Brynhild Askvik

Effects of exercise in elderly women with osteopenia or osteoporosis

A systematic review of the effects of exercise on; bone mineral density, balance and quality of life in elderly women with osteopenia or osteoporosis

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Abstract

Background: Exercise for persons suffering from osteoporosis is widely known to have positive effects. The type of exercises that influences; a) Bone mineral density (BMD); b) Balance; and c) Quality of life (QOL) is still questionable.

Objectives: To determine the effects of different exercise types on; a) BMD; b) Balance; and c) QOL in osteoporotic elderly women.

Search method: PubMed; Cochrane Library; OvidMEDLINE; and EMBASE (01.01.2000-25.01.2010); and reference list of articles.

Selection criteria: Randomized controlled trials comparing exercise and control groups and/ or comparing different types of exercise. Criteria for the subjects in the selected studies were women aged 65-85 diagnosed with osteopenia or osteoporosis (using the World Health Organization (WHO) definitions).

Main results: Thirteen studies involving 553 subjects were included. Two studies, involving 258 subjects, investigated the effects of exercise on BMD. No significant increase in BMD was found in any exercise type. Ten studies, involving 553 subjects, investigated the effects of exercise on balance. Improvement was found in; weight bearing exercise; resistance exercise; osteoporosis specific exercise; and balance exercise. Two studies, involving 178 subjects, investigated the effects of exercise on QOL. Resistance exercise and weight bearing exercise improved QOL. No improvement was found in osteoporosis specific exercise.

Conclusions: None of the exercise types showed increase in BMD in elderly women with low bone mass. Resistance exercise; weight bearing exercise; osteoporosis specific exercise; and balance exercise improve balance. Resistance exercise; and weight bearing exercise improve QOL.

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Table of context

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Abbreviations

BMD = Bone Mineral Density

CB&M = Community Balance and Mobility scale

CDP = Computerised Dynamic Posturography

CTSI = Clinical Test of Sensory Interaction

DXA = Dual-energy X-ray Absorptiometry

ECPP = Equitest Computerised Postugraphy Platform

Kg = Kilo

pQCT = peripheral Quantitative Computed Tomography

pDXA = peripheral Dual-energy X-ray Absorptiometry

QCT = Quantitative Computed Tomography

QOL = Quality of Life

QUALEFFO = The Qualitative of Life questionnaire of the European Foundation for Osteoporosis

P = Probability

RCT = Randomized Controlled Trial

SD = Standard Deviation

WHO = World Health Organization

1RM = 1 Repetition Maximum

1 Introduction

The objective of this study is to determine the effect of exercise on; a) Bone mineral density (BMD); b) Balance; and c) Quality of life (QOL) in elderly women with low bone mineral density. In a European country (Switzerland) in 2000, osteoporosis was ranked as number one for women, and number two for men among other common diseases (Lippuner et al., 2005). Without effective intervention, demographic trends alone will result in increased prevalence of low bone mass and increased number of fractures (Moskilde, 2000).

Almost half of nursing home admissions are due to falls and postural instability, and 80% of elderly persons over 80 years would rather be dead than suffer the loss of independence that a hip fracture and the following nursing home stay may bring (Salkeld et al, 2000). In the United Kingdom one in two women, and one in five men will suffer an osteoporotic fracture after the age of 50 (van Staa et al., 2001). The annual cost of all osteoporotic fractures in Europe is estimated to € 25 billion (Melton et al., 2003). Every 30 second someone in the European Union get a fracture as a result of osteoporosis, and a three-fold rise in the number of worldwide hip fractures is expected in the middle of this century. From 1,7 million in 1990 to 6,3 million by 2050 (www.who.int, a). The rise in prevalence of hip fractures seems to go above the expected rise in number of old people (Grimley-Evans et al., 1997; Kannus et al., 1999). In Finland the number of hip fractures increased with 70% over a ten years period (from 1992 to 2002) (Loonrose et al., 2006).

BMD is the most common indicator for bone strength, and is expressed in g/cm^2 or g/cm^3. Across lifetime BMD changes, and in elderly the density normally declines (Fogelman & Blake, 2000; Moskilde, 2000). Imbalance is an important risk factor for falls in person with low bone mass (Lord et al., 1994; 1991; Nguyen et al., 1993). QOL in this study covers selfreported; pain; physical function; leisure/ social life; general health perception; and mental function.

Research has shown that exercise can improve or preserve BMD in postmenopausal women (Nelson et al., 1994; Snow et al., 2000; Kemmler et al., 2004; Beck & Marcus, 1999); and reduce the prevalence of falls in the elderly population (Buchner et al., 1997; Campbell et al., 1997; Day et al., 2002). QOL increases with enhanced physical function in elderly (Wood et al., 1999).

This systematic review includes thirteen randomized controlled trials (RCT) involving 553 subjects. Pre made including and excluding criteria has been made for objectivity. A database search has been done in following databases; PubMed; Cochrane Library; OvidMEDLINE; and EMBASE (01.01.2000-25.01.2010). In addition, reference list of relevant articles have been searched.

The included studies are analysed by a methodological quality tool, and only significant results are considered in the conclusion of the thesis.

The thesis is build up as follows:

- Part 2 clarifies the variables; BMD, balance and QOL, and describes how the variables are measured in the analysed studies.
- Part 3 is the theory, with information about the population group, and how physical activity influence; a) BMD; b) Balance; and c) QOL. This part also presents previous research reviews done on the effect of exercise.
- Part 4 goes in detail of the problem and presents the hypotheses.
- Part 5 describes the methodological choices done in the project.
- Part 6 represents the results.
- Part 7 includes a discussion of the results in relation to previous studies, and quality and details of the studies.
- Part 8 consists of the conclusions and suggestions to further studies.

Part 2 and 3 have got much space, this is due to the many details that should be available for the reader.

2 Clarifications and measurement methods

This part will clarify terms used in the thesis. In addition, the measurement methods used in the included studies are described here.

2.1 Bone health

Bone is a living tissue throughout life. The bone tissue builds up by osteoblast cells and breaks down by osteoclast cells. In young people new bone is formed at a higher rate than the resorption. Therefore, the bone mass will increase until the peak around 30 years. Women have a peak bone mass about 10-30% below that of a man (Moskilde, 2000; Spirduso, 2005a). From the peak, a loss of 0% -1% per year occurs in both women and men. Bone loss in women increases to 2-6% per year at menopause and continuous 5-10 years (Spirduso et al., 2005a; McArdle, 2004). One third to one half of the bone mineral density (BMD) gets lost during this period. The increased loss as a result of the menopause is due to hormonal changes, especially the decrease in estrogen (Spirduso et al., 2005a). After the rapid loss of bone mass following menopause, the bone loss reduces to 0,5-1% per year (McArdle, 2004; Riggs, 2002). Men have an age-related compensatory bone size increase which is not seen in women. The increase may be due to mechanical loading (Moskilde, 2000).

Bone strength is the product of BMD and bone quality. Only BMD is used as the measure in this review. BMD is expressed as grams per area or volume; while bone quality includes factors like turnover, architecture, mineralization, and damage accumulation (Comacho, 2007b).

From the 8th decade the bone loss increases in both women and men. The reason is not well understood. Possible explanations could be; changes in calcium regulation hormons; decreased perfusion on bone tissue; changes in the properties of bone mineral material; and a decrease in the number and metabolic activity of the cells that produce bone (Spirduso et al., 2005a).

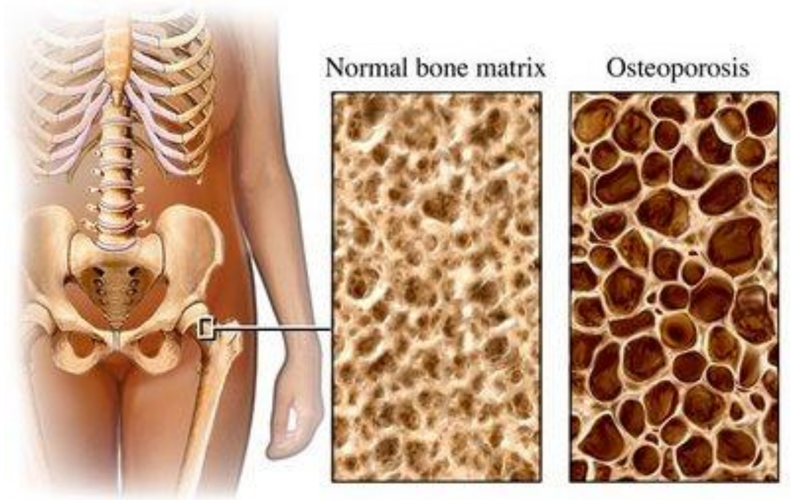

Figure 2.1.1: Normal bone and osteoporotic bone (worldclasswellness.com/bh1.php).

There are several definitions of osteoporosis. In this study the definition recommended by the WHO is used. The definition use BMD to state the disease. BMD measurements are expressed in standard deviation (SD) units called T-scores. The T-score result indicates the difference between the BMD in the subject and the ideal peak bone mass in a young adult. Measured BMD – young adult mean BMD / young adult SD = T-score. A

T-score ≤ -2,5 indicates osteoporosis; and a T-score between -2,5 and -1 is classified as osteopenia (www.who.int, b).

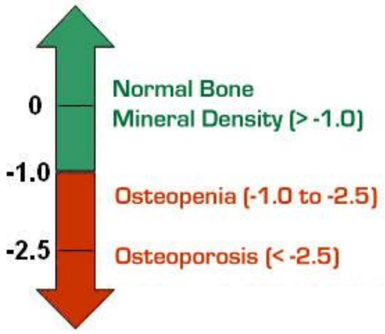

Figure 2.1.2: Scale of T-score (http://www.osteoporosis-treatment.biz/).

2.1.1 Methods to measure bone mineral density

The measure of bone mass that are most often reported in studies is BMD. BMD is believed to account for about 70% of bone strength (Spirduso et al., 2005a).

There are several ways to measure BMD. The most widely used method is Dual–energy x-ray absorptiometry (DXA). This method has high precision, short scan times and stable calibration in clinical use. For the peripheral skeleton there are special DXA devices; peripheral DXA (pDXA).

Another device that measure the BMD is Quantitative computed tomography (QCT). QCT has the advantage of determining the true 3-dimensional bone density (mg/ cm^3) compared with the 2-dimensional areal density measured by DXA. A disadvantage with this device is the high cost. Like with the DXA, there are QCT devices for the peripheral skeleton (pQCT). The advantages of the peripheral devices are; 1) they can separate the trabecular and the cortical bone; and 2) they report volumetric density (Fogelman & Blake, 2000).

A third device is quantitative ultrasound equipment. It measures the peripheral skeleton. This device has relatively poor precision and is therefore not suitable for measuring response to treatment in patients (Fogelman & Blake, 2000).

2.2 Balance

There are three main systems that contribute to the ability to maintain balance in standing and moving movements. The systems include; the sensory systems; the motor system; and the cognitive system.

The sensory systems (vision, somatosensory, and vestibular) give us information from our own actions and from the environment. We use the sensory systems when we do goal-directed action planning as well as automatic adjustments to maintain a given position or respond rapidly to a change. In addition, the pathways and structures in the nervous system that comprise the motor system are critical for action.

The motor system acts when the sensory information reaches the muscles. When the nervous systems constrain groups of muscles throughout the body to act together, action is accomplished.

The cognitive system makes us able to interpret the incoming sensations and plan the motor response. This system (including the processes of attention, memory storage, and intelligence) gives us the ability to anticipate and adopt our actions in response to changes (task demands or the environment) (Spirduso et al., 2005b).

When multiple systems fall below a minimum threshold of function, the effect will in most cases change balance ability. The changes occurring with ageing in the three systems (sensory, motor, and cognitive systems) compromises the performance of many complex movements that require speed, accuracy, balance, strength, and coordination (Spirduso et al, 2005b).

Those with low BMD seem to have different balance control strategies compared to those with normal BMD. Those with low BMD use hip strategy (bending forward in the hip) while those with normal BMD use ankle strategy (use the ankle junction) to maintain balance (Lynn et al., 1997).

Thoracic kyphosis (a spinal deformity) is common in persons with low BMD. The high prevalence of thoracic kyphosis in this group is due to spinal fractures that make the spine curve forward. Spinal fractures are often painless and therefore hard to discover (Taylor et al., 2008). Thoracic kyphosis may change the posture and influence balance.

2.2.1 Methods to measure balance

Several balance tests has been used in the studies. **Feil! Fant ikke referansekilden.** describes the test procedures used to measure balance.

Table 2.2.1. Description of the balance tests in the included studies.

Test	**Description**
Equitest compute-rised postugraphy platform	The instrument provides numerous measures of sway (Carter et al., 2001)
Clinical test of sensory Interaction	Consists of 6 sensory conditions: 1. Eyes open and firm surface. 2. Eyes closed and firm surface. 3. Eyes open, visual conflict and firm surface. 4. Eyes open and unsteable surface. 5. Eyes closed and unsteable surface. 6. Eyes open, visual conflict and unsteable surface. When the subject cannot stay at least 30 seconds in each of the 6 conditions static balance is evaluated as altered (Maduraeira, 2007)
One leg balance test	Stand on one leg. Three times on each leg. Mean time of each leg is used in the study. (Vaillant et al., 2006)
The timed up and go test	Procedure: Rise from a standard armchair, walk to a line on the floor (3 m away), turn, return, and sit down again (Podsiadlo, 1991). Timed used on the test is the result of the test (Vaillant et al., 2006).
Figure of eight running test	Procedure: run in a figure of eight around two poles placed 10 m apart (Heionen et al., 1996).

Test	Description
Step test	Procedure: stay in front of a step (7,5 cm high) without hand support. Whilst standing on one leg: place the other foot completely on to the step and return the foot as many times as possible over a 15 sec period. The test is repeated on the other leg. Total number of steps are recorded on each leg and is the results of the test (Hill et al., 1996; Devereux et al., 2005)
Community balance and mobility scale	12 items that challenge balance and mobility. 0-5 points per item. Maximal score 85. (Liu-Ambrose et al., 2004b)
The Berg balance test	14 items challenging for balance. 0-4 points per item. Maximal score 56. (Bogle Thorbahn et al., 1996; Berg et al., 1989; Swanenburg et al., 2007)
Accu sway plus system	The instrument provides centre of pressure coordinates. Measures medial-lateral and anterior-posterior sway (Swanenburg et al., 2007)
Computerised dynamic posturography	The instrument measures anterior-posterior sway. 100 = no sway. 0 = a fall. 6 conditions: Accurate proprioception: 1. Normal vision 2. Eyes closed 3. Inaccurate vision Inaccurate proprioception: 4. Normal vision 5. Eyes closed 6. Inaccurate vision (Sinaki & Lynn, 2002)

2.3 Quality of life

Quality of life (QOL) consist of several physical (e.g. physical function) and psychological (e.g. mental health) components. Health related quality of life factors are those that are influenced by health and physical function. In this study quality of life refers to health related quality of life factors. Other important factors of quality of life, such as living environment, economic status, availability of resources and climate are not affected much by exercise and physical function (Spirduso et al., 2005c). Thus, those factors are not included when quality of life is measured in the study.

2.3.1 Methods to measure quality of life

There are many ways to measure QOL (Spirduso et al., 2005c). A health related quality of life questionnaire specified for persons with low bone mass has been developed to measure quality of life in this specific group. Common factors that influence quality of life in persons with low BMD are measured (Lips et al., 1996). The questionnaire consist of 48 questions organized in five domains; pain; physical function; leisure/ social life; general health perception; and mental function (Liu-Ambrose et al., 2005). The score of the questionnaire range in a scale between 0 and 100. In a multi center study the questionnaire was validated showing adequate test-retest reliability and internal consistency (Oleksik et al., 2000).

3 Theory

3.1 Bone mineral density and bone metabolism in elderly women

The bone mineral density (BMD) in elderly individuals depends on the peak BMD they had around the age of 30; and the bone loss from the peak until current time (Moskilde, 2000; Downey & Siegel, 2006).

The bone loss from the peak to the current time is influenced by current age; gender; and other genetic and environmental factors (Riggs et al., Downey & Siegel, 2006; McArdle et al., 2004).

Osteoporosis can be categorized into either primary osteoporosis or secondary osteoporosis. Primary osteoporosis is due to age-related changes; decrease in sex hormone; or both (Downey & Siegel, 2006). There are genetic variations between individuals. 60-80% of the chance to develop osteoporosis is linked to genetic factors, while 20-40% remains lifestyle related (McArdle, 2004). Secondary osteoporosis is caused by a chronic condition that causes acceleration of bone loss (Downey & Siegel, 2006).

3.1.1 Peak bone mass

50-80% of the peak bone mass in women is determined by their genetic predisposition (Jin & Ralston, 2005; Marcus, 2001). Other factors that contribute to the overall peak bone mass product are; calcium intake; vitamin D; activity level; body weight; illnesses; and delayed puberty

(Comacho, 2007c). As previous mentioned, women have 10-30% lower peak bone mass compared to men (Moskilde, 2000; Spirduso, 2005a).

3.1.2 Age-related changes

Age-related changes enhance bone turnover from the age of 30. With aging it occur an increase in bone resorption and a decrease in bone formation (Comacho, 2007c). Two of the main factors leading to the increase in bone resorption are; decline in kidney function and decreased estrogen. Decline in kidney function leads to decreased hydroxylation of vitamin D; secondary hyperparathyroidism; and decrease in gut calcium absorption. Factors leading to decrease in bone formation are; decreased estrogen; decreased physical activity and; decreased growth hormone (Riggs et al, 2002).
The age related changes leads to a higher bone resorption than bone formation and cause bone loss (Comacho, 2007c).

In addition to the BMD, there are several factors that determine the bone strength; cortical thickness; bone size and architecture. Also those factors are affected by the age-related changes in the bone metabolism (Moskilde, 2000). In elderly with low BMD it takes at least nine to twelve months before bone measures may alter due to exercise (Biddle & Mutrie, 2008).

As previous mentioned, an increase in bone loss from the 8th decade in both women and men has been observed (Spirduso, 2005a).

3.1.3 Gender differences

Gender differences in bone metabolism include; a lower peak bone mass in women; hormonal differences; and an age related compensatory increase in bone size seen in men (Moskilde, 2000).

As mentioned previously, women have 10-30% lower peak bone mass than men (Spirduso, 2005a). This is mainly because of a larger cross-sectional area (size) in men compared to women, while the peak bone density is the same in both genders (Moskilde, 2000).

Due to the rapid bone loss occurring after the menopause, women loose more bone mass than men (McArdle et al., 2004). The rapid loss is caused by the reduction of estrogen that follows menopause (Downey & Siegel, 2006). Bone loss in men is also affected by estrogen deficiency, and seems to play a bigger role than testosterone in bone turnover (Khosla et al., 2002).

There is a compensatory age related increase in cross-sectional area seen in men, but not in women. It has been suggested that this increase is due to mechanical loading (Ruff & Hayes, 1988).

3.1.4 Other factors influencing bone mineral density and bone metabolism

Secondary osteoporosis; a chronic conditions that can cause bone loss may be due to; excess thyroxin; malignancies; gastrointestinal diseases; renal failure; and medications (Downey & Siegel, 2006).

The use of glucocorticoids is the most common cause of secondary osteoporosis; they increase bone resorption and decrease bone formation. In addition to the direct influence on bone metabolism, glucocorticoids also decrease muscle mass and muscle strength; and thus lead to decreased physical activity (Camacho, 2007c).

Other factors that contribute to bone loss are periods with immobilization or inactivity; and alcohol or tobacco use (Downey & Siegel, 2006). Immobilization seems to cause up to 40% bone loss in one year (Marcus, 2001).

Nutritional factors that have shown to affect bone metabolism are low calcium intake; high protein intake; excess sodium intake; and possible high caffeine intake (McArdle, 2004).

3.2 How bone adapt to physical activity

3.2.1 Effective mechanical loading

Load intensity verses cycle number

Load intensity seems to be much more important than cycle number in bone adaption (Lanyon, 1984; Rubin & Lanyon, 1984; Tsuzuko et al., 2001).

Studies have shown that in athletes whose activities include lifting of heavy loads show the highest bone density values compared to other athletes (Heionen et al., 1995; Robinson et al., 1995; Dickerman et al., 2000; Tsuzuku et al., 1998).

Rate of strain

In addition to the load magnitude, the rate of strain also influences the intensity of loading and thus the effect of physical activity has on bone (Marcus, 1996; Chow, 2000). “Rate of strain is a term used to describe the time over which strain develops following load application, and is roughly comparable with what is meant by *impact*.” (Marcus, 1996, p. 1139). Rate of strain has been found important in bone adaption in several studies, BMD increase more with high rate of strain compared to low rate of strain (O`Connor et al., 1982; Turner et al., 1995).

Immobilization

The negative effect of immobilization and space flight seem to be much greater than the positive effect of adding more walking to an active subject (Marcus, 1996; LeBlanc et al., 2007). Individuals who have taken part in long-duration flights in the space have shown a significant loss of regional bone mineral. 92% have lost at least 5% in minimum one skeletal site and more than 40% have experienced a loss of 10% or more at minimum one skeletal site. The lack of mechanical forces seems to cause the increased re-modeling (LeBlanc et al., 2007). Maximal one week bed rest is suggested to avoid further bone loss from immobility in elderly women (Parvez, 2004).

3.2.2 The role of cellular activity in bone adaption

Incubated cells

There are many ways mechanical load can be transducted to incubated cells, including; application of hydrostatic and shear pressures; osmotic swelling;

and stretch (Marcus, 1996). High applied strains seems to cause proliferate activity, while lower strains promote production of bone matrix proteins (Burger & Veldhuijzen, 1993).

The bone adaption to mechanical load seems to be a cellular phenomenon which involves osteocytes, osteoblasts, and bone-surface-lining cells (Marcus, 1996). The cells responsible for transducing mechanical signals into clinical mediators may not themselves experience the applied strains, but may receive the signal through strain-induced alterations in canalicular fluid flow (Reich et al., 1990; Weinbaum et al., 1994); or by generation of electrical potentials (Bassett & Becker, 1962).

Intact bone

Four steps has been outlined for the cascade which mechanical loads couple to bone adaption; mechanical sensing; biochemical coupling; cellular communication; and effector response (Turner et al., 1995).

A period of load application starts a complex series of biomechanical events in bone, and several days later there is a rise in bone forming activity (Pead et al., 1988). An increase in cellular total mRNA has been found following mechanical load (Dallas et al., 1993).

It is not completely clear how the sequence of molecular events in biochemical coupling works, but it seems to involve classical messenger molecules like cyclic nucleotides or prostaglandins (Marcus, 1996). The prostaglandin PGE_2 is rapidly and transiently released in mechanically loaded bones (Rawlinson et al., 1991).

Cellular communication is needed between signal-sensing cells and effector cells to proliferate or to alter their production of bone matrix. This communication may go through; release of grow factors or other mediators into the canalicular fluid system; or via direct cellular contacts (Marcus, 1996).

A broad range of molecules are involved in the effector responses, including; genes for cellular proliferation; genes for type I collagen, osteocalcin and osteopantin; and upregulation of mechanosensitive ion channels in osteoblast-like cells (Davidson et al., 1990; Duncan & Hruska, 1994).

The described mechanisms so far has been focusing on bone formation, but there has also been reported that mechanical load result in decreased bone resorbing activity (Klein-Nulend et al., 1990; Hillan & Skerry, 1995).

Bone adaption and electric fields

The role of electric fields in mechanical bone adaption was introduced by Bassett & Becker (1962). Bone loss due to denervation is prevented by electrical stimulation (Brighton et al., 1985); and electrical pulses also seem to increase bone formation (Rubin et al., 1989).

It has been proposed that normal functional activity, with strains arising from the ground reaction forces and muscle fiber resonance, provide the signal characteristics to which bone cells respond optimally (McLoad & Rubin, 1990).

3.2.3 Exercise recommendations to increase bone mineral density

Based on a review about osteoporosis and exercise, Sheth (1999) recommend progressive resistance training with several slow repetitions at 70-80% of one repetition maximum (1RM). He suggest that the exercise should be performed 30 minutes at least three times a week for at least one year to see an increase; and that 1RM should be adjusted monthly and that all large muscle groups should be involved in the exercise.

Turner & Robling (2003) have calculated an “osteogenic index” for exercise. The foundation of this assessment is; load applied on the bone during the training session (peak magnitude of the magnitude multiplied with the loading frequency); and the time between the exercise bouts. The time between the exercise bouts is included in the model due to a relation between the length of rest periods and load-induced bone formation; exercise with long (8 hours) rest periods enhance bone formation more than shorter rest periods (0-4 hours) in younger healthy individuals. Only after 20 cycles bone has lost more than 95% of its mechanosensitivity. Thus, Turner & Robling (2003) suggest that short intense exercise bouts frequently (e.g. 5 times per week) are more effective than longer exercise bouts less frequently (e.g. 2 times per week) to maintain and increase bone mass.

3.3 Balance

3.3.1 Age-related changes

Age-related declines are seen in all of the three systems that contribute to balance (the sensory systems; the motor system; and the cognitive system) (Spirduso et al., 2005).

Changes in the sensory systems occurs in; vision; somatosensation system; and vestibular system. Vision reduction as reduced acuity, contrast sensitivity, and depth perception is seen; and there occurs a narrowing of the visual field (Spirduso et al., 2005b). In the somatosensation system there is reduced sensitivity of cutaneous reseptors, and a decline in the number of pathways innervating these reseptors (Bruce, 1980); and a decline in the number and sensitivity of joint and muscle receptors (Spirduso et al., 2005b). In the vestibular system there is a decline in the density of hair cells (Spirduso et al., 2005b), and a reduction of the vestibulo-ocluar reflex (Wolfson, 1997).

Age-related changes in the motor system include; loss of large motor neurons in the motor cortex and other area of the motor system; a decline in nerve condition velocity; and a decline in neurotransmitters (e.g. dopamine) (Spirduso et al., 2005b).

Cognitive processes which seem to influence balance include; attention; memory; and intelligence (Spirduso et al., 2005b). 10% of persons over 80 years have a cognitive impairment (Yaffe et al., 2001).

3.3.2 Osteoporosis-related changes

In individuals with low BMD, thoracic kyphosis is common (Taylor et al., 2008).This spinal deformation seems to influence balance negatively (Lynn et al., 1997). Even persons suffering from osteoporosis without thoracic kyphosis may have a reduced ability to maintain balance compared to healthy individuals. This could be due to the strategy used to maintain stability; persons with osteoporosis seem to use a hip strategy in contrast to the ankle strategy used by healthy persons. When an individual uses a hip strategy in a situation where an ankle strategy would have been more appropriate, instability may occur (Lynn et al., 1997).

3.3.3 How exercise influence balance

Falls occurs when balance fails. The most common risk factors for falls have been indentified (Rubinstein & Josephson, 2002). Some of the risk factors are not possible to change with exercise (e.g. history of falls, visual changes, age). Common risk factors associated with falls that can be influenced by exercise include; muscle weakness (Brose et al., 2003; Hagerman et al., 2000); gait deficit (Rantanen et al., 1999; Seeman et al., 1995); impaired activities of daily living (Spirduso et al, 2005d); and depression (Singh et al., 2001). The following text will first explain the relationship between muscle strength and balance. Next, theories about gait pattern and balance will be presented.

Muscle strength

Weak muscle strength in the muscles surrounding the ankle joint limit a person's ability to use the ankle strategy to prevent a fall; and weak muscles in the hip region reduce the ability to use a hip strategy to maintain balance and also influence lateral stability. It is particularly the adductor and the abductor muscle groups that control the lateral stability, which is required during walking (Spirduso et al., 2005b). Muscle strength in quadriceps and ankle dorsiflexion strength is lower in persons that often falls compared to those that seldom falls (Lord et al., 1994).

Gait pattern

Dynamic balance is influenced by age-related changes in gait pattern. Reduced gait speed is seen due to decreased stride length and leads to; reduced arm swing; reduced rotation of the hips, knees and ankles; and increased double support time (Elble, 1997). McGibbon (2003) highlight the reduction in ankle power output during the final portion of stance phase as the cause of reduced gait speed and step length, and that it seem to influence the prevalence of falls.

3.4 Quality of life

3.4.1 Quality of life domains related to low bone mineral density

Low BMD is associated with reduced QOL. This is seen in self-reported; pain; physical function; leisure/ social life; general health perception; and mental function (Lips et al, 1999).

Pain

In persons with low BMD, pain is common. Pain is present even before the occurrence of known fractures (Binachi et al., 2005). It increases with the number of fractures; and the association between fractures and pain seems to depend on the location of the fracture. More pain is reported for fractures in the lumbar region, verses the thoracic region (Oleksik et al., 2000).

Physical function

Persons with low BMD often have reduced ability to perform activities of daily living, e.g.; taking a shower; preparing meals; gardening; walking stairs; shopping; and cleaning the house (Lips et al., 1996; D`Amelio et al., 2007). Reduced physical function may be due to fractures. According to Leidig (1990), disability does not correlate well with the number of vertebral fractures. In contrast, Oleksik et al. (2005) found a correlation between physical function and the degree of spine deformity.

Leisure/ social life

Low BMD seems to reduce social activity (D`Amelio et al., 2007; Oleksis et al., 2000). A strong correlation between physical function and social activity is reported by D`Amelio et al. (2007). They present two possible explanations for this correlation. First, they suggest that social isolation could be due to physical limitations that result from fractures. Second, decreased physical function may contribute to reduced self-esteem, and thus cause poorer perception of body image, which can lead to a reduced desire to be seen in public.

General health perception

General health perception is how a person describes her/ his health condition in general. E.g. how the person considers her/ his health compared to others at the same age (Lips et al., 1997). The perception of general health is found to be worse in persons with low BMD compared to healthy individuals (Lips et al., 1999).

Mental function

Fear of falls; moods; and independency are osteoporosis-related factors which influence the mental function in persons with low BMD (Randell et al., 1998). Independency seems to be of high value in old women; any loss to live independent in the community has a significant negative effect on their QOL. Data indicate that 22% of women who lived at home before a hip fracture, moved to a nursing home within twelve months after the fracture, and only 24% were walking as well as they did before the fracture (D`Amelio et al., 2007). The mental function seems to correlate with; physical function; social activity; symptoms (e.g. pain and sleep); and tension/ anxiety in this population group (Randell et al, 1998).

3.4.2 How exercise influence quality of life

Physiological and psychological hypotheses

Although many theories about how exercise influences QOL exist, it is no considerable agreement of the working mechanisms (Morgan, 1997; Landers & Alderman, 2007).

Several hypotheses exist based on the physiological effects on QOL. They include; cardiovascular hypothesis (Biumenthal et al., 1989); monoamine hypothesis (Morgan and O`Connor, 1988); endorphins hypothesis (Hoffmann, 1997); and thermogenic hypothesis (Koltyn, 1997).

Psychosocial hypotheses that have been proposed to affect QOL are; mastery hypothesis (Bandura, 1997); social interaction and approval hypothesis (Hughes et al., 1986); and distraction hypothesis (Bahrke & Morgan, 1978). In addition there exist many psychological theories with possible explanation of the exercise effect. Those complex theories include; self-efficacy theory; optimal stimulation theory; extraversion; sensation seeking; type A behavior pattern and self-evaluative tendencies; theory of psychological reversals; and Thayer`s multidementional activation theory (Ekkekakis & Petruzzello, 1999).

Integration of the theories

La Forge (1995) reviews the possible mechanisms from an integrating view. The integrated model he present include neurobiological systems. He suggest: “The mechanism is likely an extraordinary synergy of biological transactions, including genetic, environmental, an acute and adoptive neurobiological processes. Inevitably, the final answers will emerge from similar synergy of researchers and theoreticians from exercise science, cognitive science and neurobiology.” (La Forge, 1995, p.28.)

Including psychological theories to an integrated model will probably present an even more correct picture of the underlying mechanisms related to the positive effects of exercise on QOL (Biddle & Mutrie, 2008).

3.5 Previous reviews

Some reviews have determined the effect of exercise on BMD in postmenopausal women. Kelley (1998) found that aerobic exercise helps to maintain lumbar spine in a meta-analysis of ten studies with aerobic exercise intervention. In a study of Wolff et al. (1999) both studies with pre- and postmenopausal women were included. They found a BMD increase of 0,9% per year as the overall treatment effects for the included RCTs. Bérard et al. (1997) included only studies with subjects over 50 years. A significant effect of exercise on BMD was found in the spine. In contrast, no significant effects were seen in the forearm and femoral bones.

Ernst (1998) concludes in a systematic review that exercise is effective in preventing and treating osteoporosis. Balance and well-being / pain (domains in QOL) has been investigated by some very few of the included studies, while BMD is the dominating outcome. Several researchers suggest focusing on fall preventing rather than BMD to prevent fractures (Jarvinen et al., 2008; Marcus, 2001; Skelton & Beyer, 2003). To my knowledge there exist no reviews of the exercise effects on BMD, balance and QOL in elderly women with low BMD. Thus, this systematic review will determine the effects.

4 Problem statement

This part presents the problem, specified questions that should be answered in the thesis, and the hypotheses.

Regular exercise can have positive effects on the osteoporotic body (Spirduso et al., 2005a; Moskilde, 2000). To achieve the best effects, the type of exercise is important (Taylor et al., 2008). The objective of this study is to determine the effects of different exercise types on a) Bone mineral density; b) Balance; and c) Quality of life in elderly people with low bone mass. More specified, the following four questions will be discussed:

1. Does resistance exercise improve a) Bone mineral density; b) Balance; c) Quality of life, in elderly women with low bone mineral density?
2. Does weight-bearing exercise improve a) Bone mineral density; b) Balance; c) Quality of life, in elderly women with low bone mineral density?
3. Does osteoporosis specific exercise improve a) Bone mineral density; b) Balance; c) Quality of life, in elderly women with low bone mineral density?
4. Does balance exercise improve a) Bone mineral density; b) Balance; c) Quality of life, in elderly women with low bone mineral density?

From a scientific view, the problem is relevant for the general treatment- and coping area for persons with low bone mass. Exercise is seen as a treatment option for osteoporosis and osteopenia (Camacho, 2007a).

In a society context, there are several reasons for investigating the problem. First, the elderly population increases in numbers worldwide. This group is expected to keep on increasing over the next decades (Taylor et al., 2008). In addition to the growing elderly population, the prevalence of low bone mass is increasing (Khan et al., 2001a). This means that the target group for treatment methods, as for example exercise, is growing.

Second, exercise can prevent elderly people from get frail and dependent in daily activities. Persons with low bone mineral density (BMD) are at risk of frailty (Wood et al., 1999). Frailty is a cost for the society as well as an individual strain. Thus, a systematic exercise program of the beneficial types of exercises is important to enhance independency as long as possible (Spirduso et al., 2005d).

A third point is the high risk of bone fractures in persons with low BMD. Fractures have enormous individual consequences. In addition, fractures have high economical costs for the society. The incidence of low BMD – related fractures in women is greater than the annual combined incidence of heart attack, stroke and breast cancer (Camacho, 2007b). When the risk factors for falls get reduced, the prevalence of falls gets down. Exercise can reduce some of the risk factors; e.g. balance deficit. (Heionen et al., 1996; Lord et al., 1991; 1994; Khan et al., 2001b).

The elderly population were chosen because the prevalence of low BMD increases with ageing (Taylor et al., 2008; Moskilde, 2000). Because of physiological and psychological gender differences, only one gender was chosen in the problem statement. The prevalence of low BMD is higher in women compared to men (Taylor et al., 2008; Moskilde, 2000), thus the exercise effects on women are investigated.

The problem statement includes only people with low bone mass. There are two reasons for this. First, persons with low bone mass have some contraindications (because of weak bones) that have to be considered when exercise is practiced (Taylor et al., 2008; Khan et al., 2001a). Second, it was not possible to investigate more than one population group (elderly women with low BMD), because of the time- and size limits of the thesis.

Several determinant variables have been investigated in osteoporotic elderly women. Three variables were chosen. BMD, balance and QOL were chosen because they are important variables for persons with low bone mass (Khan et al., 2001b). In addition, together they represent both the biological- and psychological area.

The problem statement is specified. First, there are sat criteria on; age; gender; variables; and condition of subjects (low BMD). Second, exercise type is specified. Frequency, intensity and duration are not specified in the problem statement. Those factors are important when effects of exercise are investigated (Spirduso et al., 2005a), but the size of the thesis makes it impossible to include all factors.

The questions are directly transformed into the following hypotheses:

1. Resistance exercise improves; a) Bone mineral density; b) Balance; and c) Quality of life, in elderly women with low bone mineral density.
2. Weight-bearing exercise improves; a) Bone mineral density; b) Balance; and c) Quality of life, in elderly women with low bone mineral density.
3. Osteoporosis specific exercise improves; a) Bone mineral density; b) Balance; and c) Quality of life, in elderly women with low bone mineral density.
4. Balance exercise improves; a) Bone mineral density; b) Balance; and c) Quality of life, in elderly women with low bone mineral density.

5 Method

In this part there is a text about the chosen method (5.1), and then a detailed description of the other methodological choices follows (5.2-5.8).

5.1 The choice of research method

The chosen method is a systematic review. “A systematic review attempts to collate all empirical evidence that fits pre-specified eligibility criteria in order to answer a specific research question” (Green et al., 2008, p. 6).

The choice of using systematic review as the research method has several reasons. First, the problem can be answered by using this method. Second, the project can be adjusted to a suitable size for a master thesis. Third, the method does not require much economically resources.

A meta-analysis is not included in this thesis. Although meta-analyses have many advantages (Glass, 1977), this type of analyses was not found suitable in this study. First, the studies included are clinically diverse and makes a meta-analysis meaningless. Second, some of the included studies are at risk of bias and a meta-analysis can thus be misleading. When facing the two reasons given, a meta-analysis can be more of a hindrance than help (Deeks et al., 2008).

When considering only the problem statement, it would have been suitable to do a RCT. But this would not be realistic to do as a master degree project.

There would have been lack of resources and it would have gone far beyond the normal size and time of a master thesis.

5.2 Methodological challenges

One of the first challenges I met in the research process was the including and the excluding of studies. Although the problem statement have some directions of what to include and exclude, this was too wide for the including process. In this early phase I made a list of what to include and exclude (Table 5.3.1).

I found it very difficult to judge the risk of bias in the included studies without using a system. What I did to solve this problem was to analyse the studies by a tool used to identify the risk of bias. The tool is suitable and suggested to use in clinical systematic reviews (Higgins et al., 2008). The risk of bias analysis is shown in Table 5.7.1.

A methodological challenge has been how to draw the conclusions from the results. This procedure should be known to the reader to make an objective evaluation possible (Thomas, 2005). My solution to this challenge was to make it clear in a separate part of the thesis (5.8), what I based the conclusions on.

5.3 Including and excluding criteria

Table 5.3.1: Including and excluding criteria.

	Including criteria	**Excluding criteria**
Year	2000-2010	Published before 2000
Design	Randomized Control Trial (RCT)	Not RCT
Subjects	Human	Animal
Gender	Women	Men or both gender
Age	65 – 85 years	Below or above 65-85 years
Bone health status	Subjects with osteoporosis or osteopenia. With or without a history of fractures.	Subjects without osteoporosis or osteopenia
Language	English	Not in English
Intervention	Studies with exercise intervention	Studies without exercise intervention
Determinant variables	Studies with at least one of the three determinant variables: A) Bone mineral density B) Balance C) Quality of Life	Studies without one of the three determinant variables: A) Bone mineral density B) Balance C) Quality of life

5.4 The search process

A database search was done in four databases; pubmed; Cochrane Library; ovidMEDLINE; and EMBASE. In addition, reference lists of articles were searched. Table 5.4.1 show the details of the database search.

Table 5.4.1: Details of the data base search

Database	**Search strategy**	**Search details, search 1**	**Search details, search 2**
PUBMED	Osteoporosis + physical activity OR Osteoporosis + exercise OR Osteoporosis + training OR low bone mass + physical activity OR low bone mass + exercise OR low bone mass + training	Search limits: Published between: 01.01.2000 – 25.04.2008 Search result: 4316 Trials meeting the including criteria: 13	Search limits: Published between: 25.04.2008-25.01.2010 Search results: 528 Trials meeting the including criteria: 0
COCHRANE LIBRARY	Osteoporosis + physical activity OR Osteoporosis + exercise OR Osteoporosis + training OR low bone mass + physical activity OR low bone mass + exercise OR low bone mass + training	Search limits: Published between: 01.01.2000 – 25.04.2008 Clinical trials Search result: 215 Trials meeting the including criteria: 13 Included articles not found in the PubMed search: 0	Search limits: Published between: 01.01.2008-25.01.2010 Clinical trials Search result: 12 Trials meeting the including criteria: 0
OvidMEDLINE	Osteoporosis + physical activity OR Osteoporosis + exercise OR Osteoporosis + training OR low bone mass + physical activity OR low bone mass + exercise OR low bone mass + training	Search limits: Published between: 01.01.2000 – 25.04.2008 Search result: 32 Trials meeting the including criteria: 6 Included trials not found in the PubMed search: 0	Search limits: Published between: 01.01.2008-25.01.2010 Search result: 2 Trials meeting the including criteria: 0
EMBASE	Osteoporosis + physical activity OR Osteoporosis + exercise OR Osteoporosis + training OR low bone mass + physical activity OR low bone mass + exercise OR low bone mass + training	Search limits: Published between: 01.01.2000 – 25.04.2008 Search result: 21 Trials meeting the including criteria: 6 Included trials not found in the PubMed search: 0	Search limits: Published between: 01.01.2008-25.01.2010 Search result: 6 Trials meeting the including criteria: 0

5.5 Selecting studies

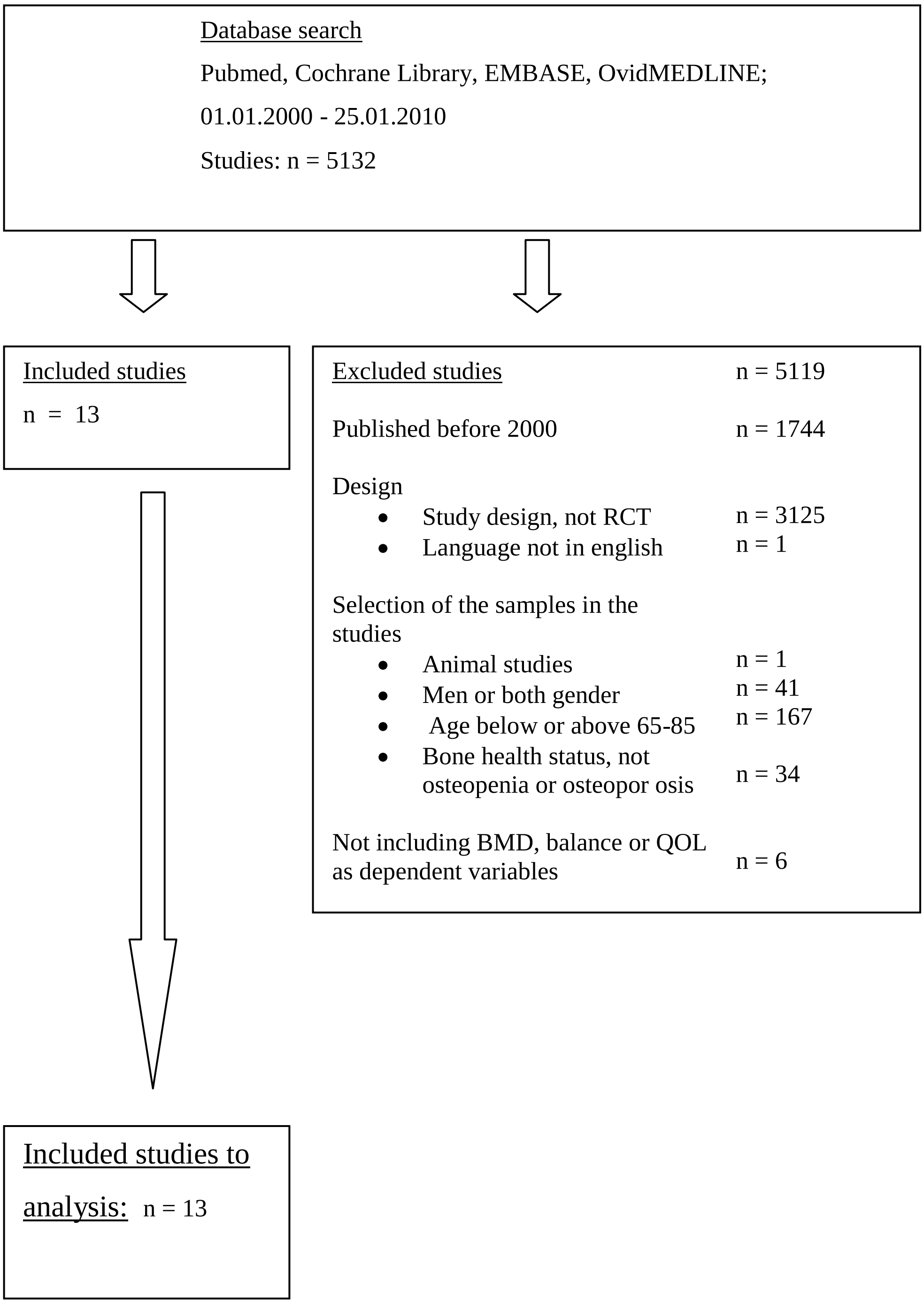

Figure 5.5.1 Flowchart of the selection process

5.6 Collecting data

The data was collected from the included studies. Table 5.6.1 show the criteria for the collected data.

Table 5.6.1: Criteria for collecting data

Test procedure:	Pre- and post test of the intervention
Determinant variables:	BMD, balance, QOL
Outcome measure priority:	Primary- and secondary outcome measures

5.7 Risk of biases

5.7.1 Risk of reporting biases

A potential bias is publication bias. Studies with positive effects may have been published more than studies with no effect. In this way the exercise intervention would be seen as more effective than it really is.

Other risk of reporting biases include time lag bias, multiple publication bias and location bias (Sterne et al., 2008).

5.7.2 Risk of methodological biases in the included studies

Table 5.7.1: Metholdological quality of the included studies

Study	Adequate sequence generation	Allocation concealment	Blind subjects for outcome	Blind assessors for subjects	Incomplete data adequately addressed	Free of selecting outcome reporting	Free of other sources of bias
Carter et al., 2001	+	+	÷	+	+	+	+
Carter et al., 2002	+	+	÷	+	+	+	+
Devereux et al., 2005	+	+	÷	÷	+	+	÷
Korpelainen et al., 2006a	+	+	÷	+	+	+	?
Korpelainen et al., 2006b	+	+	÷	+	+	+	?
Liu-Ambrose et al., 2004a	+	+	÷	+	+	+	+
Liu-Ambrose et al., 2004b	+	+	÷	+	+	+	+
Liu-Ambrose et al., 2004c	+	+	÷	?	+	+	+
Liu-Ambrose et al., 2005	+	+	÷	+	+	+	+
Madureira et al., 2006	?	?	÷	÷	+	+	?
Sinaki & Lynn, 2002	?	?	÷	+	+	+	?
Swanenburg et al., 2007	+	+	÷	÷	+	+	÷
Vaillant et al., 2005	?	?	÷	+	+	+	?

5.8 What the conclusion is based on

Objectivity is the main reason for including this part. How I arrived at the particular conclusions is described in Table 5.8.1.

Table 5.8.1: What the conclusion is based on

The conclusion is based on:	
Risk of bias:	The methodological quality of the included studies (Table 5.7.1, p.44).
Results:	Positive (P = ≤ 0.05) and negative (P = > 0.05) intervention effects (6 Results, p.46).
Size:	The size of the population groups in the included studies (Table 6.1.1, p.47)

6 Results

The first section of this part presents an overview of the included studies (6.1). Then the results are compared with the hypotheses (Table 6.1.3), and additional details about each of the included studies (6.2-6.5).

6.1 Overview of the studies

Thirteen studies involving 553 subjects met the inclusion criteria. Two had BMD as determinant variable (Liu-Ambrose et al., 2004a; and Korpelainen et al., 2006a) involving 258 subjects; ten looked at balance (Carter et al., 2001; Carter et al., 2002; Devereux et al., 2005; Korpelainen et al., 2006b; Liu-Ambrose et al., 2004b; Liu-Ambrose et al., 2004c; Madureira et al., 2006; Sinaki & Lynn, 2002; Swanenburg et al., 2007; and Vaillant et al, 2005) involving 553 subjects; and two investigated quality of life (Liu-Ambrose et al., 2005; and Carter et al., 2002) involving 178 subjects. One study (Carter et al., 2002) investigated both balance and QOL. Details of the studies and the results that are related to BMD, balance and quality of life are shown in Table 6.1.1.

The result from the studies shows that exercise can improve balance and QOL, but not BMD in elderly women with low bone mass. Table 6.1.3 shows the results in the view of the hypotheses.

Table 6.1.1: Overview of the studies included, with details and results.

(To be continuing on next page.)

Study	Subjects (n)	Age	Intervention (weeks)	Measurement	Test/ instrument used	Exercise intervention	Results
Carter et al., 2001	79	65-75	10	Balance	Figure of running 8 ECPP	Osteoporosis specific	No change in balance
Carter et al., 2002	80	65-75	20	Balance Quality of life	Figure of running 8 ECCP QUALEFFO	Osteoporosis specific	↑ dynamic balance, no change in static balance No change in quality of life
Devereux et al., 2005	50	65+	10	Balance	Steptest	Water-based balance	↑ Balance
Korpelainen et al., 2006a	160	Mean 73	130	Bone mass density	DXA pDXA	Weight-bearing	No change in BMD
Korpelainen et al., 2006b	160	Mean 73	130	Balance	Inclinometry-based method Timed ”up and go”	Weight-bearing	↑ Balance
Liu-Ambrose et al., 2004a	98	75-85	25	Bone mass density	DXA pQCT	1) Resistance 2) Agility 3) Stretch	No change in BMD
Liu-Ambrose et al., 2004b	98	75-85	25	Balance	CB&M Posture stability	1) Resistance 2) Agility 3) Stretch	↑Dynamic balance in all groups ↑ Static balance in the resistance and the agility groups, no change in the stretching group.

QUALEFFO = Quality of life questionnaire for the European Foundation of Osteoporosis. CDP = Computerized dynamic posturography.
CB&M = Community balance and mobility scale. ECPP = Equitest computerised posturography platform. CTSI = Clinical test of sensory interaction.

Table 6.1.2: Overview of the studies included, with details and results.

Liu-Ambrose et al., 2004c	98	75-85	13	Balance	Posture stability CB&M	1) Resistance 2) Agility 3) Stretch	No change in static balance in any of the groups. ↑Dynamic balance in agility group, no changes in the resistance or the stretching groups.
Liu-Ambrose et al., 2005	98	75-85	25	Quality of life	QUALEFFO	1) Resistance 2) Agility 3) Stretch	↑ Quality of life in the resistance and the agility groups, no change in the stretching group.
Madureira et al., 2006	66	65+	52	Balance	Berg balance test CTSI Timed "up and go"	Balance	↑ Balance
Sinaki & Lynn, 2002	7	70-83	4	Balance	CDP	Resistance	↑ Balance
Swanenburg et al., 2007	24	65+	12	Balance	Berg balance test Accu sway plus	Osteoporosis specific	↑ Balance
Vaillant et al., 2005	68	70+	6	Balance	Timed "up and go" One leg balance test	Dual-task, balance	No change in balance between the groups. ↑Balance from baseline to final assessment in both groups.

QUALEFFO = Quality of life questionnaire for the European Foundation of Osteoporosis. CDP = Computerized dynamic posturography.
CB&M = Community balance and mobility scale. ECPP = Equitest computerised posturography platform. CTSI = Clinical test of sensory interaction.

Table 6.1.3: The results compared to the hypotheses.

Hypothesis		
1. Resistance exercise improve	a) BMD	÷
	b) Balance	+ / ÷
	c) Quality of life	+
2. Weight bearing exercise improve	a) BMD	÷
	b) Balance	+ / ÷
	c) Quality of life	+
3. Osteoporosis specific exercise improve	a) BMD	NM
	b) Balance	+
	c) Quality of life	÷
4. Balance exercise improve	a) BMD	NM
	b) Balance	+ / ÷
	c) Quality of life	NM

+ : Significant improvement. ÷ : No significant improvement.

NR: Not measured.

6.2 Effects of resistance exercise

Liu-Ambrose et al. (2004a) found that resistance exercise improved BMD in cortical bone, but not BMD in the whole bone. The resistance exercise group increased cortical BMD with 1.4% compared to 0,4% loss in the stretching exercise group at the radial shaft (P = 0.02). The method used to measure the density in radius was pQCT. In addition to radius measurements, BMD was measured in tibia (with pQCT), total hip, femoral neck and trochanter (the three last mentioned were measured with DXA). There was no increase in BMD in the resistance group in any other bone measures. The exercise programme was done twice weekly. The resistance exercise programme was progressive. It aimed to increase muscle strength in the lower and upper extremities and the trunk. The first two weeks was used as familiarization period with the equipment and the key exercises. The intensity was initially 50-60% of 1RM, as determined at week two, with two sets of 10-15 repetitions. At week number four the intensity was progressed to 75-85% of 1RM with 6-8 repetitions (two sets). The use of medication that influence bone metabolism was not an excluding criteria.

Although the exercise program did not increase BMD, the same resistance intervention increased balance compared to the stretching exercise group ($P \leq 0,05$) measured by postural sway (Liu-Ambrose et al. 2004b). No changes were found in the CB&M between the groups. The resistance group improved the score in the CB&M significantly over time.

Liu-Ambrose et al. (2004c) found no improvement in balance after resistance exercise intervention. The intervention is previous described (Liu-Ambrose et al., 2004a). This is a study based on the same data material as in the Liu-Ambrose et al., 2004a and 2004b. The difference from those studies is the length of the intervention. This study reports the findings after 13 weeks, while the other studies report the findings after 25 weeks.

Sinaki & Lynn (2002) showed that resistance training with a posture training support was more effective to improve balance than only resistance training in women with kyphotic posture. The subjects were divided into three groups; 1; resistance exercise in subjects with deficit balance; 2; resistance exercise + posture training support in subjects with normal balance; 3; resistance exercise + posture training support in subjects with deficit balance. The results showed a significant time-group interaction between group 3 and 1 (greater improvement in balance in group 3); and between group 3 and 2 (greater improvement in balance in group 3). The resistance exercise consisted of back extensor strengthening. Posture training support was a 2-pound (ca. 1 kg) weighted kypho-orthosis and should be worn as a backpack daily for two hours during ambulatory activities.

Quality of life was improved in the resistance exercise group in a study done by Liu-Ambrose et al. (2005). The improvement, 10% ($P < 0,05$), was within the group at trial completion. Description of the intervention is described elsewhere (see Liu-Ambrose et al., 2004a).

6.3 Effects of weight-bearing exercise

Korpelainen et al.(2006a) found no increase in BMD in women that went through a weight-bearing exercise program. Bone measurements were taken at the femoral neck, trochanter and total hip. BMD was measured by DXA, pDXA and ultrasound. The exercise programme consisted of jumping and balance exercises, including walking; knee bends; leg lifts; heel rises and drops; dancing; stamping; stair climbing; and stepping up and down from benches. Use of medications that affect bone was an excluding criteria to participate in the study.

Agility exercise increased BMD of the cortical bone at the tibial shaft compared to the stretching group, the improvement of BMD in the whole bone were not significant. An increase of 0,4% versus a loss of 0,4% ($P = 0,03$) was found (Liu-Ambrose et al., 2004b). The method used to measure the density in tibia was pQCT. In addition to tibia measurements, BMD was measured in radius (with pQCT), total hip, femoral neck and trochanter (the three last mentioned were measured with DXA). There was no increase in BMD in the agility exercise group in any other bone measures. The exercise programme was done twice weekly. The agility exercise program aimed to challenge coordination, balance and psychomotoric performance (reaction time). To achieve the aim there were used ball games, relay races, dance movements and obstacle courses. The participants were given hip protectors for safety.

Also balance, measured by postural sway measurements, improved in agility exercise group measured by posture stability ($P < 0,05$) (Liu-Ambrose et al. 2004b). No changes in balance measured by the Community balance and mobility scale.

No improvements were reported in balance (CB&M) agility exercise intervention (Liu-Ambrose et al. 2004c). No improvement is shown in postural sway. The intervention is previous described (Liu-Ambrose et al., 2004a).

Weight bearing exercise improved balance in a study by Korpelainen et al. (2006b). Both the Inclinometry-based measuring method (body sway) and the Timed up and go test showed a time-group interaction of P < 0,001. The exercise intervention is described elsewhere (see Korpelainen et al., 2006a).

Quality of life was improved in the agility exercise group in a study done by Liu-Ambrose et al. (2005). 13 % improvement (P < 0,05) was found within the group at trial completion. Description of the intervention is described elsewhere (see Liu-Ambrose et al., 2004a).

6.4 Effects of osteoporosis specific exercise

After osteoporosis specific exercise no improvement was found in any balance measures by Carter et al. (2001). The exercise programme consisted of osteofit classes, which is a community-based programme for people with osteoporosis. It aims to reduce risk of falling, improve functional ability and enhance quality of life. Twice weekly the participants followed the programme that targets posture, balance, gait, coordination, and hip and trunk stability. The main part of the programme takes 40 minutes and consists of 8-16 resistance and stretching exercises with the aim to combat medially rotated shoulders, thoracic kyphosis and loss of lumbar lordosis. For the exercises there were used elastic bands and small free weights (2-5 lbs/ 1-2 kg).

Carter et al. (2002) found an improvement in dynamic balance after osteoporosis specific exercise intervention. The intervention group showed a 4, 9 % (P = 0,044) greater improvement in dynamic balance than the control group. The same subjects as in the previous mentioned study by Carter et al. (2001) are described in this study. No change was found in static balance. This study reports the results after 20 weeks, while in the Carter et al. study (2001) they reported the results after 10 weeks.

An intervention of osteoporosis specific exercise improved balance in independent living elderly women (Swanenburg et al., 2007). The intervention group had a significant greater improvement in both balance tests in the time-group interaction. The aim of the exercise programme was to improve balance abilities and reduce the risk of falling. There were three sessions per week, with duration of 70 minutes each time. Two of the three sessions consisted of progressive resistance exercise, and individual exercises that focused on the improvement of coordination, balance and endurance. The last session consisted of a group exercise programme that focused on balance exercises and games.

Carter et al. (2002) found no improvement in quality of life after 20 weeks with osteoporosis specific exercise. The intervention is described elsewhere (see Carter et al. 2001).

6.5 Effects of balance exercise

Madureira et al. (2007) found improved balance in subjects who followed a balance exercise program. In all the three balance tests in the trial, the intervention group improved balance significantly ($P < 0{,}001$) compared to the control (time-group interaction). The intervention consisted of various exercises that were aimed to challenge both static- and functional balance. After 15 minutes warm up, balance was challenged in dynamic and static positions for a period of 30 minutes. This part consisted of tandem walking, walking on the tips of the toe and on the heels, walking sideways, walking while raising the leg and the contra-lateral arm, standing on one leg, and standing in the tandem position, while gradually increasing the time of performance in the two static positions (standing on one leg and standing in the tandem position). In addition to the supervised balance exercise programme, the participants were asked to do the same exercises at home at least three times a week for 30 minutes.

Devereux et al. (2005) found an improvement ($P = 0{,}02$) in balance in the exercise group compared to the control group when they investigated the effect of water based balance exercise. Twice weekly the participants exercised. The water based exercise programme consisted of warm-up, stretching, aerobic, Tai Chi, resistance, posture, gait, vestibular, proprioception, and balance activities. The activities undertaken aimed to increase dorsiflexion, knee flexion, hip extension, and stride length; improve ankle proprioception, trunk stability, contra-lateral coordination, and stimulate righting reactions and the vestibular system.

In a study investigating the effect of dual-task verses singel-task, Vaillant et al. (2005) found no difference in balance between the groups. Balance was improved in both groups over time ($P < 0,05$), showed in within the groups measurements (comparing baseline to completion assessments). The exercise was done twice weekly. The intervention for both groups included sensory awareness exercises (messaging the soles of the feet, self-mobilization the feet); muscle strengthening exercises; proprioceptive awareness exercises for the lower limbs, trunk, and cervical spine; stretching exercises for the lower limb muscles; coordination exercises; balance and agility (ball games) exercises; functional exercises (walking forward, backward, and sideways); and exercises to minimize the adverse consequences of falls (getting up from the floor). In addition to the supervised exercise sessions, the participants got a home-exercise programme that included games to develop upper and lower limb coordination, balance exercises, and messaging the feet with a ball. The dual-task group did cognitive tasks (counting out load upward or downward, in twos (e.g. 2-4-6-8 etc.), threes, or fives; reciting poems; and saying lists of objects or places. The background of the study was that falls in elderly persons often occur when several tasks are done at the same time.

7 Discussion

7.1 Discussion of the effect of resistance exercise

Hypthesis 1a) “Resistance exercise improves bone mineral density in elderly women with low bone mass” is not strengthened by the results. There are no significant improvements in BMD in the included studies. Even though there are no significant improvements at any total bone measurements, there is significant improvement in cortical bone in one study.

In the elderly population the cortical bone seem to dominate, while the trabecular bone dominates in the young individuals. This is due to a faster decline in trabecular bone than cortical bone (Cann, 1988). The capacity of the cortical bone is believed to account for 25-30% of the total load-bearing capacity in young individuals (20-40 years); 70-80% in the elderly (70-80 years); and as much as 80-90% in osteoporotic persons (Moskilde, 2000). This may indicate that cortical BMD is more important in the elderly population compared to the young, and even more important in the osteoporotic population.

Although a significant increase is found in the cortical bone, the increase is not large enough to have a significant effect on fracture risk (Miller, 2007).

Although only one of the included studies (Liu-Ambrose et al., 2004a) has investigated the effect of resistance exercise on BMD, the methodical quality of this study is good (Table 5.7.1, p 44) and the study includes a high number of subjects (Table 6.1.1, p 47).

An increased cortical BMD is found in only one bone of the body, the radius. It may be that the intervention was too short to show an increase in other bones. The intervention time was 25 weeks, and the time of bone formation is 4-6 months. The formation time is even longer in aged subjects (Spirduso, 2005a), so the intervention time could have been too short to see an effect of the exercise in any other bones. Load, progression regiments and duration of each exercise session was as recommended, while an exercise frequency of two per week may be too low (3.2.3, p 25).

One additional point is the precession of the devices. As mentioned, the ultrasound equipment has relatively poor precession and is thus not suitable for measuring response to treatment in patients (2.1, p 10).
Second, the DXA results may be underestimating the effects of mechanical loading on bone compared to devices used on the peripheral skeleton (i.e. pDXA or pQCT) (Järvinen et al., 1999). The significant BMD improvement in the study is measured by pQCT (Table 6.1.1, p 47). Thus, the DXA measures in the study may have underestimated the effect of the intervention on BMD.

Although BMD is believed to account for most of the bone strength (2.1), the exact role of BMD in bone strength has never been determined

(Moskilde, 2000). During normal ageing there is a 70-80% decline in vertebral bone strength, while the accompanying decline in BMD is 35-45% (Moskilde, 2000). This may indicate that the decline in BMD is just one part of the total decline in bone strength.

Hypothesis 1b) "Resistance exercise improves balance in elderly women with low bone mass" is strengthened by the results of the included studies.

The time of the intervention may influence the results. Two studies with the same intervention indicate no change in postural sway (a balance test) after 13 weeks, while a significant increase is shown after 25 weeks (Table 6.1.1, p 47). Thus, it may be that 13 weeks is too short time to improve balance significantly, although the results indicate a positive direction for the resistance group after 13 weeks.

Even though no changes were found between the groups using the CB&M scale, the resistance exercise group improved the results in this test from baseline to the final assessment (Table 6.1.1, p 47).

Few exercise intervention studies with osteoporotic persons have used resistance exercise alone. Most of the studies combine resistance exercise with e.g. balance or/ and weight-bearing exercise. The included studies that are investigating the effect of resistance in this review have resistance exercise as the only exercise type (6.2). Thus, it is possible to see the effect of resistance exercise on e.g. balance.

Hypothesis 1c) “Resistance exercise improves quality of life in elderly women with low bone mass” seem to be strengthened by the results. One study shows a significant increase after resistance exercise intervention. Although only one of the included studies has investigated the issue, this study is of high quality (Table 5.7.1, p 44).

Even though questionnaires have limitations (Thomas et al., 2005), QUALEFFO is seen as a qualitative test to measure QOL in persons with low bone mass (Oleksik et al., 2000). A critical point about this specific questionnaire is the deficient of individualization (Liu-Ambrose et al., 2005). Although the lack of individualization, the QUALEFFO is suitable in clinical trials in postmenopausal women with low bone mass (Oleksik et al., 2000).

There are many explanations for the increased QOL results. Both psychosocial and biological theories exist. But the results in the study of Liu-Ambrose et al. (2005) may weaken some of the theories. The study shows a significant difference in QOL between the resistance group and the stretching group, although both activities were organized in groups. Thus, those results seem to weaken the social interaction- and the distraction theory as an explanation to improved QOL. The doubt about the distraction theory has been determined in a meta-analysis by Arent et al. (2000). Although the study has investigated the exercise – mood relationship in older adults, it may be the same in an exercise – QOL relationship.

The resistance exercise group reported significantly less pain (measured as one of the five QUALEFFO domains) at final assessment compared to baseline measurements. This may indicate that resistance exercise has a positive effect on pain reduction in this population, and thus is important in the increase of QOL.

7.2 Discussion of the effects of weight bearing exercise

Hypothesis 2a) “Weight bearing exercise improve bone mineral density in elderly women with low bone mass” is not strengthened by the results. Although weight-bearing exercise seems to increase cortical BMD in this population (Liu-Ambrose, 2004a), no significant increase is shown in the whole bones.

The issues about that the improvement in cortical bone is found only in one study and in one bone has already been discussed (7.1), and will thus not be further discussed here.

Although Korpelainen et al. (2006a) found no increase in BMD, the intervention group seems to maintain the BMD in the neck and the trochanter, while a decrease in BMD is seen in the control group over time.

One additional point with this study (Korpelainen et al., 2006a) is the control of exercise. Even though the intervention time (two and a half year) seem long enough for bone formation, twelve months of the intervention was done without supervised instruction. This home-based activity is difficult to control. Firstly, it may be that the subjects did not do all of the exercise they were supposed to do. Second, the activity done without instructors could have been done differently (e.g. lower intensity) from it was supposed to.

Hypothesis 2b) “Weight-bearing exercise improve balance in elderly women with low bone mass” seem to be strengthened by the results.

A lack of progression in the weight-bearing programme may influence the balance result score. Although the weight bearing exercise has a significantly higher score compared to the resistance- and stretching exercise groups in one test (CB&M) after 13 weeks (Liu-Ambrose et al., 2004c), no difference is to be seen between the groups after 25 weeks (Liu-Ambrose et al., 2004b). A possible reason for this could be a lack of progression in the weight bearing exercise program. Different factors may limit a progression. Firstly, safety must be considered. Second, it may be lack of established material of how to organize a progressive weight bearing program for this group.

Similar to resistance exercise, it seems like weight-bearing exercise requires more than 13 weeks to improve postural sway significantly (Liu-Ambrose, 2004c). After 25 weeks the postural sway results indicate a significant increase compared to stretching exercise (Liu-Ambrose, 2004b).

Hypothesis 2c) “Weight-bearing exercise improve quality of life in elderly women with low bone mass” seem to be strengthened by the results.

Compared to resistance- and stretching exercise, weight-bearing exercise seems to increase QOL most, although not significantly compared to resistance exercise (Liu-Ambrose, 2005). Speculations of the reasons for this can be pointed out. A possible reason could be an increase in physical function due to the weight-bearing exercise. The weight-bearing exercise group is the only group that report significantly improved physical function over time (from baseline measurement to final assessment) measured as one of the QUALEFFO domains. Perception of improved physical functioning is suggested to enhance feelings of mastery (and feelings of self-efficacy), which lead to increased feelings of well-being (Spirduso, 2005c).

An influencing psychological factor on QOL could be the interaction within the group. A higher interaction took place in the weight bearing exercise group compared to the other two groups (Liu-Ambrose et al., 2005). Thus, this could have influenced QOL.

7.3 Discussion of the effect of osteoporosis specific exercise

Hypothesis 3a) “Osteoporosis specific exercise improves bone mineral density in elderly women with low bone mass” has not been covered in this study because none of the included studies investigated this.

Hypothesis 3b) “Osteoporosis specific exercise improves balance in elderly women with low bone mass” may be strengthened by the results.

The intervention seems to influence the dynamic balance results. This is to be seen in two studies with the same intervention. While 10 weeks intervention does not show significant increase (Carter et al., 2001), an increase is to be seen after 20 weeks (Carter et al., 2002).

Although the result in static balance is not significant after osteoporosis specific exercise, a trend toward an increase is seen (Carter et al., 2002).

In contrast to the lack of significant results in the study of Carter et al. (2002), Swanenburg et al. (2007) found significant increase in static balance. Even though this is a small pilot study with some clear bias, it seems to support the positive effect of osteoporosis specific exercise on balance.

There are observed a possible ceiling effect (the subjects have reached the maximal score and have no chance to improve further) in some of the balance tests that are used. This may influence the results; the exercise intervention can be seen as less effective than it could have been if the subjects had not reached the ceiling of the test.

The osteoporosis specific programs may be suitable for frail elderly with low bone mass. Although the subjects in the osteoporosis specific studies (Carter et al., 2001; Carter et al., 2002; and Swanenburg et al., 2007) were relatively healthy (not very frail), the exercise program seems safe and manageable also for frail subjects.

Hypothesis 3c) “Osteoporosis specific exercise improves quality of life in elderly women with low bone mass” is not supported by the results.

Carter et al. (2002) suggest the reason for no increase in QOL in their study is because of a high baseline QOL score in their subjects. Although this seems reasonable, there is another possible explanation. An explanation related to the type of exercise. This discussion has already been taken (7.1 and 7.2), and will thus not be further discussed in this section.

7.4 Discussion of the effect of balance exercise

Hypothesis 4a) “Balance exercise improves bone mineral density in elderly women with low bone mass” is not investigated by any of the included studies, and this review is thus not able to cover this hypothesis. It was a mistake to use this hypothesis; balance exercise does not have the exercise regiment required to affect BMD.

Hypothesis 4b) "Balance exercise improves balance in elderly women with low bone mass" seem to be strengthened by the results. Although the studies with balance exercise intervention has some clear bias, they all indicate that balance exercise improve balance.

Even though the intervention time is short (4-10 weeks), the balance is increasing significantly.

The learning effect of the test (improved result second time due to experience from the first test) could be an issue in the improvement from baseline to the final assessment, but between the groups measurement will not be affected by this bias. The studies that are comparing balance exercise intervention with controls in this review have significant differences between the groups (6.5). Thus, the learning effect of the test does not influence the result.

Some of the balance exercises seem similar to the performance done in the tests. This may lead to a bias. The subject may score high in a test that are similar to the exercise intervention, while they may have a lower score in a balance test that differ from the exercise program. More than one balance test are used in the studies that are investigating the effect of balance exercise, and may reduce the bias.

Hypothesis 4c) “Balance exercise improves quality of life in elderly women with low bone mass” has not been covered by this study. This is because none of the included studies has investigated it.

8 Conclusion

8.1 Conclusion of findings

Based on these findings, it is apparent that exercise can improve balance and quality of life in elderly women with low bone mineral density (BMD). Improvements in bone mineral density are not significant; but significant site-specific improvements in cortical bone is found, and exercise seems to have the potential to maintain bone mineral density in some site-specific bones.

Table 8.1.1: Conclusion of the hypotheses

Hypothesis		Results	Conclusion
1. Resistance exercise improve	a) BMD	÷	÷
	b) Balance	+ / ÷	+
	c) Quality of life	+	+
2. Weight bearing exercise improve	a) BMD	÷	÷
	b) Balance	+ / ÷	+
	c) Quality of life	+	+
3. Osteoporosis specific exercise improve	a) BMD	NM	NM
	b) Balance	+	+
	c) Quality of life	÷	÷
4. Balance exercise improve	a) BMD	NM	NM
	b) Balance	+ / ÷	+
	c) Quality of life	NM	NM

+ : Significant improvement. ÷ : No significant improvement.

NM: Not measured in the included studies.

Some of the conclusions differ from the results (in the cases where there are both positive and negative results), in this cases the conclusion is based on additional information such as risk of bias and number of subjects.

When comparing the results of this systematic review with other reviews on the similar research questions, this review is the only to focus only on elderly with low bone mass. The results in this review are consistent with the suggestions from researchers on the area (Jarvinen et al., 2008; Marcus, 2001; Skelton & Beyer, 2003); they suggest a focus on fall prevention rather than a focus on BMD to prevent fractures. The results are also consistence with some previous reviews on postmenopausal women (Ernst, 1998; Kelley, 1998; Bérard, 1997) even though those reviews include studies with healthy middle-aged women. The findings stand in contrast to the results of Wolff (1999), who found an increase in BMD in a review where pre- and postmenopausal women were included.

There are some limitations in this review. First, few of the included studies investigate the effects of exercise on BMD and quality of life (QOL). Second, the type of exercise has been taken into consideration. Frequency, duration and intensity are not evaluated in this study. The intensity is not good described in the studies, but there is possible to review the frequency and duration in most of the studies.

8.2 Suggestions for further research

Further review research may be justified to investigate the effect of different exercise types on fall frequency, risk of falling, muscle strength, cardio-vascular capacity, reaction time, balance confidence, ability to perform activities of daily living, and social interaction in persons with low BMD.

Further randomized controlled trials to address the remaining questions related to intensity; frequency; and duration of exercise, is needed to find the optimal exercise prescription for BMD, balance and QOL.

References

Arent SM., Landers DM., Etnier JL. (2000). The effects of exercise on mood in older adults; a meta analytic review. *Journal of Aging and Physical Activity*, 8: 407-430.

Bandura A. (1997). Health promotion from the perspective of social cognitive theory. *Psycology and Health*, 13:623-649.

Bassett CAL., Becker RO. (1962). Generation of electric potentials by bone in response to mechanical stress. *Science*, 137:1063-1064.

Beck B., Marcus R. (1999). Impact of physical activity on age-related bone loss, in Rosen CJ., Glowacki J., Bilezikian (eds), *The aging skeleton*, New York, Academic Press, pp. 467-478.

Bérard A., Bravo G., Gauthier P. (1997). Meta-analysis of the effectiveness of physical activity for the prevention of bone loss in postmenopausal women. *Osteoporosis International*, 7:331-337.

Berg K., Wood-Dauphinée S., Williams J., Gayton D. (1989). Measuring balance in the elderly: preliminary development of an instrument. *Physiotherapy Canada*, 41:304-311.

Bianchi ML., Orsini MR., Ortolani S., Radaelli G., Betti S. (2005). Quality of life in post-menopausal osteoporosis. *Health and Quality of Life Outcomes,* 3:78.

Biddle SJH., Mutrie N. The psychology of exercise for clinical populations: exercise can be good for you even when you are ill, in Biddle SJH., Mutrie N. (eds), *Psychology of physical activity,* New York, Routledge, pp. 243-284.

Blumenthal JA., Emery CF., Madden DJ., George LR., Coleman RE., Riddle MW., McKee DC., Reasoner J., & Williams RS. (1989). Cardiovascular and behavioural effects of aerobic exercise training in healthy older men and women. *Journal of Gerontology: Medical Science,* 44:M147-M157.

Bahrke MS., Morgan WP. (1978). Anxiety reduction following exercise and meditation. *Cognitive Therapy and Research,* 2:323-333.

Bogle Thorbahn, L., Newton R. (1996). Use of the berg balance test to predict falls in elderly persons. *Physical therapy,* 76:576-585.

Brighton CT., Katz MJ., Nichols CE., Pollack SR. (1985). Prevention and treatment of sciatic denervation disuse osteoporosis in the tibia with capacitively coupled electrical stimulation. *Bone,* 6:87-97.

Brose A., Parise G., Tarnopolsky MA. (2003). Creatine supplementation enhances isometric strength and body composition improvements following strength exercise training in older adults. *Journal of Gerontology: Biological Sciences,* 58:11-19.

Bruce MF. (1980). The relation of tactile thresholds of histology in the fingers of the elderly. *Journal of Neurology,* Neurosurgery, Psyciatry, 43:730.

Buchner DM., Cress M., de Lateur B., Esselman P., Margherita A., Price R., Wanger E. (1997). The effect of strength and endurance training on gait, balance, fall risk, and health services in use in community-living older adults. *Journal of Gerontology: Medical Sciences,* 52:M218-M224.

Burger EH., Veldhuijzen JP. (1993). Influence of mechanical factors on bone formation, resorption, and growth in vitro, in Hall K. (ed.), *Bone-Bone Growth,* Melbourne, CRC Press, pp. 37-56.

Camacho P.(2007a). Treatement options, in Camacho P., Miller P. (eds), *Osteoporosis,* Philadelphia, Lippincott Williams & Wilkins, pp. 127-147.

Camacho P.(2007b). Diagnosis, in Camacho P., Miller P. (eds), *Osteoporosis,* Philadelphia, Lippincott Williams & Wilkins, pp. 1-14.

Camacho P.(2007c). Pathogenesis, in Camacho P., Miller P. (eds), *Osteoporosis,* Philadelphia, Lippincott Williams & Wilkins, pp. 15-24.

Campbell A., Robertson M., Gardner M., Norton R., Tilyard M., Buchner D. (1997). Randomised controlled trial of a general practice program of home based exercise to prevent falls in elderly women. *British Medical Journal,* 315:1065-1069.

Cann CE. (1988). Quantitative CT for determination of bone mineral density: A review. *Radiology,* 166:509-522.

Carter ND., Khan KM., Mckay HA., Petit MA., Waterman C., Heinonen A., Janssen PA., Donaldson MG., Mallinson A., Riddell L., Kruse K., Prior JC., Flicker L. (2002). Community-based exercise program reduces risk factors for falls in 65- to 75-year-old women with osteoporosis: randomized controlled trial. *Canadian Medical Association Journal,* 167(9):997-1004.

Carter ND., Khan KM., Petit MA., Heinonen A., Waterman C., Donaldson MG., Janssen PA., Mallinson A., Riddell L., Kruse K., Prior JC., Flicker L., McKay HA. (2001). Results of a 10 week community based strength and balance training programme to reduce fall risk factors: a randomised controlled trial in 65-75 year old women with osteoporosis. *British Journal of Sports Medicine,* 35:348-351.

Chow JWM. (2000). Role of nitrate oxide and prostaglandins in the bone formation response to mechanical loading. *Exercise and Sport Sciences Reviews,* 28:185-188.

Dallas S., Zaman G., Pead M., Lanyon L. (1993). Early strain-related changes in cultured embryonic chick tibiotarsi parallel those associated with adoptive modelling in vivo. *Journal of Bone and Mineral Research,* 8:251-159.

D`Amello P., Di Stefano M., Isaia G. (2007). Health-related quality of life in severe osteoporosis. *Aging Clinical and Experimantal Research,* 19:28-30.

Davidson RM., Tatakis AL., Auberbach DW. (1990). Multiple forms of mechanosensitive ion channels in osteoblast-like cells. *Pfleugers Archives,* 416:646-651.

Day L., Fildes B., Gordon I., Fitzharris M., Flamer H., Lord S. (2002). Randomised factorial trial of fall prevention among older people living in their own homes. *British Medical Journal,* 325:128-133.

Deeks JJ., Higgins JPT., Altman DG. (2008). Analysing data and undertaking meta-analyses, in Higgins JPT., Green S (eds.), *Cochrane Handbook for Systematic Reviews of interventions,* Chichester, John Wiley & Sons, pp. 243-296.

Devereux K., Robertson D., Briffa N.K. (2005). Effects of water-based program on women 65 years and over: A randomised controlled trial. *Australian Journal of Physiotherapy*, 51:102-108.

Dickerman RD., Pertusi R., Smith GH. (2000). The upper range of lumber spine bench bone mineral density? An examination of the current world record holder in the squat lift. *International Journal of Sports Medicine*, 21:469-470.

Downey PA., Siegel MI. (2006). Bone Biology and the Clinical Implications of Osteoporosis. *Physical Therapy*, 86:77-91.

Duncan RL., Hruska KA. (1994). Chronic intermittent loading alters mechanosensitive channel characteristics in osteoblast-like cells. *American Journal of Physiology*, 267:F909-F916.

Ekkekakis P., Petruzzello SJ. (1999). Acute aerobic exercise and effect. *Sports Medicine*, 28:337-374.

Elble RJ. (1997). Changes in gait with normal aging, in Masdeu, JC., Sudarsky L., Wolfson L (eds.), *Gait disorders of ageing. Falls and therapeutic strategies,* Philadelphia, Lippincott-Raven, pp. 93-106.

Ernst E. (1998). Exercise for female osteoporosis: a systematic review of randomized clinical trials. *Sports Medicine,* 25:359-368.

Fogelman I., Blake G. (2000). Different approaches to bone densitometry. *The journal of Nuclear Medicine*, 41:2015-2025.

Glass GV. (1977). Intergrating findings: The meta-analysis of research. *Review of Research in Education,* 5:351-379.

Green S., Higgins JPT., Alderson P., Clarke M., Mulrow CD., Oxman AD. (2008). Introduction in Higgins JPT., Green S (eds.), *Cochrane Handbook for Systematic Reviews of interventions*, Chichester, John Wiley & Sons, pp. 3-9.

Grimley-Evans J., Seagroatt V., Goldacre MJ. (1997). Secular trends in proximal femoral fracture: Oxford record linkage study area and England 1968-86. *Journal of Epidemiologic Community Health,* 51:424-429.

Hagerman FC., Walsh SJ., Staron RS., Hikida RS., Gilders RM., Murray TF., Toma K., Ragg KE. (2000). Effects of high-intensity resistance training on untrained older men. *Journal of Gerontology,* 55A:B336-B346.

Higgins JPT., Altman, DG. (2008). Assessing risk of bias in included studies, in Higgins JPT., Green S (eds.), *Cochrane Handbook for Systematic Reviews of interventions,* Chichester, John Wiley & Sons, pp. 187-241.

Heionen A., KannusP., Sievänen H., Oja P., Pasanen M., Rinne M., Uusi-Rasi K., Vuori I. (1996). Randomised controlled trial of effect of high-impact exercise on selected risk factors for osteoporotic fractures. *The lancet,* 348:1343-1347.

Heionen A., Oja P., Kannus P., Sievänen H., Happasalo H., Mänittäri A., Vuori I. (1995). Bone mineral density in female athletes representing sports with different loading characteristics of the skeleton. *Bone,* 17:197-203.

Hill K., Bernhardt J., McGann A., Maltese D., Berkovits D. (1996). A new test of dynamic standing balance for stroke patients: reliability, validity and comparison with healthy elderly. *Physiotherapy Canada,* 48: 257-262.

Hillam RA., Skerry TM. (1995). Inhibition of n\bone resorption and stimulation of formation ny mechanical loading of the modelling rat ulna in vivo. *Journal of Bone and Mineral Research,* 10:683-689.

Hoffmann P. (1997). The endorphin hypothesis, in Morgan WP (ed), *Physical activity and mental health,* Washington DC, Taylor & Francis, pp. 163-177.

Hughes JR., Casal DC., Leon AS. (1986). Psychological effects of exercise: a randomized cross-over trial. *Journal of Psychosomatic Research,* 10:355-360.

Jarvinen TL., Sievanen H., Khan KM., Heinonen A., Kannus P. (2008). Shifting the focus in fracture prevention from osteoporosis to falls. *Bone Mineral Journal,* 336:124-126.

Jin H., Ralston SH. (2005). Genetics of osteoporosis. *Current Rheumatology Reports,* 7:66-70.

Kannus P., Niemi S., Parkkari J., Palvanen M.,Vuori I., Jarvinen M. (1999). Hip fractures in Finland between 1970 and 1997 and predictions for the future. *Lancet,* 353:802-805.

Kelly GA. (1998). Aerobic exercise and lumbar spine bone mineral density in postmenopausal women: a meta-analysis. *Journal of American Geriatrics Society,* 46:143-152.

Kemmler W., Lauber D., Weineck J., Hensen J., Kalender W., Engelke K. (2004). Benefits fo 2 years of intense exercise on bone density, physical fitness, and blood lipids in early postmenopausal osteopenic women: Results of the Erlangen Fitness Osteoporosis Prevention Study (EFOPS). *Archieves of Internal Medicine,* 164:1084-1094.

Khan K., McKay H., Kannus P., Bailey D., Wark J., Bennell K. (2001a). Exercise prescription for people with osteoporosis, in Khan K., McKay H., Kannus P., Bailey D., Wark J., Bennell K. *Physical Activity and Bone Health,* The United States of America, Human Kinetics, pp. 181-198.

Khan K., McKay H., Kannus P., Bailey D., Wark J., Bennell K. (2001b). Exercise and fall prevention, in Khan K., McKay H., Kannus P., Bailey D., Wark J., Bennell K. *Physical Activity and Bone Health,* The United States of America, Human Kinetics, pp. 171-180.

Khosla S., Melton LJ. III., Riggs BL. (2002) Review 141: Estrogen and the male skeleton. *Journal of Clinical Endocrinology & Metabolism,* 87:1443-1450.

Klein-Nulend J., Veldhuijzen JP., van Strien ME., de Jong M., Burger EH. (1990). Inhibition of osteoclastic bone resorption by mechanical stimulation in vitro. *Arthritis and Rheumatism,* 33:66-72.

Koltyn KF. (1997). The thermogenic hypothesis, in Morgan WP (ed.), *Physical activity and mental health,* Washington DC, Taylor & Francis, pp. 213-226.

Korpelainen R., Keinänen-Kiukaanniemi S., Heikkinen J., Vänäänen K., Korpelainen J. (2006a). Effect of exercise on extra skeletal risk factors for hip fractures in elderly women with low BMD: A population-based randomized controlled trial. *Journal of Bone and Mineral Research,* 21:772-779.

Korpelainen R., Keinänen-Kiukaanniemi S., Heikkinen J., Väänänen K., Korpelainen J. (2006b). Effect of impact exercise on bone mineral density in elderly women with low BMD: a population-based randomized controlled 30-month intervention. *Osteoporosis International,* 17:109-118.

La Forge R. (1995). Exercise-associated mood alteration: a review of interactive neurobiological mechanisms. *Medicine, Exercise, Nutrition and Health,* 4:17-32.

Landers D., Alderman B. (2007). Exercise relative to other treatments for reduction of anxiety/ depression: overcoming the principle of least effort, in Morris A., Gordon S., Terry P (eds.), *Promoting Health and Fitness for Life: Invited Papers from the 11th World Congress of Sport Psychology,* Sydney, Fitness Information Technology.

Lanyon LE. (1984). Functional strain as a determinant for bone remodelling. *Calcified Tissue International,* 36:56-61.

LeBlanc AD., Spector ER., Evans HJ., Sibonga JD. (2007). Skeletal responses to space fligth and bed rest analog: A review. *Journal of Musculoskeletal and Neuronal Interactions,* 7:33-47.

Leidig G., Minne HW., Sauer P., Wuster C., Wuster J., Lojen M., Raue F., Ziegler R. (1990). A study of complaints and their relation to vertebral destruction in patients with osteoporosis. *Bone Mineral,* 8:217-229.

Lippuner K., Golder M., Greiner R. (2005). Epidemiology and direct medical costs of osteoporotic fractures in men and women in Switzerland. *Osteoporosis International,* 16, supl. 2:s8.

Lips P., Agnusdei D., Caulin F., Cooper C., Johnell O., Kanis J., Liberman U., Minne H., Reeve J., ReginsterJY., de Vernejoul MC., Wiklund I. (1996). The development of a European questionnaire for quality of life in patients with vertebral osteoporosis. *Scandinavian Journal of Rheumatology,* 25:84-85.

Lips P., Cooper C., Agnusdei D., Caulin F., Egger P., Johnell O., Kanis JA., Liberman U., Minne H., Reeve J., Reginster JY., de Vernejoul MC., Wiklund I. (1997). Quality of life as outcome in the treatment of osteoporosis: the development of a questionnaire for quality of life by the European foundation of osteoporosis. *Osteoporosis International,* 7:36-38.

Lips P., Cooper C., Agnusdei D., Caulin F., Egger P., Johnell O., Kanis JA., Kellingray S., Leplege A., Liberman U., McCloskey E., Minne H., Reeve J., Reginster JY., Scholz M., Todd C., de Vernejoul MC., Wiklund I. (1999). Quality of life in patients with vertebral fractures: validation of the quality of life questionnaire of the European foundation for osteoporosis (QUALEFFO). *Osteoporosis International,* 10:150-160.

Liu-Ambrose TYL., Khan KM., Eng JJ., Lord SR., Lentle B., Mckay HA. (2005). Both resistance and agility training reduce back pain and improve health-related quality of life in older women with low bone mass. *Osteoporosis International,* 16: 1321-1329.

Liu-Ambrose TYL., Khan KM., Eng JJ., Heinonen A., Mckay HA. (2004). Both resistance and agility training increase cortical bone density in 75-85-year-old women with low bone mass. *Journal of Clinical Densitometry,* 4:390-398.

Liu-Ambrose TYL., Khan KM., Eng JJ., Lord SR., Mckay HA. (2004b). Balance confidence improves with resistance or agility training. *Gerontonology,* 50:373-382.

Liu-Ambrose TYL., Khan KM., Eng JJ., Janssen PA., Lord, SR., Mckay HA. (2004c). Resistance and agility training reduce fall risk in women aged 75-85 with low bone mass: a 6-month randomized, controlled trial. *Journal of the American Geriatrics Society,* 52:657-665.

Lönroos E., Kautiainen H., Karppi P., Huusko T., Hartikainen S., Kiviranta I., Sulkava R. (2006). Increased incidence of hip fractures. A population based-study in Finalnd. *Bone,* 39:623.

Lord SR., Ward JA., Williams p., Anstey KJ. (1994). Physiological factors associated with falls in older community – dwelling women. *Journal of the American Geriatrics Society*, 42:1110-1117.

Lord SR., Clark RD., Webster IW. (1991). Physiological factors associated with falls in an elderly population. *Journal of the American Geriatrics Society*, 39:1194-1200.

Lynn SG., Sinaki M., Westerlind K. (1997). Balance characteristics of persons with osteoporosis. *American Congress of Rehabilitation Medicine and the American Academy of Physical Medicine and Rehabilitation,* 78:273-277.

Madureira MM., Takayama L., Gallinaro AL., Caparbo VF, Costa RA., Pereira RMR. (2007). Balance training program is highly effective in improving functional status and reducing the risk of falls in elderly women with osteoporosis: a randomized controlled trial. *Osteoporosis international,* 18(4):419-425.

Marcus R. (1996). Mechanisms of exercise effects on bone, in Bilezikian JP., Raisz LG., Rodan GA (eds.), *Principles of bone biology,* San Diego, Academic Press, pp. 1135-1146.

Marcus R. (2001). Role of exercise in preventing and treating osteoporosis. *Rheumatic Disease Clinics of North America*, 27:131-141.

McArdle WD., Katch FI., Katch VL. The micronutrients and water, in McArdle WD., Katch FI., Katch VL (eds.), *Sports & exercise nutrition,* Philadelphia, Lippincot Williams & Wilkins, pp. 45-88.

McGibbon CA. (2003) Toward a better understanding of gait changes with age and disablement: neuromuscular adaption. *Exercise and Sport Sciences Reviews,* 31:102-108.

McLeod KJ., Rubin CT. (1990). Frequency-specific modulation of bone adaption by induced electric fields. *Journal of Theoretical Biology,* 145:385-396.

Melton LJ., Gabriel SE., Crowson CS., Tosteson ANA., Johnell O., Kanis JA. (2003). Cost-equivalence of different osteoporotic fractures. *Osteoporosis International,* 14:383.

Miller PD. (2007). Assessment of fracture risk, in Camacho P., Miller P. (eds), *Osteoporosis,* Philadelphia, Lippincott Williams & Wilkins, pp. 25-47.

Morgan WP., O`Connor PJ. (1988). Exercise and mental health, in Dishman (ed), *Exercise adherence: its impact on public health,* United States of America, Human Kinetics, pp. 91-121.

Morgan WP. (1997). *Physical activity and mental health,* Washington DC, Taylor & Francis.

Moskilde, L. (2000). Age related changes in bone mass, structure, and strength – effects of loading. *Zeitschrift für Rheumatologie,* 59:1-9.

Nelson ME., Fiatarone MA., Morant CM., Trice L., Greenberg RA, Evans WJ. (1994). Effects of high-intensity strength training on multiple risk factors for osteoporotic fractures. *Journal of the American Medical Association,* 272:1909-1914.

Newhall KM., Rodnick KJ., van der Meulen MC, Carter DR., Marcus R. (1991). Effects of voluntary exercise on bone mineral content in rats. *Journal of Bone and Mineral Research,* 6:289-296.

O`Connor JA., Lanyon LE., MacFie H. (1982). The influence of rate of strain on adaptive bone remodelling. *Journal of Biomechanic,* 15:767-781.

Oleksik AM., Ewing S., Shen W., van Schoor NM., Lips P. (2005). Impact of incident vertebral fractures on health related quality. *Osteoporosis International,* 16:861-870.

Oleksik A., Lips P., Dawson A., Minshall ME., Shen W., Cooper C:; Kanis J. (2000). Health – related quality of life in postmenopausal women with low BMD with or without vertebral fractures. *Journal of Bone and Mineral Research,* 15:1384-1392.

Parvez T. (2004). Postmenopausal osteoporosis. *JK-Practitioner,* 11:281-283.

Pead M., Skerry TM., Lanyon LE. (1988). Direct transformation from quiescence to formation in the adult periosteum following a single brief period of loading. *Journal of Bone and Mineral Research,* 3:647-656.

Podsiadlo D., Richardson S. (1991). The timed “Up & Go”: a test of basic functional mobility for frail elderly persons. *Journal of American Geriatrics Society*, 39: 142-148.

Randell AG., BhaleraoN., Nguyen TV., Sambrook PN., Eisman JH, Silverman SL. (1998). Quality of life in osteoporosis: reliability, consistency, and validity of the osteoporosis assessment questionnaire. *The Journal of Rheumatology*, 25:1171-1179.

Rantanen T., Guralnik JM., Sakari-Rantala R., Leveille S., Simonsick EM., Ling S., Fried LP. Disability, physical activity, and muscle strength in older women: the women`s health and aging study. *Archives of Physical Medicine and Rehabilitation*, 80:130-135.

Rawlinson SCF., El Haj AJ., Minter SL., Taveres IA., Bennett A., Lanyon LE. (1991). Loading-related increases in prostaglandin production in cores of adult canine cancellous bon in vitro: a role for prostcyclin in adaptive bone remodeling? *Journal of Bone and Mineral Research*, 6:1345-1357.

Reich KM., Gay CV., Frangos JA. (1990). Fluid shear stress as a mediator of osteoblast cyclic adenosine monophosphate production. *Journal of Cell Physiology*, 143:100-104.

Riggs BL., Khosla S., Melton LJ. III. (2002) Sex steroids and the construction and conservation of the adult skeleton. *Endocrine Reviews,* 23:279-302.

Robinson TL., Snow-Harter C., Taaffe DR., Gillis D., Shaw L., and Marcus R. (1995). Gymnasts exhibit higher bone mass than runners despite similar prevalence of amenorrhea. *Journal of Bone and Mineral Research,* 10:26-35.

Rubenstein LZ., Josephson KR. (2002). The epidemiology of falls and syncope, in Kenny RA., O`Shea D (Eds.), *Falls and syncope in elderly patients. Clinics in geriatric medicine,* Philadelphia, Saunders, pp. 141-158.

Rubin CT., Lanyon LE. (1984). Regulation of bone foramation by applied dynamic loads. *The Journal of Bone and Joint Surgery,* 66A:397-402.

Rubin CT., McLeod KJ., Lanyon LE. (1989). Prevention of osteoporosis by pulsed electromagnetic fields. *Journal of Bone and Joint Surgery,* 71A:411-417.

Ruff CB., Hayes WC. (1988). Sex differences in age-related remodelling of the femur and tibia. *Journal of Ortheopedic Research,* 6:886-896.

Schünemann HJ., Oxman AD., Vist GE., Higgins JPT., Deeks JJ., Glasziou P., Guyatt GH. (2008). Interpreting results and drawing conclusions, in Higgins JPT., Green S (eds.), *Cochrane Handbook for Systematic Reviews of interventions*, Chichester, John Wiley & Sons, pp. 359-387.

Seeman TE., Berkman LF., Charpentier PA., Blazer DG., Albert MS., Tinetti ME. (1995). Behavioral and psychosocial predictors of physical performance: MacArthur Studies of Successful Aging. *Journal of Gerontology*, 50A:M177-M183.

Sheth P. (1999). Osteoporosis and exercise: A review. *The Mount Sinai Journal of Medicine,* 66:197-200.

Sinaki, M., Lynn SG. (2002) Reducing the risk of falls trough proprioceptive dynamic posture training in osteoporotic women with kyphotic posturing: a randomized pilot study. *American Journal of Physical Medicine & Rehabilitation,* 81:241-246.

Singh NA., Clements KM., Singh MAF. (2001). The efficacy of exercise as a long-term antidepressant in elderly subjects: A randomized, controlled trial. *Journal of Gerontology Series A: Biological Sciences and Medical Sciences,* 56:M497-M504.

Skelton DA., Beyer N. (2003). Exercise and injury prevention in older people. *Scandinavian Journal of Medicine and Science in Sports,* 13:77-85.

Snow CM., Shaw JM., Winters KM., Witzke KA. (2000). Long-term exercise using weighted vests prevents hip bone loss in postmenopausal women. *Journal of Gerontology Series A: Biological and Medical sciences*, 55:M489-491.

Spirduso W., Francis K., MacRae P. (2005a). Physical development and decline, in Spirduso W., Francis K., MacRae P (eds.), *Physical Dimensions of Ageing,* United States of America, Humna Kenetics, pp. 55-86.

Spirduso W., Francis K., MacRae P. (2005b). Balance, posture, and locomotion, in Spirduso W., Francis K., MacRae P (eds.), *Physical Dimensions of Ageing,* United States of America, Humna Kenetics, pp. 131-156.

Spirduso W., Francis K., MacRae P. (2005c). Health – related quality of life, in Spirduso W., Francis K., MacRae P (eds.), *Physical Dimensions of Ageing*, United States of America, Humna Kenetics, pp. 233-260.

Spirduso W., Francis K., MacRae P. (2005d). Physical function of older adults, in Spirduso W., Francis K., MacRae P (eds.), *Physical Dimensions of Ageing*, United States of America, Humna Kenetics, pp. 261-286.

Sterne JAC., Egger M., Moher D. (2008) Addressing reporting biases, in Higgins JPT., Green S (eds.), *Cochrane Handbook for Systematic Reviews of interventions,* Chichester, John Wiley & Sons, pp. 297-333.

Swanenburg J., Douwe de Bruin E., Stauffacher M., Mulder T., Uebelhart D. (2007). Effects of exercise and nutrition on postural balance and risk of falling in elderly people with decreased bone mineral density: randomized controlled trial pilot study. *Clinical rehabilitation,* 21:523-534.

Taylor A., Johnson M. (2008). Bone health and osteoporosis, in Taylor A., Johnson M. (eds.) *Physiology of Exercise and Healthy Ageing,* United States of America, Human Kinetics, pp. 91-111.

Tsuzuku S., Shimokata H., Ikegami Y., Wasnich RD. (2001). Effects of high versus low-intensity resistance training on bone mineral density in young males. *Calcified Tissue International,* 68:342-247.

Tsuzuku S., Ikegami Y., Yabe K. (1998). Effects of high intensity resistance training on bone mineral density in young male powerlifters. *Calcified Tissue International,* 63:283-286.

Turner CH., Owan I., Tekano Y. (1995). Mechanotransduction in bone: role of strain rate. *American Journal of Physiology,* 269:E438-E442.

Turner CH., Robling AG. (2003). Designing exercise regimens to increase bone strength. *Exercise and Sport Science Reviews,* 31:45-50.

Vaillant, J., Vuillerne, N., Martigné, P., Caillat-Miousse, J., Parisot, J., Nougier, V., Juvin, R. (2006). Balance, aging, and osteoporosis: effects of cognitive exercise combined with physiotherapy. *Joint Bone Spine* 73:414-418.

van der Wiel HE., Lips P., Graafmans WC., Danielsen CC., Nauta J., van Lingen A., Moskilde L. (1995). Additional weight-bearing during exercise is more important than duration of exercise for anabolic stimulus of bone: a study of running exercise in female rats. *Bone,* 16, 73-80.

van Staa TP., Dennison EM., Leufkens HG., Cooper C. (2001). Epidemiology of fractures in England and Wales. *Bone,* 29:517.

Weinbaum S., Cowin SC., Zeng Y (1994). A model for the excitation of osteocytes by mechanical loading-induced bone fluid shear stresses. *Journal of Biomechanic,* 27:339-360.

Wolfson L. (1997). Balance decrements in older persons: effects of age and disease, in Masdeu JC., Sudarsky L., Wolfson L. (eds.) *Gait disorders of aging. Falls and therapeutic a strategies,* Philadelphia, Lippincott-Raven, pp. 79-92.

Wolff I., van Croonenborg JJ., Kemper HCG., Kostense PJ., Twisk JWR. (1999). The effect of exercise training programs on bone mass: a meta-analysis of published controlled trials in pre-and postmenopausal women. *Osteoporosis International,* 9:1-12.

Wood RH., Reyes – Alvarez R., Maraj B., Metoyer KL., Welsch MA. (1999). Physical fitness, cognitive function, and health – related quality of life in older adults. *Journal of Ageing and Physical Activity,* 7:217-230.

Yaffe K., Barnes D., Nevitt M., Lui LY., Covinski K. (2001). A prospective study of physical activity and cogitive decline in elderly women: Women who walk. *Archives of Internal Medicine,* 161:1703-1708.

www.osteoporosis-treatment.biz/, www://osteoporosis-treatment.biz/wp-content/uploads/2008/09/osteoporosis-graph.jpg [Taken from the web 15.02.10]

www.worldclasswellness.com, www.worldclasswellness.com/bh1.php, [Taken from the web 15.02.10]

www.who.int, a. www.who.int/inf-pr-1999/en/pr99-58.html., [Taken from the web 03.02.2009] www.who.int, b. http://www.who.int/chp/topics/Osteoporosis.pdf., [Taken from the web 30.03.2009]