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Does exercise reduce the burden of fractures?

A review

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ABSTRACT – The null hypothesis that exercise has no effect on fracture rates in old age cannot be rejected on the basis of any published, randomized, prospective data. The view that exercise reduces the number of fractures is based on prospective and retrospective, observational cohort studies and case-control studies, all hypothesis-generating, not hypothesis-testing. Consistently replicated sampling bias may confirm the finding when evaluating other than randomized prospective studies. Better health, better muscle function, more muscle mass, better coordination may lead to exercise. The causal relationship could be between better health and exercise and better health and fewer fractures, not exercise and fewer fractures. The hypothesis should be tested in prospective, randomized studies evaluating hip, spine and other fragility fractures separately. Blinded studies assessing the effects of exercise can obviously not be done, but open trials can and should be undertaken to increase the level of evidence within the evidence-based system.

There are firm data supporting the view that exercise during growth builds a stronger skeleton. Exercise during growth seems to result in high peak BMD and high muscle strength. However, the Achilles heel of exercise is its cessation. Are the skeletal and muscular benefits attained during growth retained after the cessation of exercise and can any residual benefits be found in old age, the period when fragility fractures rise exponentially? Does exercise during adulthood produce any biologically important reduction in surrogate end-points for fractures other than BMD, since BMD can be influenced only marginally by exercise after completion of growth?

Recommendations for exercise should be based on evidence, not on opinion. Can continued recreational exercise maintain some of the benefits in BMD and

muscle function achieved in youth? What level of recreational exercise is needed to retain these benefits, if not fully, then at least to some extent? Dose-response relationships should be quantified. Furthermore, the effect of exercise on independent, surrogate end-points for fractures, such as bone size, shape, architecture, muscle function, fall frequency and frequency of injurious falls during defined periods in the life cycle must be determined. Absence of evidence is not evidence of absence of effect, but if we recommend exercise then should this be to children, adults, elderly, men and women with fractures, all persons? What type of exercise? For how long? Lifelong? If exercise could be implemented for most persons in society, would this reduce the number of fractures? Would the increased costs associated with the efforts to increase the activity level be lower than the reduced costs associated with any reduction in fractures? Our inability to answer these questions must be acknowledged before recommendations are made at the community level. ■

Does exercise reduce the number of fractures?

Half of all women and one third of all men will sustain a fragility fracture during their lifetime (Cooper et al. 1992). Increased morbidity, mortality and costs associated with the increased fracture incidence make it imperative to implement prevention strategies in the community (Cooper et al. 1993, Poor et al. 1995). Hip and vertebral fractures in women are the fractures most commonly discussed, but also other fragility fractures create enormous problems (Ray et al. 1997). In addition, as fragility fractures increase in men, we must also discuss the question of fracture in this cohort in the

future (Seeman 1995, Kannus et al. 1996, Center et al. 1999).

In recent years, data have become available indicating that drugs reduce the risk of fracture by about half in elderly women with bone mineral density (BMD) 2.5 SD below BMD in young healthy women, the definition of osteoporosis advocated by the World Health Organization (WHO 1994, SBU95 1995). As the evidence-based decision for drug treatment is mainly based on trials including elderly, osteoporotic women with or without fractures, it is unclear whether women with a more modest reduction in BMD can also benefit from drug treatment. Such treatment probably also reduces the fracture rate in men with low BMD, but treatment strategies in men are less well defined (WHO 1994, Orwoll et al. 2000).

General screening for detection of low BMD is not considered to be cost-beneficial, as a modest reduction in BMD implies a low absolute risk of sustaining a fracture (SBU95/1995). Drug treatment in these groups would involve the need to treat many persons to save 1 fracture event, an approach that is not regarded as being evidence-based. Instead, when the aim of the health services is to reduce the fracture rate in the community, intervention programs are needed that are effective in preventing fractures, widely accessible, inexpensive and with no adverse side effects. Exercise could have these benefits, but the question arises—does evidence-based information show that exercise reduces the number of fractures? The final and only acceptable end-point for evaluating the effects of exercise are fractures, not surrogate end-points such as BMD, balance, muscle strength or frequency of falls. However, a low absolute incidence of falls with an even lower incidence of fractures among those who fall creates a formidable challenge when randomized exercise intervention studies are planned with fracture as the end-point. When designing a study with hip fracture as the end-point, a 5-year study with $\alpha = 0.05$ and $\beta = 0.20$, a control group with a hip fracture incidence among 75-year-old women of 3–6% over a 5-year period and with a reduction in risk of 25% with exercise, sample sizes would have to be close to 7,000 persons to achieve the statistical power to detect that exercise has a fracture-reducing effect. Moreover, increasing the groups by

25% because drop-outs and nonresponders is also recommended. Thus, prospective, randomized controlled studies to evaluate the effect of exercise on the rate of hip fractures are difficult and costly to perform (Gregg et al. 1998), and no such studies are available today. A prospective study evaluating whether exercise during growth and adolescence protects against fragility fractures in old age would be virtually impossible to perform because of compliance problems and drop-outs. Therefore we have to use a lower level of evidence in the evidence-based hierarchy. The purpose of my review is to evaluate whether previous or current exercise affects the fracture rate and surrogate end-points for fracture. Finally, it must be emphasized that exercise may confer a variety of health-related effects, but in this survey I only discuss the effects on fracture rate and the muscular-skeletal system.

How strong are data suggesting that exercise reduces the risk of sustaining a fracture?

There is no hypothesis-proven evidence (randomized, prospective, controlled trial) that exercise reduces the fracture risk. No double-blinded trials can be done since it is not possible to keep the investigator or participant blinded to exercise. Moreover, there has never been an unblinded, randomized prospective trial, an unrandomized, prospective trial or an uncontrolled trial showing that exercise reduces the fracture risk, mainly because of the large cohorts needed (Gregg et al. 1998). However, lack of data from randomized trials is not proof of lack of efficacy. Going down in the evidence-based hierarchy to noninterventionist, observational, case-control studies and prospective and retrospective cohort studies, there are data which support the view that exercise reduces the fracture risk (Paganini-Hill et al. 1991). As these types of studies are the highest available evidence, we must consider these data, not forgetting that causality can never be proven in observational or case/control studies. Even meta-analyses can not exclude the risk of sampling bias, since persons with higher muscular capacity and function usually perform better in sports and are probably more likely to choose a physically active lifestyle. The genetically-inherited larger muscle mass and stronger bone may confer a lower fracture risk, not the high activity level.

Does exercise reduce the risk of sustaining a hip fracture?

In the following sections, odds ratios (all significant unless otherwise stated) for brevity are presented without confidence intervals. Most reports consistently suggest that persons with a history of a low activity level at present or in the past have a higher incidence of hip fractures than those with a higher activity level (Gregg et al. 1998, Wickham et al. 1989). Current activity, such as daily standing, climbing stairs and walking, are associated with a lower risk of sustaining a hip fracture (Cooper et al. 1988, Coupland et al. 1993). The Study of Osteoporotic Fracture (SOF), a longitudinal study following 9,704 women aged 65 years or more for 4 years, showed a 30% reduction in hip fracture risk associated with walking (Cummings et al. 1995). The same cohort followed for a mean of 8 years suggested that the incidence of hip fracture was reduced by 42% among the women in the highest quintile of current activity as compared to the least active quintile (Gregg et al. 1998). There was a dose relationship in the activity, with 2 hours or more/day of exercise reducing the hip fracture risk by 53% as compared to less than 2 hours of activity/day which reduced the incidence by 25% as compared to sedentary individuals. Sitting > 9 hours/day increased the hip fracture risk by 43% as compared to sitting < 6 hours/day (Gregg et al. 1998). The Leisure World Study (Paganini-Hill et al. 1991), a prospective cohort study following 8,600 postmenopausal women for 7 years, reported that exercise more than 1 hour/day reduced the hip fracture risk by 38% as compared to an activity level of less than 1/2 an hour/day. One study following 3,595 noninstitutionalized men and women over the age of 40 years in a population-based, longitudinal study for 10 years (NHANES I) suggested that no or a minimal activity level during recreation was associated with a 90% higher hip fracture risk as compared to recreational exercisers (Farmer et al. 1989). These findings are supported by at least 6 other prospective cohort studies (Farmer et al. 1989, Paganini-Hill et al. 1991, Meyer et al. 1993, Cummings et al. 1995, Gregg et al. 1998, Joakimsen et al. 1998) and several case-control studies (Cooper et al. 1988, Coupland et al. 1993, Johnell et al. 1995). Although nonrandomized, data consistently indicate that exercise

during growth and adulthood is associated with a reduced hip fracture risk, selection bias cannot be excluded to explain the results. The finding of a dose-response relationship in several published studies, with the risk reduction varying between 86% (Coupland et al. 1993) and 30% (Paganini-Hill et al. 1991) when comparing the most active with the least active persons, strengthens the view that moderate activity reduces the hip fracture risk in women (Gregg et al. 2000).

The data which show that exercise reduces the fracture risk in men are much weaker, since small cohorts and short follow-ups increase the risk of a type II error. However, studies with the power to evaluate the exercise-induced, hip-fracture reducing effect accord with the data in women. A longitudinal, cohort study of 3,262 50-year-old Finnish men followed for 21 years showed that vigorous physical activity at baseline reduced the hip fracture risk by 58% (Kujala et al. 2000). The Leisure World Study which included 5,049 men aged 73 years followed for 7 years, showed an inverse relationship between exercise and hip fracture risk (Paganini-Hill et al. 1991). Exercise more than 1 hour/day reduced the risk by 49% as compared to exercise for less than 1/2 hour/day. The exercise-induced, hip-fracture reducing effect in men has so far been verified by at least 4 prospective, cohort studies with adequate sample sizes (Farmer et al. 1989, Paganini-Hill et al. 1991, Meyer et al. 1993, Joakimsen et al. 1998), but also in case-control studies (Cooper et al. 1988, Grisso et al. 1991, Gregg et al. 2000).

Does exercise reduce the risk of sustaining vertebral or other fragility fractures?

In the SOF study, moderate to vigorous activity (> 2 hours/day) reduced the vertebral fracture risk by 33% as compared to no activity (Gregg et al. 1998). The European Vertebral Osteoporosis Study (EVOS) (Silman et al. 1997), including 6,646 women aged 50–79 years, of whom 884 had a vertebral deformity, showed that current walking or cycling for more than 30 minutes each day resulted in a 20% reduction in the risk of developing a vertebral deformity as compared to inactive women. In contrast, some authors suggest that a longer duration of exposure to the risk of falling during activity may increase some types of fractures. The risk

Percent of individuals with fractures

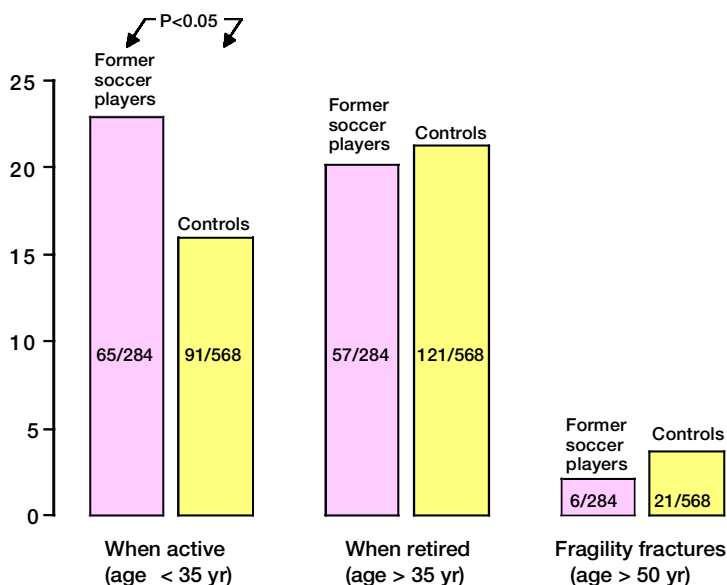


Figure 1. Percentage of persons with fractures among 284 former soccer players now 48–94 years of age and 568 age- and gender-matched controls. Adapted from Karlsson et al. 2000.

of forearm fractures was not significantly higher in women with walking as their leisure time activity than in sedentary women (Mallmin et al. 1994, O'Neill et al. 1996) and the SOF study reported the same tendency with no significant increase in the risk of sustaining a forearm fracture related to exercise (Kelsey et al. 1992) and a 13% increase in the risk of sustaining a wrist fracture (NS) in the most active persons (Gregg et al. 1998).

Data supporting the contention that exercise reduces the incidence of vertebral deformities in men are weak. The EVOS prospective study (Silman et al. 1997), which included 5,922 men, of whom 809 had a vertebral deformity, showed a 10% reduction in vertebral fracture prevalence with activity (NS). Two case-control studies with adequate sample sizes found a tendency that physical activity reduced vertebral deformities, albeit not significantly (Greendale et al. 1995, Chan et al. 1996). When including all types of fragility fractures, the results of the Dubbo epidemiological cohort study (Nguyen et al. 1996) suggest that each standard deviation of increased leisure time activity reduced all types of osteoporotic fractures by 14%, even after adjustment for differences in bone mass.

Does past exercise reduce the incidence of fractures?

What is the situation concerning fracture risks with reduced activity level after a period of active lifestyle during growth and adolescence, the scenario for many middle-aged and elderly persons? There were more persons among 284 former male soccer players now over the age of 48 who had had fractures during their active career (before age 35) than controls (23% versus 16%; $p < 0.05$), while after retirement (after age 35 years), the number of former soccer players with fractures were similar to those controls with fractures (20% versus 21%, NS) (Karlsson et al. 2000). Furthermore, the number of former soccer players who had sustained low energy fragility fractures after the age of 50 years was not lower than in controls (2% versus 4%, NS), in absolute numbers only half in former athletes, but the power to detect a significant difference was low (Figure 1). The data are supported by other studies reporting more persons with fractures among 2,622 former female college athletes now 20–80 years than among 2,776 controls (40% versus 32%; $p < 0.001$) with no difference in fracture risk after retirement (Wyshak et al. 1987). The findings of the Leisure World Study (Paganini-Hill et al. 1991) supports the findings when reporting that persons with an

Percent difference in bone mass between dominant and non-dominant arm in female tennis players with different starting age of exercise

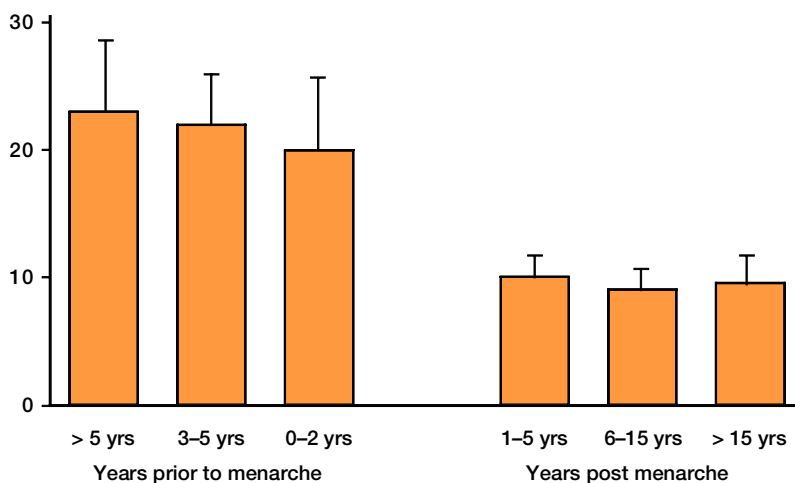


Figure 2. The side-to-side differences in bone mass of the humerus were 2–4 times greater in female tennis players who had started training before menarche than in those who had started playing up to 15 years after menarche. Bars represent 95% CIs. Adapted from Kannus et al. 1994.

activity level of more than 1 hour/day ran a lower risk of hip fracture than those active for less than 1/2 hour/day, but this effect was lost with a further reduction in activity level.

In summary, reports consistently suggest that exercise reduces the risk of hip fractures in men and women. The findings of a dose-response effect of exercise in several cohorts support this. Data suggesting that exercise reduces other types of fractures related to osteoporosis are weaker. Present studies consistently suggest that exercise in youth does not protect against fractures after retirement. Since exercise during adulthood is reported to at best cause a slight, but not significant, increase in BMD, the question remains—what is the mechanism underlying the possibly reduced fracture rate? Is the quality of the skeleton improved? Is balance or muscle strength improved? Is the incidence of falls or injuries from falls lower?

Does exercise during growth increase the accrual of bone mass and bone size?

The skeletal effects of exercise may differ in young and old persons. The mechanical threshold for old rats was higher than in young ones, but that, once activated, their cells had the same capacity as those of younger rats to enhance bone formation (Turner et al. 1995). The relative bone formation rate in the

elderly rats was 16-fold less, and the relative bone-forming surface 5-fold less compared to younger rats with similar loads (Turner et al. 1994, 1995). Similar results have been presented in other trials, showing a dramatic reduction in responsiveness of the ulnae of old turkeys to applied mechanical loads as compared to young turkeys (Rubin et al. 1992). Although data in animals can not be directly extrapolated to humans, the skeletal response to exercise must be evaluated separately in young and old persons.

Data suggesting that exercise during growth increases mineralization and/or bone size are strong. Studies of young tennis and squash players have increased our understanding of the exercise-induced skeletal effects by comparing the dominant and nondominant arm. This approach eliminates the risk of selection bias among the athletes. Tennis players were early reported to have larger bones, 10–35% greater cortical thickness and more bone mass in the playing than in the nonplaying arm (Jones et al. 1977, Huddleston et al. 1980). This observation was later confirmed by several independent reports that bone mass was up to 4 times greater in the playing than in the nonplaying arm in female players who began their tennis training 5 years before menarche as compared to those starting 15 years after menarche (Kannus et al. 1994,

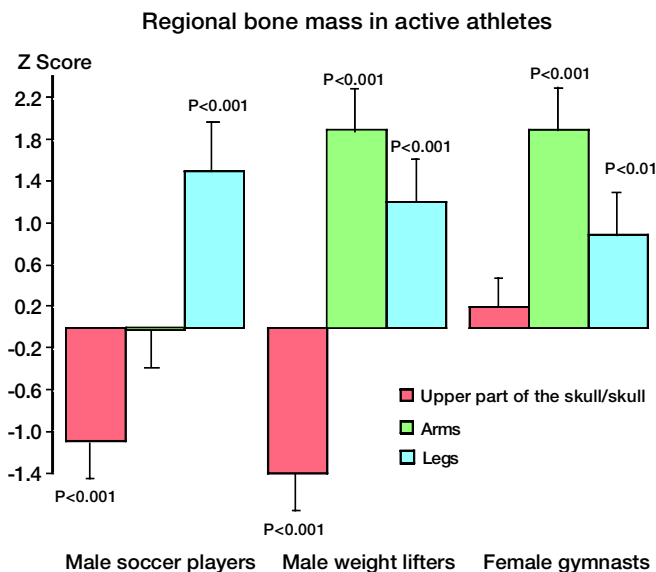


Figure 3. Bone mineral density (BMD) of the upper part of the skull / the skull, the arms and the legs, in active male soccer players, male weight-lifters and female gymnasts, expressed as Z scores (number of standard (SD) deviations above or below age-predicted mean). Adapted from Karlsson et al. 1996, Karlsson et al. 2000 and Bass et al. 1998.

Haapasalo et al. 1996) (Figure 2). The inclusion of competitive athletes who began training early also suggests that exercise during growth and adolescence can substantially increase BMD (Karlsson et al. 1993a,b, Dyson et al. 1997, Bass et al. 1998). Furthermore, cross-sectional data consistently suggest that BMD is increased by 10–20% with exercise only in weight-loaded skeletal regions. Prepubertal gymnasts had 10–30% higher BMD than controls, with the greatest difference reported in the arms compared to controls, a weight-bearing site in these athletes (Bass et al. 1998) (Figure 3). Similarly, male weight-lifters had 10–20% higher BMD in the arms than controls (Karlsson et al. 1993a,b, 1996). Both male and female soccer players had similar BMD in the arms, a region minimally loaded during soccer, while BMD in the legs was 10–20% higher than in controls, a difference of the same magnitude as in weight-lifters (Figure 3) (Duppe et al. 1996, Karlsson et al. 2000). Moreover, BMD may be lower in unloaded skeletal regions in athletes than in controls, which could suggest that a redistribution of bone occurs from unloaded to weight-loaded skeletal regions during high activity and a reverse distribution with less activity (Figure 3) (Karlsson et al. 1996, Ramne-mark et al. 1999, Magnusson et al. 2001a,b).

Currently, 6 controlled, intervention studies, some randomized and some unrandomized, comprising pre- and peripubertal boys and girls, have been published (Blimkie et al. 1996, Morris et al. 1997, Bass et al. 1998, Bradney et al. 1998, McKay et al. 2000, Fuchs et al. 2001). One study included the exercise intervention in the school curriculum (McKay et al. 2000), the others as leisure time activity on a voluntary basis. The intervention studies were short-term, 6–12 months with an increase in exercise 3 × 20–30 minutes more per week. During this period, BMD increased 1.3–5% more in the legs in the active than in the sedentary children, only 2 studies reported an increase in bone mineralization in the spine. When a similar exercise program was done in peripubertal children, the effect on the skeleton was less or not significant.

Data from prospective and retrospective cohort studies support this view that physically active children have higher BMD than sedentary controls (Slemenda et al. 1994, Cooper et al. 1995, Bailey et al. 1999). However, these observational studies may be confounded by selection bias: exercise during leisure time could be preferred by children with more muscle mass, larger bones and higher BMD due to shared genetic regulation, and not that

exercise causes high BMD. Most prospective studies show only a 1–4% increase in BMD in active persons, but cross-sectional studies usually report a 10–20% higher BMD in athletes than in controls. This could be due to a cumulative long-term effect in athletes while most prospective studies have a maximum follow-up 2 years. It is also not known whether this increase in BMD lowers the frequency of fracture and, if so, to what extent. For example, treatment with Raloxifen increases BMD by 3%, but reduces the risk of lumbar fracture by 38% (Sarkar et al. 2002).

Does exercise during adulthood increase BMD and bone strength?

Low or moderate impact exercise hardly increases BMD during young adulthood. Most studies show that aerobic exercise, at best, stops bone loss or increases BMD by less than 3%, which can have little effect on the fracture risk (Drinkwater 1993, Forwood and Burr 1993, Bouxsein and Marcus 1994). The results of weight-training are also discouraging, with most studies reporting an increase in BMD of no more than 2% (Gleeson et al. 1990, Rockwell et al. 1990, Snow-Harter et al. 1992, Friedlander et al. 1995, Lohman et al. 1995).

Similar findings have been reported in numerous randomized, prospective, short-term studies in premenopausal women (Basse and Ramsdale 1995, Heinonen et al. 1996). Prospective intervention studies in peri- and postmenopausal women with follow-ups of 6 to 24 months have evaluated activities such as walking, stepping up and down, running, jumping and strength training. They have usually found a higher BMD in the spine of less than 3% than in sedentary controls with the adaptive changes at the femoral neck described as less (Grove and Londeree 1992, Hatori et al. 1993, Revel et al. 1993, Nelson et al. 1994, Bravo et al. 1996). During the past decade, several articles have reviewed 10–20 prospective, randomized or nonrandomized studies on the effects of exercise, and shown exercise-induced beneficial effects on the skeleton in three-quarters of the studies in peri- and postmenopausal women (Bailey and McCulloch 1990, Gutin and Kasper 1992, Berard et al. 1997, Wallace and Cumming 2000). One review evaluated the effect of exercise in women between the ages 46–76 of years in 35 randomized,

prospective studies and found that 6–36 months of impact and nonimpact exercise prevented bone loss by 1–2% in the lumbar spine in peri- and postmenopausal women and that impact exercise seemed to have a similar effect, even in magnitude, on femoral neck BMD (Friedlander et al. 1995, Preisinger et al. 1995, Prince et al. 1995, Ebrahim et al. 1997).

The outcome of exercise intervention in the elderly is equally discouraging. 6–24 months of exercise in 65–80-year-old women had no effect on bone loss despite more exercise in one third of the studies and a slight increase in BMD—i.e., a maximum of 2% during the study period in some (Lau et al. 1992, Prince et al. 1995, Pruitt et al. 1995, Hartard et al. 1996, Ebrahim et al. 1997, McMurdo et al. 1997, Kelley 1998). In this age group, most of the improvement occurred in the spine and less in the femoral neck BMD (Lau et al. 1992, Ebrahim et al. 1997). It is not known whether exercise has other effects on the skeleton, such as changes in bone size, skeletal geometry or matrix properties, which may influence bone strength and no intervention studies have yet been published in adult men.

No randomized, prospective studies have been done to evaluate the skeletal effects of lifelong exercise. The Rancho Bernardo Study (Greendale et al. 1995) showed that both current and lifetime exercise were correlated with hip BMD—i.e., differences in BMD between persons in the highest and lowest categories of exercise being 5% and 8%, respectively. These findings were confirmed by Brahm et al. (1998), who reported that high lifetime occupational and leisure time activity was associated with high BMD in 61 women and 61 men aged 22–85 years.

Does cessation of exercise confer residual high BMD after retirement?

Only a few, short-term, longitudinal studies have evaluated the effect on BMD of cessation of exercise. Michel et al. (1992) reported a decrease of 16% in the BMD of the spine in 9 middle-aged male runners who stopped their running career, as compared to no loss in 3 persons who continued running over a 5-year period. Similarly, 12 women, aged 19–27 years increased their muscle strength in the trained leg by 24% and leg BMD by 2% during

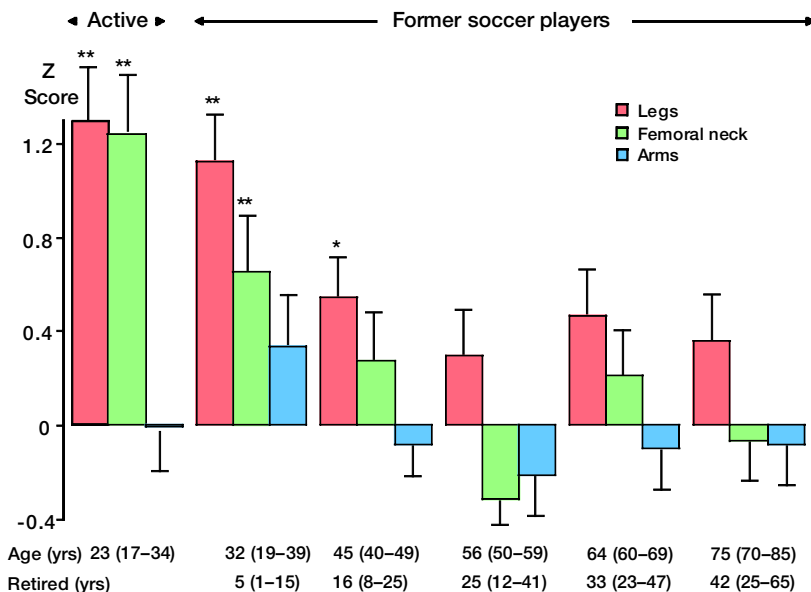


Figure 4. Bone mineral density (BMD) of the legs, femoral neck and arms in active and former soccer players expressed as Z scores (number of standard (SD) deviations above or below age-predicted mean). Adapted from Karlsson et al. 2000. * $p < 0.05$, ** $p < 0.01$.

12 months with unilateral leg presses 4 times a week, but the BMD returned to its pretraining level after no more than 3 months of detraining (Vuori et al. 1994). No long-term studies evaluating the structural changes in the skeleton with reduction or cessation of exercise exist. Only 3 cross-sectional studies evaluated the BMD effects of cessation of exercise after the age of 65 years, when fragility fractures increase exponentially (Karlsson et al. 1995, 1996, 2000, Khan et al. 1996). Leg BMD has been reported to be 10% higher than in age-matched controls in male soccer players who had been retired for 5 years, 5% higher in those retired for 16 years, but no higher in those retired for 42 years (Figure 4). The decrease in BMD with age in the legs was 0.33% /year in the former soccer players as compared to 0.21%/year in the controls. A residual, but not significantly higher leg BMD was reported in the legs in the former players aged 70 or more. However, the difference was significant when adjusted for differences in body composition relative to the controls. No differences were found in the spine or hip before or after adjustment for confounders, indicating that after 3–5 decades of retirement, no residual BMD benefits could be found (Karlsson et al. 1993a, b, 1995, 1996, 2000, Khan et al. 1996). Similar data have been

presented, evaluating both male weight-lifters and female ballet dancers (Karlsson et al. 1993a, b, 1995, 1996). There are problems with cross-sectional studies spanning 7 decades because of secular trends in exercise (Karlsson et al. 2000). Intensity and duration of training in young persons were perhaps less vigorous 5 decades ago. However, the duration of activity in the oldest former soccer players was at a level that gave the same high BMD during their active career as in soccer players active today (Karlsson et al. 2001).

A lower level of activity may retain some BMD benefits acquired during an active career. The findings in the male soccer study accord with this view by showing a correlation between current activity level and femoral neck BMD ($r = \sim 0.25$) (Karlsson et al. 2000). This was also shown in a 4-year longitudinal study of 13 formerly competitive male tennis players in which all players at baseline were Finnish national top level players with an average training frequency of 8 hours' exercise/week. No changes were seen in the differences in bone mineral content between the arm used for playing and the one not used after not training for 2 years, but these athletes were still playing a mean 3 hours/week (Kontulainen et al. 1999). Perhaps continued activity, but at a lower level, preserves the exer-

cise-induced, beneficial skeletal effects acquired during growth and adolescence, but currently we have no data on the amount of exercise needed to preserve exercise-induced skeletal benefits also after an active career.

Does exercise increase muscle size and muscle strength?

Muscle size, muscle strength, neuromuscular fiber recruitment, and balance decline with advancing age, traits often regarded as surrogate end-points for fractures (Roman et al. 1993, Lipsitz et al. 1994, Lord and Ward 1994, Hakkinen et al 1995, Tracy et al. 1999).

It is unclear whether the age-related decrease in muscle size and strength can cause the age-related decrease in BMD or whether the decrease in these two variables, both predicting fracture, can occur with no causal relationship. Grip strength correlated with BMD in all measured locations in 649 postmenopausal women (Kritz-Silverstein and Barrett-Connor 1994) and quadriceps strength and femoral neck BMD were correlated in 109 men and 231 women aged 20–89 years (both $r = 0.6$) (Hyakutake et al. 1994), as in the data reported in most studies. Muscle strength has been described as an independent predictor of femoral neck BMD in some (Hyakutake et al. 1994, Pocock et al. 1989, Snow-Harter et al. 1990), but not all studies (Seeman et al. 1996). It is unclear whether muscle strength partially determines the BMD or whether strength and BMD covariate only because of similar genetic regulation, since these persons with a large skeleton and a high BMD probably also have a larger muscle volume (Hyakutake et al. 1994, Kritz-Silverstein and Barrett-Connor 1994, Pocock et al. 1989, Snow-Harter et al. 1990).

Muscle strength seems highly adaptable to exercise in the elderly as well and an increase of up to 200% with exercise has been reported in octogenarians. This increase is far greater than the corresponding increase in the muscle volume and BMD. Tracy et al. (1999) reported a 27% increase in quadriceps strength, a 12% increase in quadriceps muscle mass and a 14% increase in muscle quality, defined as strength per unit of muscle mass for a 9-week program of resistance exercise for the quadriceps 3 days/week in 12 men aged 65–75 years. The corresponding increase in

11 women aged 65–73 years was 29%, 12% and 16%, respectively. Lord et al. (1995) confirmed these findings by reporting 29% increase in quadriceps strength, while BMD remained unchanged in those aged 60–85 years after a 12-month period of exercise and Ryan et al. (1998) reported up to a 98% increase in strength with no changes in femoral neck BMD after a 16-week training program. A similar training program for 21 men aged 61 years gave a 39% increase in upper body and a 38% increase in lower body strength, but also a 3% increase in femoral neck BMD (Ryan et al. 1994). Moreover, a decrease in activity level causes rapid changes in muscular strength. Kontulainen et al. (1999) reported that muscle volume, measured as differences in forearm circumference between the playing and nonplaying arm, diminished from 6% to 3% with a reduced training level during 2 years, and Fiatarone et al. (1990) reported a 32% loss of muscle strength after no more than 4 weeks with no training.

The exercise-induced muscle response is probably of greater significance than the BMD response in the elderly for reduction of the risk of fracture by exercise through improved mobility, speed of movement and ability to prevent or reduce the severity of falls. The specific neuromuscular mechanisms responsible for the increase in muscle quality with exercise are unknown. Neuromuscular recruitment with increase in motor unit recruitment or discharge rate increased activation of synergistic muscles, decreased activation of antagonistic muscles and alteration in muscle architecture may all contribute (Hakkinen and Komi 1983, Narici et al. 1989, Fiatarone et al. 1990, Pyka et al. 1994, Hakkinen et al. 1998).

Does exercise reduce the number of falls?

Impairments of balance and gait are known risk factors for a fall (Overstall et al. 1978, Tinetti et al. 1986, Wolfson et al. 1986, Lipsitz et al. 1994, Lord and Ward 1994). Among persons aged 65 years, living in the community, 30% fell in the course of a year and the frequency of falls increases with age so that 40% of 80-year-olds fell at least once a year (Tinetti et al. 1988, Campbell et al. 1989). Observational, cohort studies and case-control studies indicate that a fall precedes more than 90% of hip and forearm fractures, but only 5% of all falls

lead to a fracture and fewer than 1% of all falls result in a hip fracture (Tinetti et al. 1988, Nevitt et al. 1989, Grisso et al. 1991, Hayes et al. 1993, Greenspan et al. 1994). The tendency to fall seems to be a predictor for hip fractures. Cummings et al. (1995), in the prospective SOF study, reported that a history of falls increased the risk of hip fracture, where the fracture risk increased by 30% with each fall during the first 5 recorded falls.

Prospective, randomized or unrandomized intervention studies and observational cohort studies consistently indicate that exercise improves balance, coordination, muscle strength, reaction time, protective responses during a fall, lean body mass and mobility, all surrogate end-points for fractures (Tinetti et al. 1988, Nevitt et al. 1989, 1991, Meyer et al. 1993, Fiatarone et al. 1994, Hu and Woollacott 1994, Nelson et al. 1994, Province et al. 1995, Daly et al. 2000). Several observational studies have found a reduction in the number of falls with exercise (Tinetti et al. 1988, 1995, O'Loughlin et al. 1993, Graafmans et al. 1996). Hornbrook et al. (1994) in 1611 persons with an intervention program and 1571 controls 65 years and older, found that the fall frequency had been reduced by 15% with exercise, Tinetti et al. (1994) in 301 men and women 70 years and older reported that 35% of those exercising fell as against 47% of the controls. Several randomized controlled trials have evaluated the effect of exercise and the risk of falling. The first longitudinal study which reported that exercise reduces the risk of falling was The Frail and Injuries: Cooperative Studies of Interventions Techniques (FICSIT) including 60-75-year-old persons. The authors reported that 10-36 weeks of various training programs reduced the number of falls by 17%. The best results were reported with 15 weeks of Tai-Chi training, resulting in a 47% reduction in multiple falls during the 4-month period (Wolf et al. 1996). Since this study, 4 newer randomized controlled trials have confirmed that exercise reduces the number of falls (Buchner et al. 1997, Campbell et al. 1997, 1999a, Lehtola et al. 2000) while 4 other randomized controlled trials could not detect a reduction with exercise (McMurdo, et al. 1997, Campbell et al. 1999b, Rubenstein et al. 2000, Steinberg et al. 2000). Some studies even imply that the most active persons are at the same risk of sustaining a

fall as the most inactive (Tinetti et al. 1988, 1995, O'Loughlin et al. 1993, Graafmans et al. 1996), probably due to a longer exposure to risk during the activity in the most active elderly. Two recently published reviews concluded that exercise alone does not protect against future falls (Campbell et al. 1999a, Gillespie et al. 2000). However, Gregg et al. (2000), summarizing 6 randomized studies, asserted that exercise reduces the fall frequency. It seems that the outcome in one population of elderly can not automatically be extrapolated to another population and that intervention studies concerning nursing home populations with a fall as end-point show less promising results. Additional questions arise as to how much exercise; its frequency and duration are needed to maintain the level of function achieved and are there any differences between populations?

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