

Physical activity, skeletal health and fractures in a long term perspective

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Abstract

Exercise during adolescence, especially during the pre-pubertal years, builds a skeleton with a high bone mineral density (BMD) and possibly a larger skeleton with a different skeletal architecture. This would lead to a stronger skeleton more resistant to trauma. These changes could be of biological significance for fracture reduction, if they were maintained into old age where fragility fractures exponentially rise. The Achilles heel of exercise is its cessation. Most BMD benefits achieved by exercise appear to be eroded with cessation of exercise. Reduced exercise intensity after a period of high activity, may maintain some residual BMD benefits into old age. A decreased fracture rate in the population could perhaps be achieved by promoting a physically active life style with lifelong high activity. But what happens if the activity in former athletes is reduced to the same level as in individuals who never exercised? The null hypothesis that exercise has no effect on fracture rates in old age cannot be rejected on the basis of any published, randomised, prospective data. Instead we have to rely on retrospective observational and case control studies, all hypothesis-generating, not hypothesis-testing. Existing data suggest that there could be a reduced fracture risk in former athletes. This notion may be correct, but consistently replicated sampling bias may produce the same observation and any biological explanation for this fracture reduction is unclear. Residual structural skeletal benefits, improved muscle strength, coordination and balance are all traits possibly maintained in former athletes after their active career. These traits may possibly reduce the number of fractures in later life.

Keywords: Athletes, Bone Mass, Exercise, Fractures, Retirement

The fragility fracture problem

About 50% of all women and 30% of all men during their lifetime will suffer a fracture related to osteoporosis¹. As these injuries are associated with increased morbidity, mortality and impose a financial burden on the community, it is imperative to prevent these types of fractures^{2,3}. Today we know that anti-resorptive drugs reduce the fracture risk by about 50%. This however is shown in women, but probably also occur in men, with a bone mineral density (BMD) 2.5 standard deviations (SD) below the young normal mean; the definition of osteoporosis used by the World Health Organization (WHO)^{4,5}. Even if the relative risk is the greatest in individuals with

osteoporosis, most fractures in absolute numbers are derived from the much larger population of subjects at a more modest increased risk. These are individuals with BMD between 1.0 to 2.5 SD below the young normal mean and defined as osteopenia according to WHO⁵. In this group, no drug trials have been made showing that drugs reduce the incidence of fractures. Neither is treatment of all women from the age of 50 years and onwards, irrespective of their BMD, recommended because a similar approach would not be regarded as evidence based therapy and it is not feasible or cost effective⁶. Thus, we must search for other prevention strategies when the public health burden of fractures should be reduced. Society needs community based interventions that are safe, accessible to virtually all individuals independent of age and inexpensive to implement. Exercise seems to be an ideal strategy to fulfil these demands, but what evidence exists implying that exercise reduces the numbers of individuals with fractures? The purpose of this review is to examine the hypothesis that exercise during growth and adulthood leads to increased bone strength and reduces the fracture risk, not only during periods with a high level of exercise, but with advancing age when the activity level usually is low.

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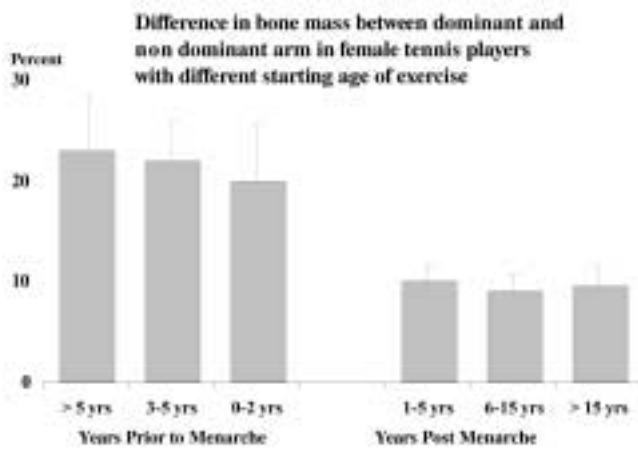


Figure 1. The difference in BMD between the dominant and the non-dominant humerus was two to four times higher in female tennis players who had started training before menarche compared with those who took up tennis up to 15 years after menarche. Bars represent 95% CI's. Adapted from Kannus et al.¹³.

In this review, I have cited the existing literature. Most of the literature evaluates bone strength by bone mineral density (BMD). I am aware of the importance of other traits and that BMD is not the final answer for bone strength⁷⁻¹⁰. There are a few data in retired athletes using pQCT and MRI. What data that does exist are present in this review^{11,12}.

Exercise, bone strength and fracture risk—study design problems

Physical activity is a pivotal area of research because decisions regarding the role of exercise in the individual and community depend on these findings. When exercise is undertaken during growth, remodeling and modeling changes such as endocortical accrual and perhaps trabecular thickening may be transient, i.e. exercise induced bone mineral density (BMD) benefits may be eroded by retirement. In contrast, changes in bone size and shape, achieved by exercise may be permanent. Furthermore, the property of bone as a material and the amount of fatigue damage in a bone also affect the strength of the bone. If the effects of exercise derived in adolescence and youth or adulthood are totally eroded by time, then could exercise be used as a prevention strategy for fracture reduction? Why take up exercise in the first place? Having a high BMD in young years does not influence the fracture frequency in society, as even young adults with low BMD for their age usually do not reach the level of osteoporosis and usually do not sustain fragility related fractures. If the aim is to reduce the fracture burden in the community, then physical activity must confer long term benefits in older age. After about 60 years of age fragility fractures exponentially rise and become a substantial problem. If the effects of exercise during youth can be main-

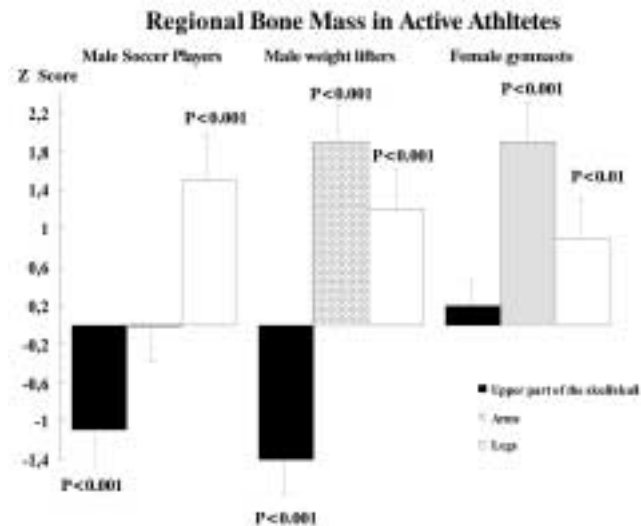


Figure 2. Bone mineral density (BMD) of the upper part of the skull / skull, the arms and the legs, in active male soccer players and male weight lifters expressed as Z scores (number of standard deviations [SD] above or below age predicted mean). Adapted from Karlsson et al.^{37,41}.

tained, at least in part, by lesser levels of exercise in adulthood, then information is needed defining the level and type of exercise needed to sustain a biologically worthwhile benefit in BMD. Absence of evidence is not evidence of absence of effect, but if we recommend exercise then should this be to children, adults or to elderly with or without fractures? What type of exercise? For how long? How many fewer fractures will result in the community from a community based exercise campaign like the anti-tobacco campaign? The higher level of proof to show that exercise reduces the number of individuals with fragility fractures must come from well designed and executed prospective randomized studies. Blinded studies obviously cannot be done, as neither researchers nor participants can be blinded to physical activity, but open trials can and should be undertaken.

Presently we only have short term prospective data that follows changes in BMD with retirement from physical activity. There are few published long term cross-sectional studies and these are always subjected to the risk of selection bias. Healthier individuals, subjects with larger musculoskeletal size and larger BMD, may choose to be more active, while less healthy persons exercise less because of their reduced health. The reduced health may lead to lack of exercise, BMD loss and fractures and the causal link may be between the reduced health, low BMD, fracture, and the reduced health and lack of exercise, not low BMD and fracture and the lack of physical activity. Furthermore, most studies addressing these questions are retrospective analyses using BMD as a surrogate end point for bone strength. When former athletes and controls are compared, most studies do not evaluate structural skeletal discrepancies and

Bone mass in male active soccer players, and former active soccer players and controls

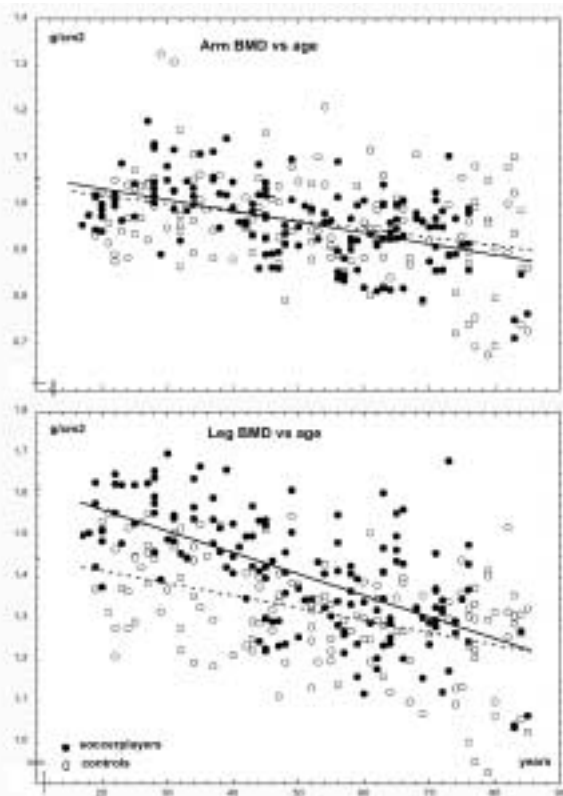


Figure 3. Bone mineral density (BMD, g/cm²) of the legs and arms in active and former active male soccer players and controls versus age.

virtually no one uses the clinical relevant end point, fractures. Studies designed to expressly address these important questions are needed before inferences from the data can be made with a higher level of confidence.

Exercise during growth and adulthood

In the following sections, all presented differences are significant unless otherwise stated but for brevity these are presented without confidence intervals or p-values. Exercise seems to increase BMD by a biologically significant amount with most obvious benefits achieved during growth (Figure 1)¹³⁻²⁵. Randomised, prospective intervention studies in pre- and peripubertal children indicate that even moderate exercise may increase BMD by a biologically significant magnitude. It is during these years when the highest level of skeletal benefits appear to be achieved by physical activity^{14-17,19-22}. In contrast, a similar exercise regime that led to increased accrual of BMD during the pre- and peripubertal years did not enhance the accrual of BMD during the post-pubertal years^{18,19}. Also, bone size and skeletal architecture, both independently providing bone strength, may be affected by

exercise during growth^{11,22,24-28}. If exercise is conducted at a competitive level, the benefits in BMD and bone size may reach even greater levels and the modelling and remodelling effects may continue also after completion of growth (Figure 2)^{26,29}. Interestingly, there could be a redistribution of BMD from unloaded to weight loaded skeletal regions during extreme activity (Figure 2). Furthermore, both periosteal and endosteal surfaces may be affected, but the magnitude varies according to whether the surface is anterior, posterior, medial or lateral and whether the surface is proximal, central or distal within the bone²⁷. Moreover, induced periosteal and endosteal responses may depend on the type of load applied, the magnitude of, direction and speed of applied force as well as whether the child is early or late in pubertal development^{13,30,31}. Exercise after completion of growth seems to have less influence on the skeleton than during growth, with at best an increase of a few percentage points in the spine BMD and possibly also in the femoral neck BMD³².

The Achilles heel of exercise – an increased bone loss with retirement?

Currently only short term prospective data exists that follows former athletes after retirement from high levels of exercise. There are reports supporting and opposing the hypothesis that exercise confers BMD benefits that are maintained after cessation of exercise^{12,29,33-35}. Differences observed in bone mineral content (BMC) between the playing and non-playing arm in tennis players remained undiminished after detraining, suggesting benefits in BMC were maintained with reduced activity level³⁶. However, two years of detraining may be insufficient to detect changes that occurred in this small sample. Additionally, the former tennis players in this study continued with about 3 hours of exercise per week and this may have been sufficient to preserve the BMC benefits achieved during their active careers. This notion is supported by findings of a correlation between proximal femoral BMD and current activity level in retired male soccer players ($r = \sim 0.25$). This also suggests that continued exercise may maintain some of the benefits of sport achieved in youth³⁷. Furthermore, lifetime tennis players aged 70-84 years were found to have 4-7% higher radial bone mineral content (BMC) in dominant versus the non dominant arm³⁸. These individuals remained playing but at a lower levels of intensity than during youth, so perhaps exercise on a more recreational level may retain exercise-induced skeletal benefits. These studies support the notion that residual benefits are found in retired athletes and their continued activity may contribute to these beneficial results. Most studies on former athletes continued levels of activity and exercise that were generally greater than the average individual^{29,36,38-46}.

In contrast, prospective data are less promising. Michel et al. reported in a 5 years prospective study that spine BMD decreased by 13.4% in middle aged runners who ceased to

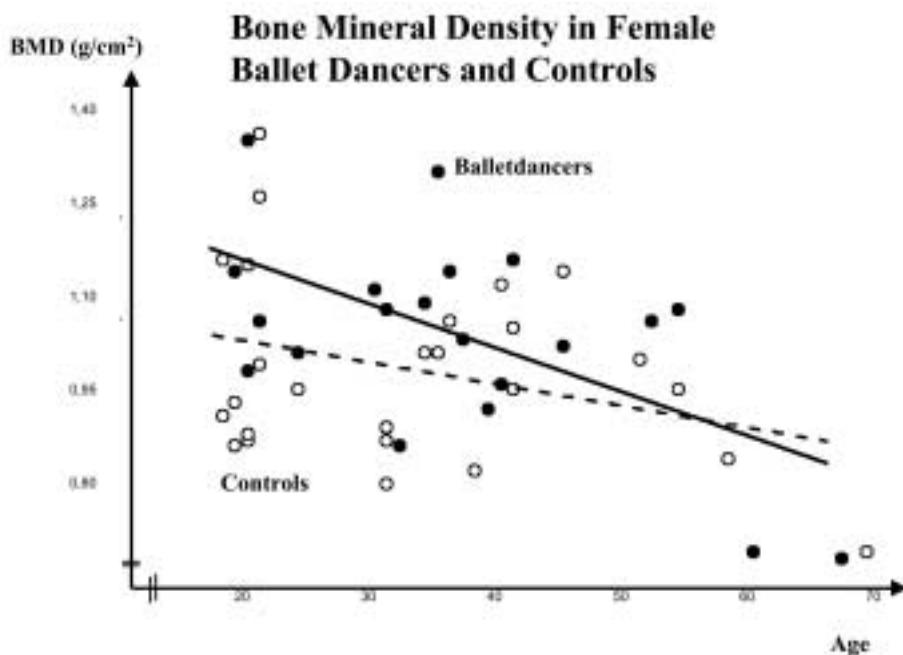


Figure 4. Bone mineral density (BMD) of the femoral neck in active and former active female ballet dancers and in controls in relation to age. The slopes differ significantly ($p < 0.05$) when comparing the groups. Adapted from Karlsson et al.⁴².

run compared to a 3.8% loss in individuals who continued to run³⁹. Similarly, Vuori et al. reported BMD to return to pre-training levels with cessation of exercise in 12 women aged 19 to 27 years doing unilateral leg presses four times a week for 12 months and then followed by 3 months of detraining⁴⁰. However, as these studies include only a small sample of retired athletes, conclusions must be drawn with caution. So far the largest cohort of retired athletes followed prospectively for several years included 97 male ice hockey and soccer players and 49 controls²⁹. The athletes had at baseline a higher BMD than controls (0.8 standard deviations, SD) at the femoral neck. Four years after retirement from exercise, the differences between the athletes and controls had decreased by 0.3 SD at the femoral neck. Additionally, the loss in BMD in the retired athletes was greater than the loss measured in both the athletes who proceeded with exercise and the controls. However, in spite of the reduced benefits with retirement of exercise, BMD was still higher in the retired athletes than in the controls, but now only 0.4 SD in the femoral neck. Thus, prospective studies following retired athletes over years imply that exercise induced BMD benefits seem to diminish with retirement^{29,39,40}.

There presently exist only cross-sectional data on retired athletes at ages where fragility fractures would exponentially increase. Retired soccer players have high BMD during the first two decades after cessation of high physical activity, but the residual benefits in BMD are lower than in active soccer players³⁷. Leg BMD was 10% higher than age-matched controls in players retired for 5 years, 5% higher in players retired for 16 years, but no higher in players retired

for 42 years (Figure 3). The diminution in leg BMD was 0.33%/year in the former soccer players, ~50% higher than the 0.21%/year diminution in controls (Figure 3). Residual benefits were seen in former soccer players over the age of 70 years. Their leg BMDs were about 6% greater than controls; a difference that was significant when adjusted for differences in body composition. No benefits were seen in the hip or any other skeletal region. Thus, three to five decades after cessation of the active athletic career most exercise induced skeletal benefits seem to be lost (Figure 3)^{29,41-44,47}. Duppe et al. supported this view when reporting BMD to be higher in 25 former female soccer players now aged 40 years and retired for 10 years, however less than during the active career⁴⁶. Former male weight lifters have higher total body BMD by 8% in 35 - 49 years olds, by 6% in 50 - 64 year olds but no higher in former lifters aged 65-79 years^{41,43,44}. Data in former ballet dancers support the notion of a higher BMD loss after retirement. Diminution in femoral neck BMD across age was higher in both female and male former dancers (Figure 4)⁴². Benefits of about 10-15% are found also in retired female gymnasts, lower than in active gymnasts (20-25%) suggesting maintenance of biologically worthwhile effects for at least 10 years after retirement²⁶. Most data consistently imply that BMD is maintained by about 5-10% above the age-predicted mean in athletes retired for 10-20 years, around half compared to the benefits found in currently active athletes but in the long term perspective, no benefits seem to be maintained^{29,41-44,47}.

Perhaps these negative observations are incorrect. Secular trends in exercise may be responsible^{37,45}. Training in youth was possibly less vigorous in the older retired soccer

Physical activity and the risk to sustain a hip fracture

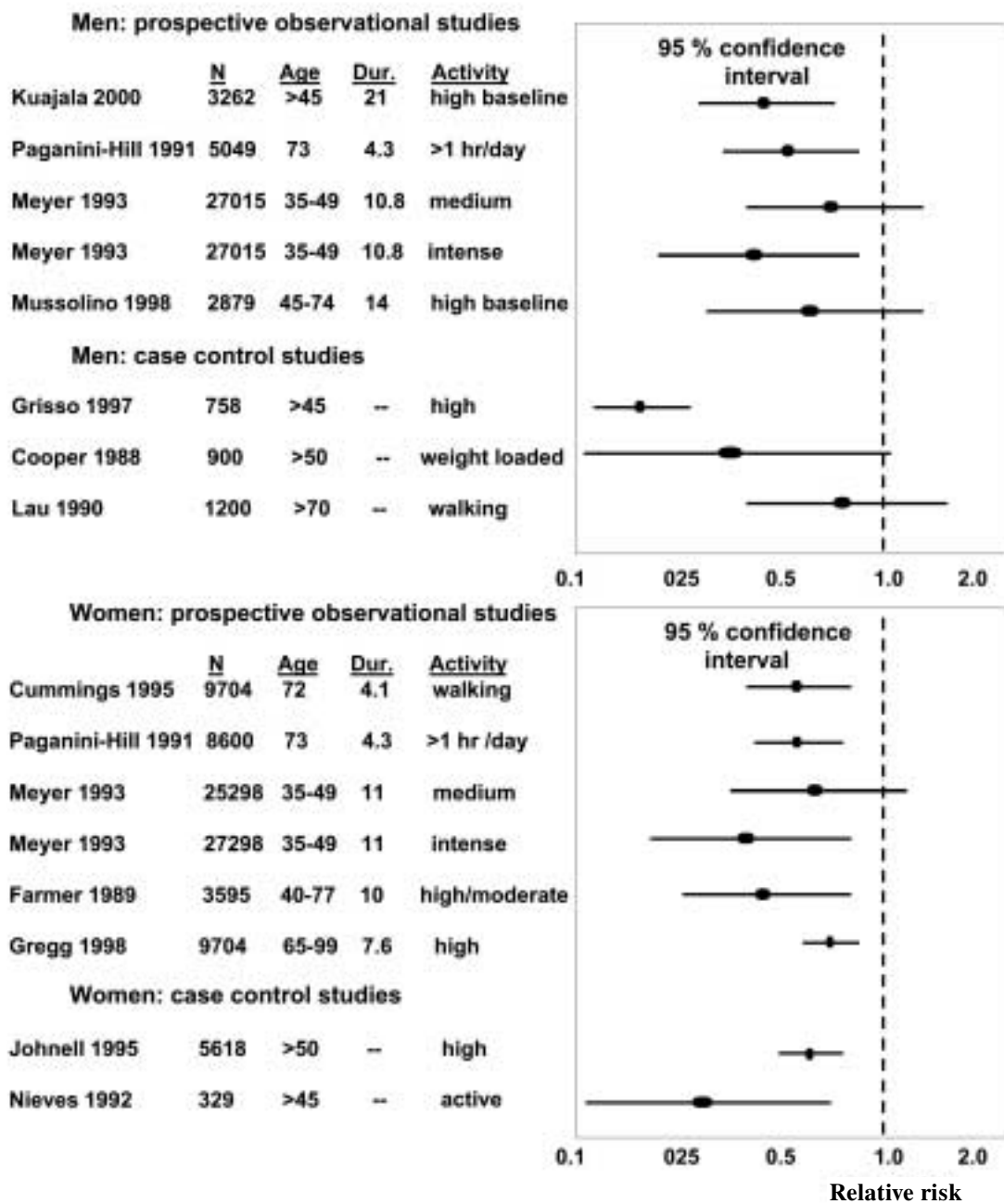


Figure 5. Relative risk of sustaining a hip fracture with a higher level of exercise. Original study, numbers (N), age (years), duration of observation (years) and compared activity levels with 95 % confidence interval (95 % CI) for the odds ratio presented. A 95% CI below 1.0 indicate that exercise is associated with reduced number of fractures.

players compared with younger players today, so they may have attained a lower peak bone mass. More sedentary living, a less working load or less recreational physical activity and greater intake of alcohol may have produced greater bone loss in retired athletes. However, there were virtually no differences in work load, life style, recreational activity,

smoking habits, alcohol consumption and nutritional habits between male or female soccer players and controls as assessed by questionnaire^{29,37,45}. These data are consistent with the notion that benefits are retained for many years after retirement but BMD loss proceeds at a higher rate than in controls so that benefits are largely lost in old age, the

Physical activity and the risk to sustain fragility fracture

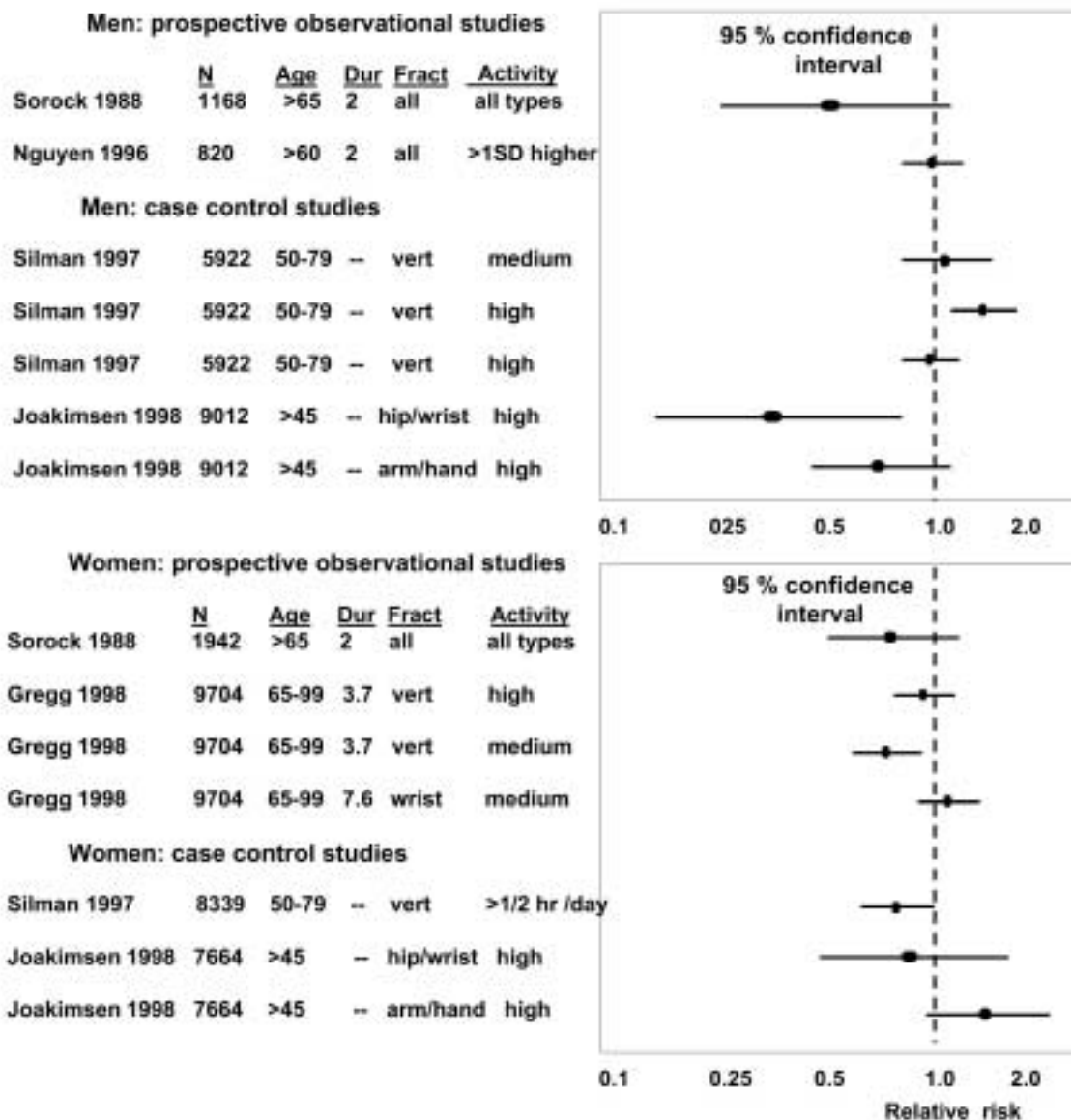


Figure 6. Relative risk of sustaining other fragility fractures with higher level of exercise. Original study, numbers (N), age (years), duration of observation (years) and compared activity levels with 95 % confidence interval (95 % CI) for the odds ratio presented. A 95% CI below 1.0 indicate that exercise is associated with reduced number of fractures.

time the benefits are needed most. Continued activity at lower levels after retirement may preserve some of these BMD benefits but what levels of recreational activity should be performed to maintain any benefits need to be defined.

Are exercise induced structural changes of the skeleton preserved with retirement?

Haapasalo et al. reported that exercise caused enlargement in bone size (humerus, radius shafts, and distal

humerus) without a change in volumetric bone density¹¹. This benefit was maintained after retirement. Twelve former national-level male tennis players retired for 1 to 3 years had higher, side to side differences in BMC (20%), total cross-sectional area of bone (18%), cortical area (22%), bone strength index (30%), principle moments of inertia at all sites, and cortical wall thickness (15%). The side to side cross-sectional area of the marrow cavity difference was higher at the proximal humerus (19%) and radial shaft (29%). Volumetric density of cortical bone was lower at the

Proportion of individuals with fractures in former male athletes after retirement and in controls

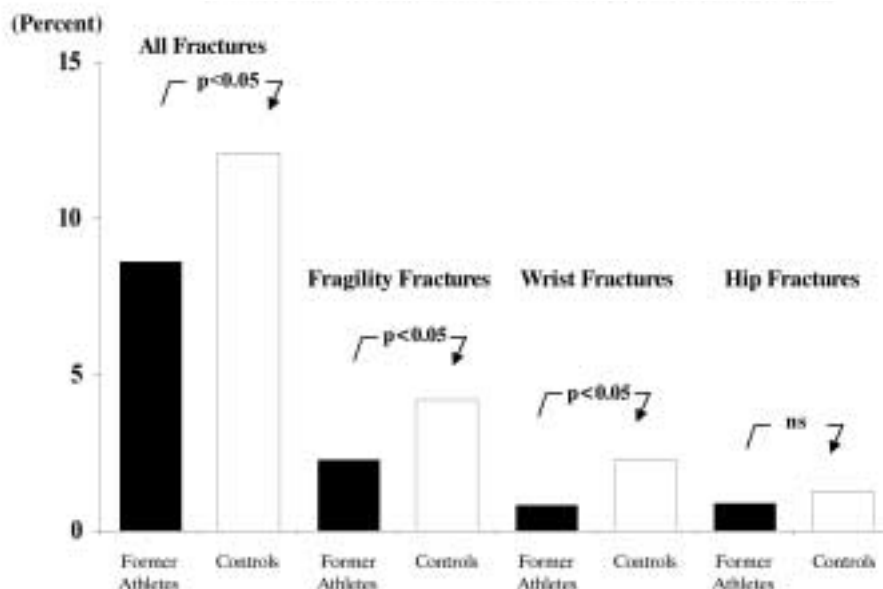


Figure 7. Proportion of individuals with fractures among 663 former male athletes now 50 to 94 years of age and 943 age- and gender-matched controls.

distal humerus and trabecular bone but side to side differences were not significant. The marrow cavity was larger in the playing arm suggesting a greater endocortical expansion during activity or that bone loss occurred on the endocortical surface after retirement¹¹. These observations fit with the notion that exercise produces enlargement of bone size that is permanent after retirement but any endocortical thickening due to endocortical apposition may be partially or completely. Bone size was also evaluated in 90 former male soccer players and weight lifters (mean age 67; range 50-92) who had retired from their exercise career (mean 27 years; range 3-65). They were compared with 77 sedentary age- and gender- matched controls using dual energy X-ray absorptiometry (DXA) and Quantitative Ultrasound Calcaneus (QUS). In this study both femoral neck area and lumbar spine width was larger in the former athletes than the controls⁴⁵. Additionally, the QUS, usually regarded as a measurement of skeletal architecture, was higher in the former athletes than the controls. These data indicate that exercise induced structural changes in the skeleton may be preserved in former athletes into old age, in contrast with the exercise induced benefits in BMD. If so, this would maintain bone strength and reduce the numbers of fragility fractures in former athletes compared with sedentary controls.

Fracture risk during activity

Data from retrospective and prospective observational and case control studies consistently suggest that activity is

associated with reduced fracture risk. Current physical activity is statistically associated with a lower risk of hip fractures in both men and women (Figure 5)⁴⁸⁻⁵⁰. Additionally, there is a relationship between activity levels and a reduced risk of hip fracture⁵¹⁻⁵³. Data suggesting that exercise reduces other types of fractures related to osteoporosis are not as convincing, though several reports suggest a non-significant reduction in also other types of fragility fractures associated with higher current levels of physical activity (Figure 6)^{48,49,54}. This may be correct, but consistently replicated sampling bias may produce the same observation. Higher musculoskeletal mass, better health, coordination and a better balance may facilitate physical activity and exercise and these qualities may also lead to a reduced fracture risk, not the reverse. This possibility cannot be excluded. Observational data is hypothesis generating, never hypothesis testing.

Fracture risk after cessation of exercise

What happens with bone strength and fracture risk when the level of exercise is reduced, a common occurrence when individuals reach middle age? Karlsson et al. evaluated 284 retired male soccer players all above age 48 years with age- and gender-matched controls. A greater proportion of former soccer players had fractures when they were active and under 35 years of age compared to controls (23 versus 16%, respectively) but the fracture prevalence was no lower in former soccer players over 35 years of age compared with controls (20 versus 21%, respectively)³⁷. The proportion of for-

mer soccer players over 50 years of age with fragility fractures was no less than controls (2 versus 4%, respectively). The sample size was small so that a type 2 error could be present and for this reason the study was extended. The incidence of fractures in 663 former elite athletes (mean age 69 years; range 50-93 years) who had participated in impact loading sport and were retired (mean 34 years; range 1-62 years) were compared with 943 gender- and age-matched controls^{29,45}. The proportion of subjects with fractures was no lower in former athletes than controls (25.9% versus 25.2%, respectively). In contrast, after age 35 years (after retirement), there were fewer former athletes with fractures than controls (8.9% versus 12.1%, respectively). Additionally, the proportion of subjects with fragility fractures sustained after age 50 years was lower in the former athletes compared with controls (2.3% versus 4.2 %, respectively) as well as the proportion of individuals with distal radius fractures (0.8% versus 2.3%, respectively) (Figure 7)^{29,45}. The proportion of individuals in this cohort with fragility fractures was similar to the previous published study³⁷, however now with a greater statistical power to conclude that there was a reduced incidence of fragility fractures in former male athletes. The causality for the reduction in fracture incidence in former athletes was undefined. Residual benefits in the former athletes, other than in the skeleton, as neuromuscular function, co-ordination, balance and fall frequency as well as selection bias may also explain the results.

In contrast, Wyshak et al. compared 2,622 former female college athletes with 2,776 controls at age 20-80 years. It was found that the former college athletes had higher lifetime occurrence of fractures compared to controls (40.5% versus 31.9%, respectively). No fewer fractures were found in the retired athletes compared with the controls (29% versus 32%, respectively)⁵⁵. This study suggests that any protective effect of exercise against fractures is not sustained after retirement. However, as this study included individuals from age 20 years and with the activity level poorly defined, perhaps there were too few elderly individuals and too few with an activity level conferring a greater BMD to fully evaluate the longer term risk to sustain fragility related fractures. There could also be a gender difference as this study was conducted in females. Furthermore, the Leisure World Study indicates that individuals with an activity level of > 1 hour/day had reduced risk of hip fracture but the beneficial effect was lost in if the activity level was reduced⁵³. However, the level of exercise may have been too low and conducted only during adulthood as to lead to any long term skeletal benefits and a reduction in the number of individuals with fragility fractures.

The above cited studies evaluating the incidence of fractures in former athletes, do not describe the type of trauma associated with the fractures. In the studies by Karlsson et al., fractures usually associated with osteoporosis (fractures of the distal radius, the proximal humerus, the spine, the pelvis, the hip and the tibial condyle) sustained after age 50 years were regarded as fragility related fractures. However,

we acknowledge that a small proportion could be based on high energy trauma, unfortunately this was not possible to determine as the questionnaire in the study did not evaluate the type of trauma.

Summary and conclusion

The most compelling evidence for a beneficial effect of exercise on bone mineral density (BMD) is during growth. Even moderate exercise increases BMD during growth and high impact loading activities such as soccer, ice hockey, gymnastics, weight lifting and racket sports are associated with high regional BMD. The higher BMD is the result of a periosteal surface modelling increasing bone size and endosteal (endocortical, trabecular, intracortical) surface modelling and remodelling, resulting in thicker cortices and thicker trabeculae. Whether the cortices also are less porous, due to fewer or smaller haversian canals, is not known. Physical activity may prevent age-related BMD loss or restore previously lost bone in individuals above age 65 years, the age when fragility fractures exponentially rise. But this increase in BMD is of a questionable biological significance for fracture reduction.

Two other critical questions are whether reduction in exercise is followed by the loss of any benefits derived during growth and adolescence and whether exercise on a more recreational level can sustain any benefits achieved by more vigorous exercise during growth or adulthood. Most prospective data following athletes indicate a higher BMD loss in retired athletes in comparison with both athletes who continue with exercise and controls. Additionally, cross-sectional long-term data suggests the benefits in BMD are lost in former athletes after 3-5 decades of retirement. Residual benefits in bone size, shape and architecture may, however, be permanent. When looking at the clinical relevant endpoint, fractures, it seems that there are fewer former athletes with fractures than among individuals who never exercised. In conclusion, exercise may well reduce fracture risk during periods with physical activity but also in later years when activity levels are reduced, but the quality of the evidence supporting this notion is weak.

Acknowledgements

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