently influenced by both IKES and GRF were trochanter BMD and total hip BMD. IKES explained some variance of all of the other hip BMD measurements. FFM predicted hip bone density at some regions; namely, femoral neck, upper neck, and Ward’s triangle; as well as being a strong predictor of the hip geometry variables, CSMI and CSA. Body mass was the only predictor of spine BMD and FSI.
Table 6.3: Predictors of bone mineral density and geometry according to stepwise linear regression models: beta-coefficient (SE)

| Variables entered if F<0.05. Statistics are shown for those variables entered into the model. The p value listed here is for the individual variable entry to the final model. The r^2 value represents the amount of variance explained by the model with current and preceding variables included. *p<0.05, **p<0.01, ***p<0.001 |

<table>
<thead>
<tr>
<th>Lumbar spine BMD</th>
<th>Constant</th>
<th>Body mass</th>
<th>Height</th>
<th>FFM</th>
<th>IKES</th>
<th>GRF</th>
<th>r^2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Femoral neck BMD</td>
<td>1.323 (0.367)**</td>
<td>-0.686 (0.272)*</td>
<td>0.015 (0.003)***</td>
<td>0.005 (0.002)</td>
<td>0.33</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Upper neck BMD</td>
<td>1.177 (0.409)**</td>
<td>-0.679 (0.303)*</td>
<td>0.013 (0.004)***</td>
<td>0.008 (0.002)**</td>
<td>0.32</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lower neck BMD</td>
<td>0.593 (0.089)***</td>
<td>0.006 (0.001)***</td>
<td>0.004 (0.002)*</td>
<td>0.30</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ward’s BMD</td>
<td>1.378 (0.448)**</td>
<td>-0.837 (0.332)*</td>
<td>0.015 (0.004)***</td>
<td>0.29</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trochanter BMD</td>
<td>0.47 (0.067)***</td>
<td>0.006 (0.001)***</td>
<td>0.005 (0.002)**</td>
<td>0.24</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Shaft BMD</td>
<td>0.636 (0.111)***</td>
<td>0.006 (0.002)***</td>
<td>0.007 (0.002)**</td>
<td>0.25</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total hip BMD</td>
<td>0.525 (0.091)***</td>
<td>0.003 (0.002)*</td>
<td>0.005 (0.002)*</td>
<td>0.011 (0.0)</td>
<td>0.28</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FSI</td>
<td>2.232 (0.202)***</td>
<td>-0.01 (0.003)**</td>
<td></td>
<td></td>
<td></td>
<td>0.10</td>
<td></td>
</tr>
<tr>
<td>CSMI</td>
<td>-10906.5 (4666.7)*</td>
<td>7135.7 (3500.3)*</td>
<td>190.1 (40.5)***</td>
<td></td>
<td></td>
<td>0.48</td>
<td></td>
</tr>
<tr>
<td>CSA</td>
<td>44.3 (12.7)**</td>
<td>1.743 (0.326)***</td>
<td>0.134 (0.047)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

6.4 Discussion

This study found that hip BMD measurements were positively associated with muscle function and maximal voluntary impact forces as assessed by IKES, GRF, or both, and these associations persisted after inclusion of body size and composition. Correlations with strength and GRF were generally similar. Lumbar spine BMD and FSI were positively and negatively associated with body mass respectively. Femoral neck CSMI and CSA were most strongly associated with FFM, although CSA was also independently associated with GRF and IKES. Broadly speaking, hip BMD thus appears to be most strongly related to muscle function, whilst hip geometry is most strongly related to FFM.

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The finding that all bone variables except for FSI were associated with muscle function supports previous observations that greater muscle strength is associated with greater bone mass (Schonau et al. 1996, Sinaki et al. 1996), so individuals with larger and stronger muscles also have stronger bones (Myburgh et al. 1993). However, maximal voluntary muscle force is dependent upon muscle size, which is largely determined by overall body size (Bamman et al. 2000, Hakkinen et al. 1986), with muscle CSA accounting for approximately 50% of the difference in strength between untrained individuals (Maughan et al. 1984). Body size and composition were associated with hip BMD and geometry in this study and others (Cui et al. 2007, Faulkner et al. 2003, Nichols et al. 1995), so the associations between muscle function and bone could be mediated by body size and composition, rather than any effect of muscular activity or impact forces on bone. FFM was at least as strong a predictor of bone mass as the muscle function measures, but the relationships of BMD and CSA at the hip were independent of body size and FFM, indicating that muscle forces may affect bone at these sites.

There have been previous reports of proximal femur bone geometry relating to lean mass, but these findings have been in children (Petit et al. 2005). In this study, FFM was the variable most strongly related to CSMI and CSA in adult women. Since a larger body has more FFM, the present observation is also consistent with Nordstrom et al. (1998) who concluded that bone CSA is largely determined by parameters relating to body size. Furthermore, other researchers have observed that body size variables, particularly lean (i.e. muscle) mass, are more closely associated with the density of weight-bearing bones than non-weight bearing bones, thereby implying that there is a mechanical-loading component in relationships of body size and BMD (Doyle et al. 1970, Edelstein and Barrett-Connor 1993). The relative contribution of the lean component to BMD has been reported to differ by age or menopausal status, with lean mass being the strongest predictor of BMD in premenopausal women (Nichols et al. 1995) but FM being more strongly related to BMD than lean mass in postmenopausal women (Khosla et al. 1996) or in women with lower levels of FM in whom this component of body composition constitutes a greater part of the weight-bone relationship (Gjesdal et al. 2007). The positive associations between FFM and BMD could also be due to the finding that contributions of muscle to the extraglandular production of oestrogen might be similar to that of fat (Matsumine et al. 1986). Circulating oestrogen levels may therefore be higher in those with large muscle mass as well as those with large adipose tissue mass, consequently resulting in protection against bone loss (Turner et al. 1994).
The FSI represents the ratio of estimated compressive yield strength of the femoral neck to the expected compressive stress of a fall on the greater trochanter, and has been reported to be lower in fracture patients than healthy individuals (Faulkner et al. 2006). FSI is calculated from a number of variables, including body mass, height, age, and various geometric parameters (Yoshikawa et al. 1994). FSI was not associated with muscle function, but was negatively associated with body mass. Presumably, this is because increased body mass increases the estimated stress from a fall without adequate compensatory increase in estimated bone strength. However, this is only a theoretical hypothesis and the reverse is normally observed: an association between low body mass and greater risk of fracture (LaFleur et al. 2008). As muscle strength and FFM contributed to hip BMD and geometry, it is perhaps surprising that they were not related to FSI. One explanation is that any increase in bone strength associated with greater muscle strength was only adequate to compensate for greater body mass.

Neither measure of muscle strength in the present study explained spine BMD. Instead, body mass was the only independent predictor of spine BMD in the regression model. It has been proposed that, unlike the strain applied on the hip by muscle contraction, loads on the spine are produced primarily by body mass, pre-stress exerted by the ligaments, and externally applied loads, i.e. high-impact GRFs (Tyldesley and Grieve 2002). Although we found GRFs to be associated with spine BMD, this association disappeared on adjustment for body mass, so it seems that body mass was mediating this association and there is no independent association of the maximal GRF that can be generated in hopping with spine BMD. Body mass also predicted BMD at the lower neck and not the upper neck, which is in agreement with the finding in older people that daily gravitational loads induced by the weight of the body from standing and walking maintain lower rather than upper neck BMD (Mayhew et al. 2005). However, because we found IKES to be the strongest predictor of upper neck BMD, it may be possible to prevent bone loss in this skeletal region by maintaining muscle strength; although not only of the knee extensors, because these muscles alone would not affect the hip. Rather, hip flexion/extension more specifically loads the hip, and since knee flexion/extension often occurs with hip flexion/extension during everyday activities, (e.g. during chair/stair ascent, squatting, running, and jumping), it could be that knee flexion/extension strength correlates with hip flexion/extension strength. Another fragile site that is not highly loaded in walking but comes under compression during the sideways falls that lead to hip fracture is the posterior end of the femoral neck (Lotz et al. 1995) and the intertrochanter (Kaptoge et al. 2003b). Muscle strength and maximal voluntary impact forces were related to
BMD at most hip regions, independently of body size, thereby implying that maintaining the function of muscles that load the hip might maintain BMD at these susceptible hip sites that are less loaded by walking.

One of the unique aspects of the study was the exclusion of regular exercisers. This served to limit the potential muscular and impact-loading effects of regular exercise on current bone status that would otherwise confuse associations between muscle function and bone properties. Muscle strength and BMD are only two of many biological features that increase during growth (Vicente-Rodriguez 2006), hence the observed correlation between muscle strength and bone is possibly one that developed during childhood and persisted into adulthood, regardless of physical activity levels. Despite identifying themselves as non-exercisers, physical activity during childhood, a period when the skeleton is thought to best respond to mechanical stimuli (Bass et al. 1998, Warden et al. 2007), or even during prior years to the current study; may have resulted in present associations since there is evidence that gains in BMD and bone structural properties during puberty persist during detraining (Binkley and Specker 2004, Kudlac et al. 2004). Existing studies that demonstrate increases in muscle strength without concomitant increases in BMD (Heinonen et al. 1996a, Vuori et al. 1994) contradict the muscle-bone relationship. In contrast, numerous studies show parallel increases in muscle and BMD (Dornemann et al. 1997, Hawkins et al. 1999, Sinaki et al. 1996). Differences in study duration probably led to these varied findings since muscle and bone follow a very different time course of response (Schlessl et al. 1998), so the shorter studies may have been sufficient in duration to observe changes in muscle, but not long enough for bone to physiologically change. Moreover, there is equal evidence that cessation of exercise in both the short- and long-term results in bone loss (Snow et al. 2001, Valdimarsson et al. 2005, Winters and Snow 2000). To clarify, the graded childhood activity levels from the questionnaires were entered into analyses, but did not correlate with any of the bone measurements taken. These findings offer reassurance that the results presented here were not confounded by the effects of exercise, past or present.

Measuring GRFs may provide a surrogate measure of the strain experienced by bone (Bassey et al. 1997, von Stengel et al. 2007), so whilst takeoff force provides an indication of lower extremity muscle functional strength and power (Bosco and Komi 1980, Cordova and Armstrong 1996), the peak landing GRF an individual can experience during a maximal hop test may also indicate the gravitational loads imposed on their skeleton during those occasions in daily living when high-impact movements are performed, e.g. bounding down the stairs to answer the phone.
However, the magnitude of GRFs produced cannot be separated from the influence of muscle function (muscle strength is needed in order to hop higher, which contributes to greater GRFs) or the dependence of this value on body mass (heavier individuals are also likely to generate higher GRFs). Another limitation of using this measure is that technique and familiarisation can determine the height hopped and hence the landing force. For example, depending on the degree of arm swing in a countermovement jump, the height reached can increase more than 10% due to increased vertical momentum (Luhtanen and Komí 1978). Obviously, the validity of any test that assesses voluntary maximal effort is largely dependent on volition (Ikal and Steinhaus 1961), thus it cannot be confirmed that the true ability of each individual was recorded. Yet since the data in this study came from the baseline tests of a long-term intervention study, it is more likely that the subjects were most highly motivated during this first testing session when all the tests were new to them. Moreover, they had 3 attempts to attain a maximal score. Inter-individual variation was minimised by giving very precise instructions and a demonstration to the participants as well as allowing them all the same number of practice hops beforehand and the same duration of rest in between attempts (30s).

Testing maximum isometric leg extension has been employed previously to assess leg muscle strength (Bassey et al. 1992) but one potential limitation is that measurements of muscle strength, bone density, and bone geometry were available for a limited number of muscle groups and skeletal sites, and the measured sites may not correspond to those most loaded by the knee extensor muscles. As mentioned in Chapter 2, the quadriceps femoris group of muscles attach at the femoral shaft and may extend to the greater trochanter but do not directly load the femoral neck. Considering the site-specificity of exercise training (Kerr et al. 1996, Winters-Stone and Snow 2006), measurements of muscle function in hip abduction and flexion would have strengthened the study because the agonistic muscles cross the hip and insert at the greater and lesser trochanter, thereby transferring greater forces to the femoral neck. As highlighted previously, more muscle groups than just the knee extensors are activated during hopping so testing their strength could expose more skeletal sites to osteogenic loading than were examined here. Furthermore, bone structure at other sites might have been identified as being more strongly related to muscle function.

The low activity levels of the participants in this study may have strengthened the independent associations between muscle and bone that were observed, as it has been proposed that high physical activity weakens the relationship between muscle strength and BMD in an individual (Nordström et al. 1996, Pettersson et al. 1999).
thresholds of “high” vs. “low” activity levels are not defined, so it is possible that the results presented may have differed if participants did either moderately more or less exercise. Nevertheless, the over-riding, persisting limitation of these cross-sectional analyses is that it cannot be confirmed that it is only muscle that is affecting bone. Higher BMD values cannot be inferred from greater muscular strength, because as described earlier, there are other possible explanations for the observed associations between muscle and bone in addition to the direct loading of the skeleton.

6.5 Conclusions

These findings imply that BMD and CSA are associated with muscle function in sedentary women. Although weaker, once adjusted for body mass, height, and FFM, these associations remained significant. In a regression model, muscle function is more strongly associated with hip BMD than hip bone geometry, but was not a predictor of lumbar spine BMD. Since lower limb functional measures do not appear to influence spine BMD, assessment of muscle groups relevant to the spine are needed. FFM was the strongest predictor of hip structural properties, as measured by DXA. Further research is necessary to determine whether it is solely muscle influencing bone or if their strong correlation is caused by the sharing of other common intrinsic determinants. Given the other benefits of superior muscular function on extraskeletal risk factors for fractures (Korpelainen et al. 2006), it would seem desirable for untrained women to endeavour to maintain muscle strength and composition.
7.1 Implications

In the human model, the determination of a dose-response relationship is hindered by a lack of the appropriate technology to directly evaluate mechanical loading and skeletal competence. *In vitro* loading of bone does not duplicate the *in vivo* physiologic conditions and neuromuscular responses to loads applied to the skeleton. While animal studies aid in determining mechanisms of bone's response to mechanical loading, they do not obviate the need for human clinical trials to evaluate the effects of exercise on skeletal competence and fall prevention. My research has demonstrated hip BMD can positively respond to brief, high-impact exercise over a short period of time and also result in improvements in neuromuscular function and postural stability, which are factors that reduce the risk of falling and subsequent fracturing (National Institutes of Health, 2000). A critical feature of the exercise intervention in addition to its efficacy was its feasibility, reflected by the high overall compliance rate achieved by the exercisers as a whole (86.8%). Their feedback indicated that the programme was easily fit into their daily life. Considering the challenges of inadequate time, interest, and motivation that many people face regarding regular long-term exercise, convenience and acceptability is an important aspect of exercise prescription for osteoporosis prevention. Therefore, in addition to introducing hopping exercises as a strong scientific model to study bone's response to mechanical loading, the programme also seems to have the potential to deliver the required osteogenic loads to the skeleton in a way that is convenient, acceptable, and comfortable. Furthermore, this thesis added to knowledge regarding predictors of bone geometry, which also contributes to bone strength alongside bone mass and density. Body composition was more strongly associated with bone geometry than ground impacts, a finding that is consistent with the absence of effect the high-impact intervention had on structural parameters of bone and the absence of change in both FFM and bone geometry. Both the cross-sectional and intervention studies also demonstrated impact forces to be related to BMD. Despite the consistency between findings of these two studies, the intervention study has advantages in experimental design that makes its results more robust. The following discussion will consider their implications and further research that could develop from these outcomes.

It was demonstrated that it is possible to increase BMD at a clinically relevant site with relatively little time, providing the exercises are performed regularly. The present
findings could have valuable implications for the exercise prescription to optimise peak bone mass. In the U.K., it is recommended that activities to improve bone health, muscle strength and flexibility are needed “at least twice a week” (Department of Health 2004); whilst the American College of Sports Medicine Position Stand on physical activity and bone health advises weight-bearing endurance activities 3–5 times per week and/or resistance exercise 2–3 times per week (Kohrt et al. 2004). These vague recommendations make it clear that the exercise prescription for bone health is not fully understood. Animal models indicate that more frequent exercise is more effective (Turner 1998), but until now, neither an animal or human study has attempted to compare the effects on bone of differing weekly frequencies. My findings indicate that more frequent exercise is more beneficial in humans, which would also serve to enhance bone health by strengthening the established association between muscle function and BMD. Further research is now needed to support this inference, as the present results might only be relevant to high-impact exercise and it is possible that an equal or even greater response might be observed with less frequent exercise if it was performed for a longer duration of time.

7.2 Strengthening the current study design

The hopping exercises can be confidently identified as causing the increases in hip BMD because the changes in the trained leg significantly differed from the changes in the control leg. If it were some other factor(s) influencing the change in BMD, then both legs would have been affected rather than just the one. The unilateral design of the exercise intervention is the major strength of the study design, in that comparing the two legs of the same individual enables the elimination of confounding factors. To my knowledge, only two unilateral exercise interventions in premenopausal women have been conducted in the past, but exercise effects were not apparent due to weaknesses in methodology (Heinonen et al. 1996a, Vuori et al. 1994). Even though these interventions continued for a year, perhaps their low compliance rates meant that the exercise was not performed frequently enough for bone to detect the need to adapt, and perhaps using RT as an intervention is insufficiently osteogenic compared to high-impact exercise. Despite the strength of the findings from the recently completed tightly controlled study, there are still certain limitations that may have weakened results, which if addressed, could strengthen future studies of similar design.
CHAPTER SEVEN

Placebo effect

Considering some of the significant changes observed in controls, an improvement of the study design for next time would be to conduct the intervention so that control subjects were unaware that they were controls. They would still be informed that the study aimed to investigate effects of exercise on bone and would still be allocated to an exercise frequency group, but instead they would be instructed to only perform the mobilising exercises and stretches without any hopping. This would ensure that nobody felt like they were “missing out”, which could have led some controls to take up some exercise outside the study.

It was not an option in the present study, because I had to administer and monitor the intervention as well as take measurements, but findings could be further strengthened if the person conducting the tests was “blind” to which group each subject was in. Or indeed, making all participants “blind” to the study and not just controls would be most advantageous. Obviously, those assigned to an exercise group would have to know how many days per week to do the training, but if they were not told fully about the study’s specific aim of comparing bone’s response to different exercise frequencies and instead given more general information that it was simply an investigation into the effects of exercise on bone, then it could be possible to conduct this study so that neither the subjects or researchers can “anticipate” results. It would certainly be difficult for significant findings from a unilateral, double-blind, RCT to be criticised.

Outcome measurements

As has been highlighted numerous times, bone strength reflects the integration of bone density and bone geometry. It is only useful if the loading-induced increases in bone mass are appropriately used to build mechanically strong bone structures, but unfortunately, I did not have equipment at my disposal to measure this element of bone quality. There is evidence that exercise has positive effects on cross-sectional geometry that are not necessarily evident in density measures (Haapasalo et al. 2000), and it is suggested that bones tend to primarily adjust their apparent strength, rather than BMD or BMC in response to changes in their functional environment (Adami et al. 1999). This is presumably achieved through the apposition of bone to endosteal or periosteal surfaces or by diminished resorption at the endocortical surface (Faulkner et al. 2003). Moreover, DXA cannot differentiate between trabecular bone and cortical bone, of which the latter contributes most to bone strength (Adami
et al. 1999). In order to better understand the effects of exercise on skeletal health, structural parameters other than areal bone mass or density must be included.

Research in animals has found that despite an absence of differences in DXA-measured BMD/BMC between impact-loaded and unloaded groups, the impact-loaded rats had significantly higher (>14%) failure load at their femoral neck, thereby indicating a positive redistribution of bone mineral (Jarvinen et al. 1998). The authors consequently speculated that if similar changes in the cross-sectional and mechanical characteristics of bones without simultaneous changes in BMD/BMC are translated in humans too, the results of longitudinal exercise studies that show no or only mild exercise-induced gains in BMD and BMC (Ernst 1998) must be re-evaluated (Jarvinen et al. 1999). It could be that the true increases in bone strength were superior to those indicated only by changes in BMD and BMC. More exercise studies have now measured bone structural parameters in addition to BMD to provide a more complete understanding of the effects of exercise on total bone strength, but the majority are cross-sectional in nature (Heinonen et al. 2002, Lai et al. 2005, Nikander et al. 2006). The few intervention studies were carried out either in older, postmenopausal women (Karinkanta et al. 2007, Uusi-Rasi et al. 2003) or in children, whose natural growth patterns would show different changes in bone structure compared to adults (Binkley and Specker 2004, Heinonen et al. 2000).

In the present study, a number of structural parameters were assessed but these were obtained from the DXA scans, so the accuracy of outcomes depended on the accuracy of DXA. Limitations include those related to scanner design or performance, those related to quality control, and those fundamental to the measurement method, such as imprecise and inconsistent positioning (Beck 2003). If the scanning position and the regions of analysis are not accurately reproduced in serial measurements, error in projected dimensions and consequent geometry can occur. The assumptions made of cross-sectional shape and of the relative distribution of trabecular and cortical bone within the different regions are also not completely accurate. Consequently, it is necessary to re-evaluate the appropriateness of current bone measurements for evaluating the skeletal response to exercise and other treatments. DXA can provide an overall picture of bone status, but as mentioned before, it overlooks interior bone structure and periosteal alterations that can independently and considerably influence bone strength. However, although bone mass is only one component of overall bone strength, it accounts for more than 80% of its variability (Beck and Snow 2003), thus using DXA is still a very useful indicator of bone status. It would have been preferable to supplement the DXA measurements in this study with ones from pQCT, because
accurately measuring bone structural parameters may have uncovered a relationship between muscle function and hip geometry, (which was not evident in current correlations), but we had to "settle on measuring what is measurable rather than what is relevant" (Ernst 1998). Similarly, taking more measurements of muscle function (e.g. a hip flexor strength test) could reveal more associations between specific muscle groups and bone, or other predictors of bone geometry (e.g. muscle volume (Vaiontönnä et al. 2007)), especially as about 60% of work done during a jump is produced by muscles other than the knee extensors (Bobbert and Casius 2005). However, in order to successfully conduct a large intervention study in a relatively short period of time with finite resources, there had to be a limit on the number of tests developed.

*Measurement error*

Measurement error and Intrasubject variability can present problems in the assessment of BMD change in an individual subject. It can be questioned as to whether observed change is simply due to random error, the limitations of instrument performance, or if it is indeed true biological change (Nguyen et al. 1997). In this study, having two operators performing the DXA scans on two different Lunar machines could have also introduced variability in bone measurements, even though standardised protocol was adhered to, because each instrument could have provided consistently different results. Hangartner (2007) reported clinically significant BMD shifts of 1.5% and 2.1% for two separate Lunar densitometers over a 4-year period. However, variability from this source should have been reduced since any BMD shifts in the scanners would have been minimal over 6 months and every participant had their pre- and post-intervention measurements performed on the same scanner by the same operator.

Change over time can be detected reliably only if it exceeds measurement error, as the proportion of error in detecting change is usually considerably larger than the degree of absolute change. In clinical and research settings there is still confusion about the interpretation of measured changes and the comparative performance of techniques is difficult. Therefore, calculating the "least significant change" (LSC) is recommended by the International Society for Clinical Densitometry (Binkley et al. 2007) to identify clinically meaningful change in an individual and to serve as a universal reference so that techniques can be comparable across studies. However, applying the LSC criteria to the current study was inappropriate because the aim was to identify significant changes in a group and not on an individual basis. Although the
unilateral study design increases the effects of measurement error as twice as many measurements are taken, increasing the sample size reduces these effects (overestimation in one person is likely to be counterbalanced by underestimation in another), so based on power estimations, the study's sample size should have adequately overcome measurement error issues.

**Chance findings**

Since statistical significance was set at $p<0.05$ in analyses, there is always the 5% probability that the significant results were actually chance findings, and since the intervention study was powered at 80%, there is a 20% chance that a significant result was not detected. The current sample size was largely an estimation from bilateral exercise studies, so now that the study has been completed, the results can be used to examine if there was sufficient power in analyses. Using the difference in response between legs in femoral neck BMD of G7, observed power was calculated to be 52%. This means that the negative findings, or absence of effects, cannot be regarded as conclusive, as it would seem that there is almost a 50% chance that something significant was missed! It was subsequently calculated that, at least for measurements at the femoral neck, a sample size of 54 participants per group would have given the intended 80% power (mean difference in response between legs = 0.021, mean standard deviation of change = 0.038). The multitude of comparisons made would have further increased the likelihood of a chance finding, although some of the exercise effects on bone remained after performing post hoc tests that controlled for multiple comparisons. Moreover, the concomitant changes observed in neuromuscular variables strengthen the credibility of the BMD results. The muscular system responds to training before the skeletal system (Folland et al. 2007) so it is unlikely that significant changes in both would be a result of chance.

**Calcium intake**

A significant difference was noted between groups in their dietary intake of cereal servings, a food group that is fortified with calcium. Despite neither this variable nor daily servings of dairy products contributing to the variance in BMD change, results are unreliable because the food frequency questionnaires used provided only a very crude indication of dietary habits. Considering that calcium has a permissive influence on bone's response to exercise (Specker 1996), it could be that levels may not have reached the required "threshold" to fully express the effects of the exercise intervention, even though it was ensured that all participants consumed sources of
calcium everyday. A more accurate measurement of calcium intake would be useful, but the more accurate methods, such as a weighed food record, is more time-consuming and can be less valid due to under reporting or under eating (Black et al. 1993). The increased demand on participants might have also reduced compliance.

**Hopping technique**

Hopping technique significantly influences hop height and the GRFs that are consequently produced. First, counter-movement jumps have longer flight times than squat jumps due to the increased range of motion (Elvira et al. 2001) and in a countermovement jump, the lower the centre of mass drops (i.e. a greater knee angle and hence deeper countermovement) up to an optimum muscle length, the more distance is available for the push phase of the jump, which increases the work performed and hence impulse at take-off and final jump height (Kvorning et al. 2006). A larger countermovement also enables a greater eccentric muscle stretching phase that will store more elastic energy during the stretch-shortening cycle and thus lead to greater concentric muscle contraction to propel the body upwards (Harman et al. 1990).

Second, arm swing exerts another influence on hopping performance, because the contribution of the arms towards higher propulsion of the body can be more than 10%, which translates into increased peak force production and ultimately jump height (Luhtanen and Koml 1978). It can be argued that a squat hop while keeping the arms immobile would have provided a more standardised protocol due to large variations in countermovement hop technique as well as ensuring that arm movement did not mask peak force production generated by the lower limb muscles, but the counter-movement style is a much more natural movement than starting from a crouched position (Linthorne 2001), an important consideration for the unathletic population in the present study. Moreover, imposing no restrictions in terms of body position, knee angle, or degree of arm swing allowed subjects to jump more freely, safely, and potentially more maximally.

Third, the speed of hopping plays a role in the attenuation of landing forces. It has been demonstrated that for the same height during continuous jumping, internal forces on bone are higher when the jumps are performed quickly compared to slowly (Bassey et al. 1997). Force-time curves have illustrated that during fast jumping the landing and take-off fuse together; an action that is fast enough for muscles to reuse the absorption of stored elastic energy that occurs during eccentric contraction upon
landing for take-off (McNitt-Gray 1993). On the other hand, landing forces during slow jumping are attenuated if the subject flexes their hips and knees to a greater extent in preparation for the next jump, because the time interval over which the landing force is absorbed by the leg musculature increases (McKay et al. 2005). A longer contact time with the ground means a longer coupling time between eccentric and concentric contraction, thus reducing effectiveness by not taking advantage of the elastic recoil during the concentric phase of the jump (Aura and Viitasalo 1989, Bosco et al. 1983). These differences in hopping technique were apparent during testing sessions. Some participants hopped quickly so that the 10 hops became one fluent movement, whereas others hopped slowly so that each hop involved a separate countermovement (i.e. they straightened up after landing before lowering themselves again for the next hop.) Factors that also influence the ability to attenuate landing forces are age and skill level, with younger and more skilled individuals able to produce a higher peak GRF during landing and to attenuate impact forces more than older and less skilled individuals (Johannsen et al. 2003). The correlation between peak GRF and age were not examined in the existing analyses, but studying a sedentary population may have reduced the chance of force attenuation.

Fourth, toe-to-heel landings appear to reduce GRF compared to full footed landings (Dufek and Bates 1990). Although not noted, this difference was audible in the current study, as the noise made on the force plate from those who landed full footed was very loud, thereby creating high impact forces. Considering the site-specificity of osteogenic exercise, landing technique may have also determined the extent of osteogenesis at the calcaneus. Subjects who did not touch their heel to the ground with each hop would not have experienced the same loading on their calcaneus as those who had their whole foot touching the ground when landing full footed. The hopping exercises were performed barefoot, but a previous high-impact study found that wearing trainers significantly increased GRF and implant forces at the hip because subjects were able to jump almost 20% higher when wearing shoes (Bassey et al. 1997). Future use of the current intervention could consider requesting exercisers to keep their shoes on while doing the hopping exercises, although the advantage of not wearing shoes is that participants do not have to worry about having the appropriate footwear (i.e. trainers), especially if they travel or are away from home.

In this study, the degree of arm-swing, knee-bend, and type of foot landing during the hopping exercises were self-determined by the participants so the variation in technique could have affected the GRFs produced and hence strain on bones. However, it was emphasised that they should progress to hopping as high as possible,
which would require sufficient arm-swing and knee-bend in the countermovement; and it is likely that they maintained the same hopping technique throughout the intervention, which is most important when the aim of this longitudinal study was to examine change over time. Besides, it was a home-based intervention so it would have been difficult to ensure all exercisers hopped exactly the same way, and since they were non-athletic individuals, it was more important to ensure that they felt comfortable with the exercise routine. Regardless of the variation in technique, hopping exercises, like jumping, are still faster and more strenuous than average daily locomotive activities such as walking, jogging, and cycling (Aura and Viitasalo 1989). It must be emphasised that the principal interest in the present research was to measure peak landing GRF in order to assess the resulting impact on the relevant weight-bearing bones, not to serve as a direct indication of muscle power. Rather, it is the peak GRF during the propulsion phase of a jump/hop that may provide a mean to estimate lower limb function (Cordova and Armstrong 1996). Nevertheless, it is recognised that complementing the IKES measurements with measures of takeoff GRF would have improved the intervention study’s evaluation of the effects of the exercise programme on muscle strength and power.

Assessment of jumping/hopping performance

The literature identifies three main techniques to assess vertical jump performance (Garcia-Lopez et al. 2005), each which may produce considerably different scores, even when different methods are used to analyse the same jump. Firstly, jump height can be considered as the vertical difference between two body landmarks and can be measured relatively simply by the traditional jump and reach test or by sophisticated cinematography or video techniques. Secondly, jump height can be estimated from flight time, which can be measured using timing devices such as contact mats, force plates, and laser beams. Thirdly, jump height can be calculated by applying equations for takeoff velocity and impulse where values are taken from the force-time curve produced by a force plate. Aragon-Vargas (2000) conducted a comprehensive evaluation of the reliability and accuracy of examples of each type of technique, namely calculating displacement of the body’s centre of mass, measuring time spent in the air, and calculating impulse from force plate data. All methods were able to explain more than 90% of the variability in jump height and their estimated prediction error was close to 20mm. Taking together the reliability coefficients and standard error of measurement values of all tested methods, despite not being the most accurate (it showed a discrepancy of about 118mm), the value obtained from the flight time method was the most stable and consistent (i.e. reliable). However, the
author comments that it cannot be differentiated as to whether a method shows less variability because it truly has a smaller error of measurement or because it is simply less sensitive and so cannot clearly discriminate between different trials. On the other hand, Hatze (1998) analysed the flight time method to have an error of 3.6% relative to the force plate Impulse method, which had a total precision error of 0.41% and was thus used as the reference procedure in his investigation. Errors in the flight time method are attributed to the assumptions made by Bosco et al. (1983) when the applied equations were first developed, none of which hold true. First, the propulsion period is not equal to half the total contact time, second, the vertical velocity of the centre of mass does not increase linearly during the propulsion phase, and lastly, the position of the body's centre of mass at takeoff and landing are not identical (Hatze 1998). As mentioned in Chapter 3, the flight time method is criticised for overestimating jump height, yet at the same time there is evidence that it actually underestimates jump height by 118mm relative to the criterion Vertical Jump Performance Test (Aragon-Varas 2000). Jump performance has also been found to strongly correlate with the rate of force development in an isometric leg press test (Marcora and Miller 2000) and with power in a double leg press (Thomas et al. 1996), thereby demonstrating that certain field tests may be comparable to laboratory tests.

Overall, as long as the same method is used at baseline and post-intervention and that it is shown to be reliable and valid, it may not be so critical that different techniques give slightly different values, since assessment of hop/jump performance in the current study was to compare height before and after the training intervention. It would seem that obtaining the actual true value of hop/jump height was not the most important outcome in this study but rather identifying change over time was. Above all else, investigators must often select a certain method according to their means and the equipment at their disposition.

Progression

Progression is not required to achieve an initial response, but according to the mechanostat theory, in order for bone mass to continue to increase, bone needs to be continually overloaded (Frost 1987). Other exercise studies have increased intensity of exercise by using weighted vests and elastic bands (Winters-Stone and Snow 2006) or by increasing the height of benches that are jumped off (Helnonen et al. 1996). During the present intervention where the volume, frequency, and type of mechanical loading remained the same, height and speed of hopping offered the two ways that bone could be stimulated by increasing GRFs and muscle contraction forces. Exercisers
were encouraged to always hop as high and as fast as they felt comfortable doing, but because they performed the exercise alone, their progression was voluntary. It could be argued that the increases in hop height that were observed were only a result of a greater effort when they knew they were being tested or a natural learning from familiarisation (Elvira et al. 2001), for the reliability study exposed the possibility of a learning effect taking place simply from greater familiarity with the testing protocols from one occasion to the next. Future studies based on the intervention study design should therefore incorporate a familiarisation testing session before the baseline tests begin. Nevertheless, it seems unlikely that any learning effects would have affected the outcome of the present intervention study, as the same protocol and same number of trials were applied to each subject. Furthermore, it is unlikely that improvement was due to a conscious increase in volition. If anything, it was more likely that they were most highly motivated at the start of the study when everything was new to them, which would be when their performance was the worst. Besides, the exercisers' ability to hop significantly higher over the course of the study is evidence that adaptation occurred and, according to principles of training, for adaptation to occur, there must have been an overload of the system (Drinkwater 1994). The significant difference in response detected between the trained and control leg confirm adherence to the hopping programme, yet perhaps the size of effect would have been larger if a more reliable method of progression was included, for example supplying participants with weights to strap around their waist. However, this may have made the intervention much less feasible and might have reduced compliance.

Study duration

It was my original intention to conduct a 12 month-long intervention because that was what time allowed for (even though a year is viewed as an insufficient length of time to accurately assess the relationship between mechanical loading and BMD because the skeleton is much slower to respond to physical activity than other biological systems (Dolan et al. 2006).) However, this turned out to be unfeasible for a number of reasons. The number of participants initially recruited was limited by the time and energy demands of testing and, after losing participants who withdrew during the first 6 months and who were leaving the country (international students made up a large portion of the first cohort), the remaining sample size was inadequate to make it worthwhile to continue for another 6 months. Because preliminary results were encouraging and indicated that 6 months may be long enough to observe exercise-induced effects on bone, it was decided that it would be more important to ensure that the sample size criterion was met in order to report changes with confidence.
Therefore, a second 6-month study was conducted, which increased the study's sample size but also enabled improvements to be made in the running of the second intervention, which resulted in a lower drop out rate. Nevertheless, although important findings were produced in 6 months, it is possible that a longer intervention could reveal more differences between groups or effects in other regions of bone. It could be argued that only changes in the femoral neck and Ward's triangle were apparent because trabecular bone responds at a more rapid rate than cortical bone (Einhorn 2001), but if the intervention was continued for longer, a bigger effect may take place in the shaft and trochanter because, although slower to do so, cortical bone is more responsive than trabecular bone (Adami et al. 1999).

7.3 Developing future research

It remains unclear if the time-course for adaptation or modelling thresholds differs between types of bone. It appears that the more distal portion of long bones in both humans and animals show a greater response to loading (Haapasalo et al. 1996, Mosley et al. 1997), although this could be explained by the probability that loading is greater at these regions. In animals, loading stimulated periosteal bone formation only on the distal side of rat ulnae (Mosley and Lanyon 1998), and side-to-side differences in cortical bone area, cortical wall thickness, and bone strength index were considerably greater (15-20%) in tennis players' distal rather than proximal humerus (Haapasalo et al. 2000). It would seem that long bone adaptation to mechanical loading is site-specific, not homogenous; thus one region of long bones cannot represent the entire bone's response. However, this is expected because the magnitudes, directions, and types of load would vary along its length, so the loading characteristics would have varied considerably along the proximal end of the femur where we took our measurements. Animal studies demonstrate that adaptation in a single bone cross-section varies in the medial-lateral and anterior-posterior direction and is dependent on the strain magnitude, type, and location along the length of the bone (Judex and Zernicke 2000, Mosley and Lanyon 1998). My observations of varying adaptive responses at the different regions of the femur emphasises the site-specificity of bone's adaptive response. The ideal intervention for low bone mass at a particular skeletal site should therefore select exercises that have been identified as improving bone density at that particular region. Prescribing a targeted and efficient programme for the individual increases the likelihood that each person benefits the most from their time and effort invested in physical activity. Ideally, conducting a long-term study that follows a group of premenopausal women into and through the menopause would offer insight into the rates of bone adaptation in different regions.
and provide the most accurate information about whether or not exercise-induced increases in BMD ultimately translate into meaningful changes in fracture incidence. Unfortunately, such a long-term exercise study would be unfeasible due to poor compliance.

Performing the hopping exercises may be preferred over other forms of osteogenic exercise, especially for individuals who are not disposed to exercising, because a lot of time and motivation are not required to do it. It is not necessary to travel to a specific venue at a certain time, to change clothes, or indeed even to break into a sweat! Despite the positive effects on skeletal health, the present exercise programme cannot be the sole recommendation for premenopausal women as it does not encompass all aspects of overall health. It is vigorous but too brief to alter cardiorespiratory homeostasis (50 hops can be completed within a few minutes) that is required to improve cardiovascular function and prevent cardiovascular-related diseases (U.S. Department of Health and Human Services 1996). Current exercise recommendations prescribe weight-bearing endurance exercise (Kohrt et al. 2004), but some people are put off by structured exercise and prefer to do other activities that are physical but non weight-bearing. This includes the majority of participants in the present study who did not participate in regular, structured exercise, but were still physically active, e.g. they did yoga, cycled to work, or did heavy gardening. Therefore, recommendations could be modified to advise a brief bout of exercise similar in type to the hopping exercises used here to be incorporated into daily routine instead of prescribing only weight-bearing exercise, so that individuals will have more choice as to what types of activities they choose to do to maintain overall health and fitness.

The high-impact nature of the hopping exercises makes them unsuitable for some populations, especially frail, older individuals; so the next step would be to modify the exercises in order for women of all ages to ensure their present and future bone health. Further characterisation of activities that are osteogenic for premenopausal women is needed, which will allow refinement of exercise programmes as well as the design of novel and effective exercise interventions to increase peak bone mass. Of course it needs to be confirmed that the same benefits would apply to men who also suffer from reduced bone mass and osteoporotic fractures, although not as prevalently as women. Since many of the individuals who have established osteoporosis are on medication, it would also be useful to investigate how the current exercise programme interacts with drug therapies.
Furthermore, it is necessary to establish the time-course of bone adaptation to exercise as to how permanent the exercise-induced increases in BMD are. A detraining study, whereby half of the exercisers cease daily hopping at 6 months while the others continue for another 6 months, would be a relevant study to follow on from the present one. Results would enable the exercise prescription for bone health to be even more precisely defined, as they would indicate whether or not exercise needs to be performed indefinitely or if the amount/frequency can be reduced after a certain increase in BMD has occurred. Complementing areal BMD measurements with those from QCT would enable adaptations in bone structure to be identified. The possibility of the exercise having even greater effects on variables related to bending stiffness and strength would give the exercise programme far-reaching implications for future use.

Other avenues of research that could follow the present study include closer determination of exercise frequency. Performing the hopping exercises everyday induced a greater response in hip BMD than exercising at lower weekly frequencies, raising the question as to whether the response would be further enhanced by exercising more than once per day. There are a multitude of different combinations that could be applied to exercise frequency and a larger study would be able to compare several different groups. However, the application of scientific findings to real life situations must always be considered and it is unlikely that people would successfully integrate exercise into their daily living more than once per day, no matter how brief.

7.4 Final conclusions

Prior to the research covered in this thesis, it was already well-established that muscle strength is associated with BMD and that exercise can reduce skeletal fragility, predisposition to falls, and fall impact. What was not known was how often people; especially young, non-athletic women who need to maximise their peak bone mass before the menopause; should do such exercise. Neither were the determinants of bone geometry in this population widely investigated. A programme consisting of brief bouts of high-impact, multi-directional, unilateral exercises has been shown to serve as a useful model to closely examine the effects of exercise on maintaining bone strength and muscle function in terms of its effectiveness on bone, acceptability to participants, and tightness in experimental design. Using this intervention, it was concluded that more frequent exercise is most beneficial for increasing bone mass at clinically relevant sites. Frequent exercise performed in the long-term could also result
in a greater proportion of FFM which, in light of their strong association, may positively influence bone structural parameters' and hence contribute to a mechanically more competent skeleton. There is now the potential to apply this study design to investigate other important aspects of exercise prescription and lifestyle intervention that could help improve the frightening prospect currently facing women: that there is a 50/50 chance that they will suffer an osteoporosis-related fracture in the second half of their life. It remains to be seen if these exercise-induced increases in bone mass ultimately translate into a reduction in the risk of osteoporosis-related fractures.
References


BASS, S.L., 2000. The prepubertal years - A uniquely opportune stage of growth when the skeleton is most responsive to exercise? Sports Med, 30(2), pp. 73-78.


~ REFERENCES ~


~ REFERENCES ~


REFERENCES


REFERENCES


REFERENCES


REFERENCES


Nuti, R.; Martini, G.; Frediani, G.; Valenti, R.; Giovani, S.


REFERENCES


REFERENCES


GET HAPPY HOPPING TO BUILD BONE!

Could a couple of minutes hopping make your bones stronger?
Here is your chance to make sure that your own bones are strong
and healthy!

As long as you are a female between 18 and 45 years-old and
don't do more than 1 hour per week of high-impact exercise, we
would like to invite you to join our study that will help osteoporosis
prevention.
You will be randomly assigned to be in a training group or the control
group. People in the training group will be divided into separate
groups of training frequency – 2, 4, or 7 days per week.
The training involves a simple routine of hops that take no more than
2 minutes to do. You can hop anywhere and no special equipment
is needed. Control participants will simply continue their normal lifestyle.
All participants will visit our lab 3 times during the study – at the
beginning, mid-point (3 months), and at the end (6 months) – so we
can take measurements that will show the effects of the hopping
training on your bones and muscles.

What would you get out of taking part in this study?
Well, you will receive accurate bone scans; if you hop, your bone
density, muscle strength, balance, and coordination should improve;
you will be contributing to important health-related research; and
hopefully, you will have fun!

If you are interested, get in touch with us for more information (under
no obligation to participate). Ask your friends to join you too!

Please contact:

Chrissie Bailey (Human Sciences Research Student)
C.A.Bailey@lboro.ac.uk
Tel: 01509 228159 or 07786706886

OR

Dr Katherine Brooke-Wavell (Human Biology Lecturer)
K.S.F.Brooke-Wavell@lboro.ac.uk
Tel: 01509 222749
RESEARCH: EXERCISE MAY INCREASE BONE DENSITY

Could hopping help stop osteoporosis?

by LYNDSEY EMMETT

It is an activity usually associated with frogs and small children.

Now Loughborough University experts believe hopping could hold the key to preventing a painful bone condition.

They want volunteers to spring into action to find out if it can help stop osteoporosis.

One in three women over the age of 50 suffers from the condition which weakens bones and leaves them susceptible to fractures.

It has already been proven that exercise can increase bone density and previous research showed jumping was particularly effective.

A recent study by Dr Katherine Brook-Warell and PhD student Christine Bailey found hopping was even better.

VOLUNTEERS

Now, they are investigating how often people would need to hop for it to have an effect.

They want 50 women between the ages of 18 and 45 to volunteer to take part in the study.

Volunteers would have to hop for two minutes every day for six months.

Christine Bailey, 23, who came up with the idea for the study, said: 'I found out when I was 18 that I had low bone density and although I don't have any problems now, it's something that could cause me problems in later life.

'I do the exercises myself and I'm hoping other women will take part too.

'Instead of waiting for it to happen, it's better to try and prevent osteoporosis by doing these exercises.' Dr Brooke-Warell, who is supervising the study said:

'The hopping volunteers will be asked to do for the study will be easy to fit into their daily routine, as they can be done at home in just a few minutes without the need for any special equipment.

'Jumping up and down puts pressure on bones and with hopping all the weight goes down onto one leg, so we will be able to make a comparison with the other leg at the end of the study.'

Findings from the research will help determine how people can improve bone strength with the minimum amount of exercise.

Louise Hart, of the National Osteoporosis Society said:

'We know weight-bearing exercise is one of the most important things you can do to improve the strength of your bones, especially during the key development years up to your late 20s, and this may be able to tell us more.'

Every three minutes someone has a fracture due to osteoporosis and an estimated three million people UK suffer from it.

Anyone interested in the project is asked to contact Christine Bailey by 01509 229129.
LIFESTYLE QUESTIONNAIRE

Participant name or number: ___________________________ Date: _____________

1. Are you currently on a specific kind of diet? (e.g. weight-loss, vegetarian etc.) YES NO
   If YES, please give details: ______________________________________________________

2. Please list any vitamin/mineral supplements you regularly take:
   ____________________________________________________________

3. Approximately how many units of alcohol do you drink per week?
   (1 unit = ½ pint beer, 1 glass wine, 1 shot spirit) __________

4. Do you smoke? YES NO
   If YES, on average how many cigarettes per day? ______

5. Does your mother/father or grandmother/father have osteoporosis? ______________________

6. Please give details of any regular or seasonal exercise you do:
<table>
<thead>
<tr>
<th>Type of exercise</th>
<th>Duration (min/hr)</th>
<th>Frequency (per week/month)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

7. How would you describe yourself compared to your peers when you were at school?
   a. Not very active/sporty (i.e. just participated in compulsory school P.E. classes) __________
   b. Average (i.e. did some after-school/lunchtime sport) __________
   c. Very active/sporty (i.e. did structured training for competitive sport out-of-school) __________

8. What is your current occupation? __________________________________________

9. Are you left-handed or right-handed? ______

10. Have you ever broken a bone? YES NO
    If YES, please give details: ______________________________________________________

11. How many children have you had? ______

12. How old were you when you had your first period? (Please be as accurate as possible)
    ______ years ______ months

13. Have you always had regular periods (10-13 cycles per year)? YES NO
    If NO, please give details: ______________________________________________________

14. Are you currently on the Pill? YES NO
    If YES, for how long? ___________________________
Please define approximately how often and how much of the following food items you usually consume.

<table>
<thead>
<tr>
<th>Food Item</th>
<th>Frequency →</th>
<th>&gt;6 times/d</th>
<th>4-6 times/d</th>
<th>2-3 times/d</th>
<th>1 time/d</th>
<th>5-6 times/wk</th>
<th>2-4 times/wk</th>
<th>1 time/wk</th>
<th>1-3 times/mo</th>
<th>Rarely or never</th>
</tr>
</thead>
<tbody>
<tr>
<td>Milk (any kind, for all uses)</td>
<td>1 glass</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hot chocolate/Horlicks</td>
<td>1 mug</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yoghurt (any kind)</td>
<td>1 pot</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hard cheese (incl for cooking)</td>
<td>1 matchbox</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Soft cheese</td>
<td>1 matchbox</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ice-cream (except sorbet)</td>
<td>2 scoops</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chocolate (except dark)</td>
<td>5 squares</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cream/custard</td>
<td>1/2 cup</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dairy-based dessert, e.g. rice pudding/mousse</td>
<td>1 serving</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cereal (any kind)</td>
<td>1/2 cup</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White bread (or similar bakery products)</td>
<td>1 slice/roll</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wholemeal bread</td>
<td>1 slice/roll</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eggs</td>
<td>1 egg</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White fish or salmon</td>
<td>1 serving</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Shrimps/prawns</td>
<td>1 serving</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Sardines</td>
<td>2 small</td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>Almonds</td>
<td>1 handful</td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Brazil nuts/Hazelnuts</td>
<td>1 handful</td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Sesame seeds</td>
<td>1 handful</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chickpeas/Kidney beans</td>
<td>1 serving</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Soya bean/Tofu</td>
<td>1 serving</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spinach</td>
<td>1 cup</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other green vegetables/salad (raw or cooked)</td>
<td>1 cup</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
**NUTRIENT SURVEY**

The following questions are about the food that you *usually* eat. Unless otherwise indicated, please give the number of *times per week* that you eat the following foods by ringing the appropriate number – e.g. White bread, if you eat white bread everyday, ring 7. If you eat the food less than once a week, but more often than once a month, ring M. If you eat the food only once a month, rarely, or never, ring R. It would be helpful if you could complete every line even if you do not eat the food item in question.

**BREAD**

<table>
<thead>
<tr>
<th>Item</th>
<th>No. of slices/rolls per day</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. White bread</td>
<td>7 6 5 4 3 2 1 M R</td>
</tr>
<tr>
<td>2. Brown bread</td>
<td>7 6 5 4 3 2 1 M R</td>
</tr>
<tr>
<td>3. Wholemeal</td>
<td>7 6 5 4 3 2 1 M R</td>
</tr>
<tr>
<td>4. Bread rolls (all types)</td>
<td>7 6 5 4 3 2 1 M R</td>
</tr>
<tr>
<td>5. Crackers/crispbread etc.</td>
<td>7 6 5 4 3 2 1 M R</td>
</tr>
</tbody>
</table>

**BREAKFAST CEREALS**

<table>
<thead>
<tr>
<th>Item</th>
<th>No. of slices/rolls per day</th>
</tr>
</thead>
<tbody>
<tr>
<td>6. Grapenuts/Ready Brek/Rice Crisples/Special K/Sugar Puffs</td>
<td>7 6 5 4 3 2 1 M R</td>
</tr>
<tr>
<td>7. Cornflakes/Muesli/Shredded Wheat/Sulatna Bran/Weetabix</td>
<td>7 6 5 4 3 2 1 M R</td>
</tr>
<tr>
<td>8. Bran Flakes/Puffed Wheat</td>
<td>7 6 5 4 3 2 1 M R</td>
</tr>
<tr>
<td>9. All bran/Wheat bran</td>
<td>7 6 5 4 3 2 1 M R</td>
</tr>
</tbody>
</table>

**FRESH FRUIT**

10. Number of apples eaten per week __________
11. Number of pears eaten per week __________
12. Number of oranges or grapefruit eaten per week __________
13. Number of bananas eaten per week __________

**VEGETABLES**

<table>
<thead>
<tr>
<th>Item</th>
<th>No. of slices/rolls per day</th>
</tr>
</thead>
<tbody>
<tr>
<td>14. Potatoes: boiled or baked</td>
<td>7 6 5 4 3 2 1 M R</td>
</tr>
<tr>
<td>15. Potatoes: instant or mashed</td>
<td>7 6 5 4 3 2 1 M R</td>
</tr>
<tr>
<td>16. Potatoes: chips/fried</td>
<td>7 6 5 4 3 2 1 M R</td>
</tr>
<tr>
<td>17. Green vegetables/salads</td>
<td>7 6 5 4 3 2 1 M R</td>
</tr>
<tr>
<td>18. Carrots</td>
<td>7 6 5 4 3 2 1 M R</td>
</tr>
<tr>
<td>19. Parsnips, Swedes, turnips, and other root vegetables</td>
<td>7 6 5 4 3 2 1 M R</td>
</tr>
<tr>
<td>20. Baked beans/lentils/butter beans</td>
<td>7 6 5 4 3 2 1 M R</td>
</tr>
<tr>
<td>21. Onions (cooked/raw/pickled)</td>
<td>7 6 5 4 3 2 1 M R</td>
</tr>
<tr>
<td>22. Garlic (cooked/raw)</td>
<td>7 6 5 4 3 2 1 M R</td>
</tr>
<tr>
<td>23. Spaghetti and other pasta</td>
<td>7 6 5 4 3 2 1 M R</td>
</tr>
<tr>
<td>24. Rice (all types except pudding rice)</td>
<td>7 6 5 4 3 2 1 M R</td>
</tr>
</tbody>
</table>

**FATS**

25. What do you usually eat on bread?
   - Butter
   - Margarine (please specify brand): ____________________________
   Either

26. How many tubs of butter do you use on average *per month*? _______
27. How many tubs of margarine do you use on average *per month*? _______
28. How many tablespoons of cooking oil do you use on average *per week*? _______

29. How often do you use a frying pan, deep fryer, or wok with...
   - lard or dripping: 7 6 5 4 3 2 1 M R
   - cooking oil: 7 6 5 4 3 2 1 M R
MILK PRODUCTS

30. How much milk do you drink per day in tea/coffee, in milky drinks, with cereal etc.?
   None at all  <½ pint  ½-1 pint  More than 1 pint

31. How much cream do you use per week (for all uses)? _____ pints
32. How much cheese do you use per week (for all uses)? _____ grams
33. How much yoghurt do you eat per week? _____ grams

EGGS

34. Approximately how many eggs do you eat or use in cooking/baking per week? _____

MEAT

Approximately how often do you eat the following meats?

35. Beef (including minced beef)  7 6 5 4 3 2 1 M R
36. Lamb  7 6 5 4 3 2 1 M R
37. Pork/bacon/ham  7 6 5 4 3 2 1 M R
38. Veal  7 6 5 4 3 2 1 M R
39. Chicken/turkey or other poultry  7 6 5 4 3 2 1 M R
40. Tinned meat (all types)  7 6 5 4 3 2 1 M R
41. Sausages  7 6 5 4 3 2 1 M R
42. Meat pies or pasties  7 6 5 4 3 2 1 M R
43. Liver/kidney/heart or other offal  7 6 5 4 3 2 1 M R

Approximately how often do you eat the following fish?

44. White fish (cod/haddock/plaice/fish fingers, etc.)  7 6 5 4 3 2 1 M R
45. Oily fish (kippers/mackerel/tuna/sardines/salmon, etc.)  7 6 5 4 3 2 1 M R
46. Shellfish (mussels/prawns/crab, etc.)  7 6 5 4 3 2 1 M R

SUGARS & SNACKS

47. How much sugar do you use per week (for all uses)? _____ grams
   How often do you eat the following items?

48. Biscuits  7 6 5 4 3 2 1 M R
49. Sweets/jellies  7 6 5 4 3 2 1 M R
50. Ice-cream/chocolate  7 6 5 4 3 2 1 M R
51. Potato crisps  7 6 5 4 3 2 1 M R

DRINKS

Approximately how often do you take the following drinks?

52. Water  7 6 5 4 3 2 1 M R
53. Fruit juices and squashes  7 6 5 4 3 2 1 M R

Are these usually... Natural juices Squashes Fizzy drinks More than one (please ring)
54. Approximately how many cups of tea do you drink per week (all kinds)? _____ cups
   Do you take sugar with it?  YES NO If so, how many teaspoons?_____
55. Approximately how many cups of coffee do you drink per week? _____ cups
   Do you take sugar with it?  YES NO If so, how many teaspoons?_____

ALCOHOL

56. Do you take some drinks containing alcohol...
   Everyday Most days Weekends and occasionally In the week Weekends only
   Not every week Special occasions only Never
57. Which type of alcoholic drink do you normally take?
   Beer, stouts or cider  Wine  Sherries, Port  Spirits, Liqueuers
   Combination of these Other alcoholic drinks None
58. When you drink, how many would you normally have?
   Beers, stouts, cider  _____ pints
Wine
Sherries, etc.
Spirits, etc.

DIETS

59. Are you on any special diet?  NO
   Slimming diet suggested by your GP
   Slimming diet prescribed by yourself
   Diabetic diet
   Other medical diets (please specify): ______________
   Vegetarian diet
   Vegan diet

60. How many persons (both adults and children) normally eat in your household?
   No. adults (including yourself) ______
   No. children 5-16 years of age ______
   No. children 1-4 years of age ______
   No. babies <1 year of age ______

Thank you very much for your help in completing the questionnaire. Please contact us if you have any problems completing it.

Have you any comments particularly about the dietary questionnaire that you think may be helpful?

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Feedback Questionnaire - 6 months

Participant name: __________________ Date: ____________

Hopping frequency: _____ x per week Hopping leg: ______

Read the following statements and circle the numbered response that best expresses how you feel according to the rating scale below. Please be honest!

1 = Very strongly agree
2 = Agree
3 = Indifferent
4 = Disagree
5 = Strongly disagree

1. I feel that I am hopping higher now compared to at the start of the study. 1 2 3 4 5

2. My hopping leg feels much stronger now compared to my non-hopping leg. 1 2 3 4 5

3. My balance whilst hopping is better now compared to at the start of the study. 1 2 3 4 5

4. I experienced muscle soreness during the past 3 months. Please give details: ____________________________________________________________ 1 2 3 4 5

5. I experienced injury during the past 3 months. Please give details: ____________________________________________________________ 1 2 3 4 5

6. I think I was a good participant in this study. If not, why not? ____________________________________________________________ 1 2 3 4 5

7. Doing the hopping became more of a chore as time went on. 1 2 3 4 5

8. I would continue hopping if the study went on for longer. 1 2 3 4 5

9. Taking part in this study has improved my knowledge about bone health. 1 2 3 4 5

10. I think I will now try to do more physical activities that are good for my bones. 1 2 3 4 5

11. I would choose to do this study again 1 2 3 4 5

Any other comments?

________________________________________________________________________________________________________________________________________________________________
## TRAINING LOG: WEEKS 1-12

**Name:**

**Frequency/week:**

**Hopping leg:**

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<th>Weekly total</th>
<th>Comments (i.e. reasons for missed sessions, discomfort? etc.)</th>
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Hopping routine to be done barefoot on a hard surface *as high and as fast as possible*:

1. 10 vertical hops
2. 10 clockwise hops
3. 10 anti-clockwise hops
4. 10 torso twisting hops
5. 10 vertical hops

= 50 hops in total