The link between physical activity and bone strength across the lifespan

Weight-bearing physical activity plays an important role in bone health across the lifespan. During childhood, short bouts of high-impact activity augment bone-mass accrual and enhance bone's structural characteristics that contribute to overall bone strength. Along the age continuum, physical activity in adulthood serves to maintain bone mass and strength and in later life, to diminish bone loss. While the specific exercise prescription for bone strength in women and men is not known, a combination of resistance training and impact exercise may offer the best strategy to promote bone health in older adults and ultimately, reduce fracture risk. In this review we discuss the central role that physical activity plays in promoting bone health across the lifespan. Specifically, we focus on the adaptations in bone structure and strength to weight-bearing physical activity.

KEYWORDS: bone strength ▪ exercise ▪ lifespan ▪ physical activity

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Learning objectives

Upon completion of this activity, participants should be able to:

- Describe bone changes over different life stages and their assessment
- Identify the relationship between physical activity and bone strength among children
- Identify the relationship between physical activity and bone strength among adults
- Describe research into the effect of physical activity on the prevention of falls and fracture among adults

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> *"Lack of activity destroys the good condition of every human being, while movement and methodical physical exercise save it and preserve it."*
>
> – Plato

We have known for some time that bone has a remarkable capacity to adapt in order to achieve mechanical competence. In 1638, Galileo described how bone structure is configured to be as light as possible (a hollow diaphysis) without compromising its strength [1]. By 1892, Julius Wolff and others had linked mechanical loads to bone architecture [2], but the clinical relevance of this relationship was not yet understood. More recently, Harold Frost espoused the mechanostat – not unlike a room thermostat – where in theory, bone adapts its strength in response to strain thresholds that turn the 'bone building machinery' on or off [3,4]. Frost contended that the strength of load-bearing bones is a result of their response to the largest voluntary loads the bones experience and that:

> *"healthy bones must be stronger than the minimum needed to keep voluntary loads from breaking them suddenly or from fatigue"* [4].

The most unfortunate consequence of an imbalance between bone strength and imposed loads is fracture.

Fractures are a significant cause of morbidity and mortality, particularly in developed countries [5], and are associated with enormous healthcare costs [6]. In light of this disease burden and current evidence that indicates rising fracture rates among the elderly [5,7], interventions that aim to reduce the risk of fracture warrant attention [8]. In clinical settings, bone-specific medications may be the intervention of choice; however, physical activity may be an effective, nonpharmacological strategy to prevent osteoporosis [8].

There is a substantial body of evidence to support the role of physical activity in augmenting bone mass during the growing years, to conserve it during adult life and to diminish its decline in later life. The majority of exercise intervention trials have monitored changes in bone mineral content (BMC [g]) or areal bone mineral density (aBMD [g/cm^2]) using dual-energy x-ray absorptiometry (DXA). However, it is now well known that DXA is unable to assess changes in bone geometry or to identify specific adaptations in cortical and trabecular bone compartments. Importantly, DXA is also unable to identify small changes in bone dimensions that translate into substantial increases in bone strength.

With the advent of three-dimensional imaging technologies, such as peripheral quantitative computed tomography (pQCT), the more complex adaptation of bone structure to physical activity in the growing, adult and aging skeleton can now be assessed. Importantly, these tools also permit us to identify the mechanisms that underpin the bone strength adaptation to weight-bearing physical activity. However, the specific exercise programs that best promote bone-mass or strength accrual across the lifespan have yet to be clearly defined.

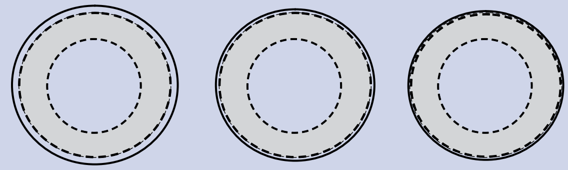
Therefore, in this review, we first aim to introduce the mechanisms by which bone adapts to load-bearing physical activity in the growing, adult and aging skeleton. Second, we will describe the imaging tools that quantify changes in bone geometry structure and strength in response to weight-bearing regimens. Third, we summarize the current literature and focus on physical activity programs designed to enhance bone strength during growth and with aging. Finally, we share our perspective on how the field of physical activity and bone health may evolve over the next decade.

Bone adaptation to physical activity

Physical activity is a comprehensive term that includes any body movement that expends energy [9]. Categories of physical activity include work- and leisure-time physical activity (LTPA) – LTPA includes household tasks, activities of daily living, exercise and sport [9]. Current recommendations suggest that children and adolescents should engage in 60–90 min/day of moderate-to-vigorous physical activity (MVPA) [201,202], and older adults should engage in 30 min or more of moderate physical activity 5 days/week to achieve health benefits [10]. Although the specific physical activity prescription for bone health is not well-defined for all age groups, we know that loads associated with weight-bearing activity play a critical role in shaping the architecture of the skeleton across the lifespan.

Functional adaptation – matching bone mass and architecture to functional demands – is determined by strain or deformation of bone tissue [11]. During voluntary activities, muscle forces are thought to produce the greatest loads on the skeleton and to be the primary source of mechanical strains [12]. In turn, strain characteristics, including magnitude, distribution and rate, influence mechanically adaptive bone modeling and remodeling through feedback loops [3]. For example, an increase in strain magnitude beyond a customary level, or setpoint, leads to modifications in bone structure (i.e., periosteal apposition). These adaptations lead to enhanced mechanical competence and return bone strains at the skeletal site back to the 'customary' strain. This regulatory system controlled by the strain environment is commonly referred to as the 'mechanostat' [3]. The customary strain level and the ability of the skeleton to respond appropriately to changes in the strain environment are determined, largely, by genetics [13]. However, other factors, such as nutrition and hormones, also influence skeletal adaptations during growth and with aging.

Importantly, the growing skeleton has a greater capacity to adapt to loads associated with weight-bearing exercise than the mature skeleton. This was clearly demonstrated in several studies of racquet-sport athletes, where age at training initiation significantly influenced the structural differences between playing and nonplaying arms [14]. Specifically, female athletes who began their training prior to menarche demonstrated significantly greater side-to-side differences in bone strength (bone strength index [BSI], measured by pQCT) than athletes who began their training after menarche (FIGURE 1). During growth, bone can adapt its strength in response to mechanical stimuli via several mechanisms; bone cross-sectional area can increase owing to the addition of new bone on the periosteal surface (periosteal apposition), cortical thickness can increase owing to both periosteal apposition and reduced endocortical resorption and tissue density can increase through modifications to cortical and/or trabecular microarchitecture (i.e., increased trabecular thickness) [15,16]. By contrast, the adult skeleton adapts primarily through changes in material properties such as increased cortical or trabecular density or altered bone-mass distribution [17,18]. However, in response to a loss of bone mass at menopause, bone may undergo periosteal expansion as a mechanism to maintain bone strength and resist fracture [19].



Side-to-side difference	Young starters	Old starters	Controls
Total CSA	12.3	5.3	3.4
Cortical CSA	20.0	9.2	3.1
Cortical BMD	-0.8	-0.7	-0.9
Bone strength	26.5	10.2	4.0

Figure 1. Demonstrates mean side-to-side differences in humeral midshaft total-bone cross-sectional area, cortical cross-sectional area, (volumetric) cortical bone mineral density and bone strength (bone strength index; density-weighted polar section modulus) between the playing and nonplaying arm of female racquet-sport athletes as measured with peripheral quantitative computed tomography. The solid line represents the playing arm (or dominant in controls) and the dashed line represents the nonplaying arm (or nondominant in controls). Players who began playing before puberty accrued significantly more bone strength compared with players who began playing after puberty and controls.
BMD: Bone mineral density; CSA: Cross-sectional area.
Adapted from [14] and [16].

Measurement of bone strength

As outlined above, skeletal adaptations to weight-bearing physical activity involve more complex structural and architectural changes than simply an increase in bone mass. Ultimately, changes in the bone's material and structural properties influence whole bone mechanical competence or strength [20]. BMC and aBMD obtained using DXA are commonly used clinical surrogates for bone strength. However, these two-dimensional DXA measures are unable to assess bone geometry and microarchitecture, which directly influence overall bone strength in the trabecular and cortical bone compartments. This was clearly illustrated in a study of postmenopausal women by Adami and colleagues [17]. Exercise-induced changes in BMC or aBMD were minimal or nonexistent, yet modifications to pQCT-derived cortical bone area of the ultradistal radius were observed in the exercise group. Owing to the limitations of DXA, there has been a paradigm shift and the focus of bone research has broadened beyond bone mass to encompass the key concept of bone strength and the bone properties that underpin it.

A number of imaging modalities and software applications are available to more accurately capture bone structural adaptations to physical activity and estimate the effects of physical activity on bone strength. These include pQCT, MRI and hip structure analysis (HSA) from DXA images. The most recent evolution, high-resolution pQCT (XtremeCT [Scanco Medical AG, Bruettisellen, Switzerland]), evaluates bone microstructure in the growing [21,22] and adult [23] skeleton and together with finite element analysis, estimates bone strength of the distal radius and tibia [24]. Together, these innovative tools allow researchers to address more complex questions and help to further our understanding of bone adaptations to physical activity during growth and with aging.

Across these modalities, investigators use a number of parameters to describe bone structure, or cross-sectional geometry, at various skeletal sites including bone cross-sectional area, periosteal and endosteal circumferences, cortical thickness and the cross-sectional moment of inertia (CSMI). In HSA studies, section modulus (Z) is commonly used as a measure of bone's resistance to bending forces at the femoral neck (FN). In pQCT studies, common estimates of bone strength include the BSI, which incorporates cross-sectional area and volumetric BMD (vBMD) and estimates bone strength in compression at distal sites [14,25], and the polar strength–strain index (SSIp), which is a density-weighted section modulus and estimates bone's resistance to torsion at shaft sites (FIGURE 2) [26]. The CSMI is also used as an indicator of bone strength in bending or torsion at shaft sites [27]. Importantly, since bone strength cannot be measured directly in clinical studies, these outcomes are all used as estimates of bone strength. In the present review, we use the term 'bone strength' and provide the specific variable that was used to estimate bone strength in brackets.

Physical activity programs for children's bone health

In has been almost two decades since childhood was recognized as a crucial time to adopt lifestyle habits known to prevent osteoporosis [28]. There is now a substantial body of evidence to support the influential role of weight-bearing physical activity for optimizing bone-mass and strength accrual during growth [29]. This contention is well supported by numerous excellent reviews that have been published in the last several years [16,30,31], since all concluded that appropriate physical activity positively influences the normal pattern of bone-mass and strength accrual. Despite this body of knowledge, we still do not know the optimal exercise prescription to enhance bone strength in children, nor do we know the precise timing of the 'window of opportunity' when the growing skeleton is most responsive to exercise-induced loads.

To effectively enhance children's bone health, physical activity programs must be evidence-based and reflect what is known about bone's response to loading. The majority of the school-based interventions conducted to date were comprised of high-impact activities designed to incur 'physiological loads' on the growing skeleton [3]. A number of jumping-based programs [32–38] were also based, in part, on Charles Turner's 'three rules for adaptation' [39]: adaptation is driven by dynamic loading; short bouts of loading are more osteogenic than long bouts; and adaptation is 'error-driven', meaning that abnormal strains drive structural change. In addition, the design of jumping programs [38,40] was based on results from animal studies that suggested short bouts of dynamic activity followed by rest periods were more effective than longer bouts of activity [41]. These jumping- or circuit-based programs were most often implemented in schools and were incorporated into physical education (PE) or the regular classroom where large numbers of children could be reached. Importantly, if an exercise program is to be sustained, it must be simple and deliverable by trained or untrained individuals (often generalist teachers). The Bounce at the Bell component of Action Schools! British Columbia (BC) provides one example of a successful school-based program. Since the jumps took only a few minutes, they could easily be incorporated into the daily classroom routine, did not require additional equipment or space and were associated with low teacher burden. An alternative school-based approach was to modify the PE curriculum or increase the time devoted to PE. These strategies were effective for enhancing bone-mass accrual in boys and girls [42–44]; however, further study is required to determine if this approach is an effective means to augment bone strength. In addition, the demands placed on teachers and schools to adapt and deliver a modified school curriculum may limit the feasibility and sustainability of these programs in many countries.

Most of the evidence that supports the effectiveness of the various physical activity programs in enhancing children's bone health comes from DXA-based trials [31]. These studies ranged from 3–48 months and the children assigned to exercise intervention groups gained significantly more bone mass at several skeletal sites, including the FN and lumbar spine, compared with children in control groups [15,34–36,38,40]. However, as discussed, the limitations of DXA do not permit the investigation of bone structural adaptations. Of the intervention trials conducted in the last 10 years that evaluated exercise, only six used technologies such as HSA, MRI and pQCT to evaluate exercise-induced changes in bone geometry, vBMD and estimated bone strength (TABLE 1) [15,34–38,40,43,45].

In the longest school-based randomized, control trial (RCT), MacKelvie and colleagues reported that after 20 months of the Healthy Bones Study (HBS) high-impact circuit training program, boys in intervention schools demonstrated a significantly greater increase in FN cross-sectional area compared with boys in control schools [35]. This structural adaptation suggests that periosteal apposition had increased and this explains the associated greater gain in FN bone bending strength (section modulus). Interestingly, the intervention-related gains in FN bone strength were not observed in boys after only 7 months [McKay H, University of British Columbia, Vancouver, BC, Canada, Unpublished data] but were observed in girls [15]. The difference in timing of structural adaptations to the HBS intervention between sexes is likely to be related to maturity status. Whereas the majority of boys were prepubertal at baseline, 60% of the girls were early pubertal and it was in this group that the greater gains in FN bone strength occurred [15]. Thus, the advanced maturity status of boys over the second year of the study and/or the prolonged intervention may explain the later adaptation at the FN. The absence of exercise-related gains in bone strength (and bone mass) at the FN in prepubertal boys and girls is in agreement with findings from other school-based studies [38,43] and suggests that although exercise-related periosteal apposition is thought to occur during prepuberty when the bones undergo rapid expansion owing to normal growth [16,46], early puberty may be a window of opportunity for structural adaptations at the FN. It is also possible that a more intense intervention may be required to elicit an osteogenic effect at the hip during prepuberty. Fuchs and colleagues [32] observed significantly greater gains in total-hip BMC in exercising prepubertal boys and girls than in controls following 7 months of a jumping program that was associated with ground reaction forces nine times that of body weight. This is considerably higher than the two to five times body weight across other studies [35,38]. It is not known whether this high-impact activity also results in significant structural changes at the FN or other skeletal sites.

Although HSA estimates bone strength at the clinically relevant FN, deriving three-dimensional properties from two-dimensional DXA images has known limitations. Thus, HSA results must be interpreted with these in mind. In order to more accurately capture exercise-related changes in bone cross-sectional geometry and vBMD, several intervention studies used pQCT at the weight-bearing tibia [34,36,40,45]. Of these studies, Action Schools! BC was the first RCT to demonstrate that short bouts of classroom-based physical activity significantly impact tibial bone strength [36,40]. At the distal tibia, prepubertal boys in the intervention group had greater gains in the estimated bone strength (BSI) than boys of the same maturity in control schools. This was mainly due to exercise-related gains in vBMD as opposed to an increase in cross-sectional area. This finding is consistent with resistance to the primarily compressive loads at this site being a function, in large part, of trabecular density [21] and agrees with pQCT results from a jumping intervention [34] as well as cross-sectional athlete studies [47]. At the tibial midshaft where bending and torsional loads predominate [48], we applied a novel method of pQCT analysis to further explore observed trends for greater gains in torsional bone strength (SSIp) in intervention boys [36,40]. The moderate gains in bone strength (SSIp) were associated with an approximately

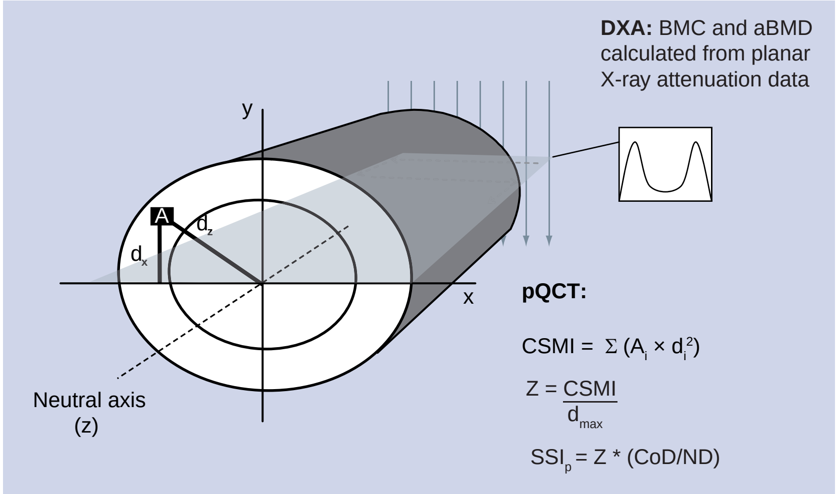


Figure 2. Long bone that demonstrates the difference between two-dimensional measures of bone mineral content and areal bone mineral density by dual energy x-ray absorptiometry calculated from planar x-ray attenuation data and the three-dimensional measures of bone cross-sectional geometry, and estimates of bone strength obtained with peripheral quantitative computed tomography. The CSMI (mm^4) describes the distribution of bone material about a specific axis and is calculated as the integral sum of the products of A_i and d^2 of the corresponding voxel to the bending (x, y) or torsion (z) axes. Z (mm^3) estimates bone's resistance to bending and is calculated as the CSMI divided by the maximum distance from the bending axis to the outer surface (d_{max}). The SSIp (mm^3) is a density-weighted estimate of bone strength in torsion and is calculated as the product of the section modulus and the ratio of CoD and the ND (SSIp = 1200 mg/cm^3) [26].
A: Area of each pixel; aBMD: Areal bone mineral density; A_i: Area of each voxel; BMC: Bone mineral content; CoD: Cortical bone density; CSMI: Cross-sectional moment of inertia; d^2: Squared distance; d_x: Distance of the pixel from the corresponding bending axis; d_z: Distance of the pixel from the corresponding torsion axis; ND: Normal physiological bone density; pQCT: Peripheral quantitative computed tomography; SSIp: Polar strength–strain index; Z: Section modulus.
Adapted from [27].

Table 1. Randomized, controlled and controlled exercise intervention studies in boys and girls with bone geometry and strength outcomes.

Study	Subjects	Subjects & study design	Intervention	Results (% difference EX vs CON)	Ref.
DXA with HSA					
Petit *et al.* (2002)	Girls: n = 174; pre- and early pubertal; 57% Caucasian and 34% Asian Mean age: Prepubertal: 10.0 ± 0.6 years Early pubertal: 10.5 ± 0.6 years	7-month RCT Group allocation (randomized by school, stratified by number of subjects and ethnicity as per MacKelvie *et al.* [33,35]): EX: n = 86 (43 prepubertal, 43 early pubertal) CON: n = 88 (25 prepubertal, 63 early pubertal) Imaging: DXA with HSA analysis Compliance: 61%	Program: School-based, high-impact jumping program integrated into school physical education classes. GRF = 3.5–5 times that of BW Frequency and duration: 10–12 min, three times per week for 7 months Progression: Number of jumps and height of jump (progressed through levels). Started with 50 jumps per session and progressed to 100 jumps per session	Prepubertal: EX and CON Early pubertal (EX > CON, $p < 0.05$): NN CSA: +2.3% NN C.Th: +3.2% NN ED: NS NN bone strength (Z): +4.0% IT ED: -1.4% IT C.Th: NS IT CSA: NS IT bone strength (Z): NS FS: NS	[15]
MacKelvie *et al.* (2003) MacKelvie *et al.* (2004)	Boys and girls: n = 139; pre- and early pubertal; 57% Caucasian, 34% Asian and 9% other ethnicity Mean age: Boys: 10.2 ± 0.5 years (EX) and 10.1 ± 0.5 years (CON) Girls: 9.9 ± 0.6 years (EX) and 10.3 ± 0.4 years (CON)	20-month RCT Group allocation (randomized by school, stratified by number of subjects/school and ethnicity): EX: n = 64 (31 boys, 32 girls; boys all prepubertal, girls pre- and early pubertal at baseline) CON: n = 76 (33 boys, 43 girls; boys all prepubertal, girls pre- and early pubertal at baseline) Imaging: DXA with HSA analysis Compliance: 61%	Program: School-based, high-impact jumping program integrated into school physical education classes. GRF = 3.5–5 times that of BW Frequency and duration: 10–12 min, three times per week for 2 school years (20 months) Progression: Number of jumps and height of jumps advanced every 8–10 weeks: Year 1: 50 (baseline) to 100 (final) jumps; year 2: 55 (baseline) to 132 (final) jumps	Boys [35]: TB, LS, PF and TR BMC: NS FN BMC: +4.3% ($p < 0.01$) NN CSA and SPW: +2.5–2.6%, NS NN ED: +2.9%, NS NN C.Th: NS NN CSMI: +12.4% ($p < 0.05$) NN bone strength (Z): +7.5% ($p < 0.05$) Girls [33]: TB, PF and TR BMC: NS FN BMC: +4.6% ($p < 0.05$) LS BMC: +3.7% ($p < 0.05$) No 20-month HSA results for girls	[33,35]

BA: Bone area; BMAD: Bone mineral apparent density; BMC: Bone mineral content; BSI: Bone strength index; BUA: Broadband ultrasound attenuation; BW: Body weight; CoA: Cortical bone area; CoD: Cortical bone density; CON: Control; CSA: Cross-sectional area; CSMI: Cross-sectional moment of inertia; C.Th: Cortical thickness; DXA: Dual energy x-ray absorptiometry; ED: Endosteal diameter; EX: Exercise group; FN: Femoral neck; FS: Femoral shaft; GRF: Ground reaction force; HSA: Hip-structural analysis; IBS: Index of bone structural strength; I_{max}: Maximum second moment of area; I_{min}: Minimum second moment of area; IT: Intertrochanteric region; LS: Lumbar spine; LS3: Third lumbar vertebrae; NN: Narrow neck; NS: Not significant; PF: Proximal femur; pQCT: Peripheral quantitative computed tomography; RCT: Randomized, control trial; SPW: Sub-periosteal width; SSIp: Polar strength–strain index; TB: Total body; ToA: Total bone cross-sectional area; ToD: Total bone mineral density; TR: Trochanter; Z: Section modulus.

Table 1. Randomized, controlled and controlled exercise intervention studies in boys and girls with bone geometry and strength outcomes.

Study	Subjects	Subjects & study design	Intervention	Results (% difference EX vs CON)	Ref.
DXA with HSA (cont.)					
Weeks *et al.* (2008)	Boys and girls: n = 79; 53% Caucasian; Tanner stage 5 (postpubertal) Mean age: 13.8 ± 0.4 years	8-month RCT Group allocation (randomized by individual): EX: n = 42 (30 girls, 22 boys) CON: n = 37 (23 girls, 24 boys) Imaging: DXA: TB, FN and LS Ultrasound: calcaneus Compliance: 80%	Program: Jumping activity included in physical education class Frequency: 10 min (~300 jumps), two times per week for 8 months Progression: Maximum of 300 jumps was achieved gradually	Boys: TB BMC: +4.3% (p = 0.03) FN BMC, BA and CSMI: NS LS BMC, BA and BMAD: NS LS bone strength (IBS): NS Calcaneal BUA: NS Girls: No significant differences in change between groups for any outcome	[37]
Macdonald *et al.* (2008)	Boys and girls: n = 410; pre- and early pubertal; 35% Caucasian, 53% Asian and 12% mixed ethnicity Mean age: Boys: 10.2 ± 0.5 years (EX), 10.3 ± 0.7 years (CON) Girls: 10.2 ± 0.6 years (EX), 10.2 ± 0.5 years (CON)	16-month RCT Group allocation (randomized by school, stratified by school size): EX: n = 293 (151 boys, 142 girls) CON: n = 117 (62 boys, 55 girls) Imaging: DXA with HSA analysis Compliance: 74% with ‘Bounce at the Bell’	Program: Action Schools! BC program (Classroom Action) and Bounce at the Bell; 5–12 countermovement or side-to-side jumps per session performed in the classroom. GRF = 3.5–5 times that of BW Frequency and duration: Classroom Action– 15 min, five times per week for 16 months; Bounce at the Bell – 3 min, three times per day, four times per week for 16 months Progression: Number of jumps increased every month up to a maximum of 36 jumps per day	Boys: TB BMC: +1.7% (p = 0.03) LS BMC: +2.7% (p = 0.05) PF and FN BMC: NS FN CSA and SPW: NS FN bone strength (Z): NS Girls: Intent-to-treat analysis TB and LS BMC: NS FN BMC: +2% (p = 0.2) FN CSA: +2% (p = 0.1) FN SPW: NS FN bone strength (Z): +3.5% (p = 0.1) Efficacy subgroup analysis FN BMC: +3.7% (0.04) FN CSA: +3.7% (p = 0.04) FN SPW: NS FN bone strength (Z): +5.4% (p = 0.05)	[38]

BA: Bone area; BMAD: Bone mineral apparent density; BMC: Bone mineral content; BSI: Bone strength index; BUA: Broadband ultrasound attenuation; BW: Body weight; CoA: Cortical bone area; CoD: Cortical bone density; CON: Control; CSA: Cross-sectional area; CSMI: Cross-sectional moment of inertia; C.Th: Cortical thickness; DXA: Dual energy x-ray absorptiometry; ED: Endosteal diameter; EX: Exercise group; FN: Femoral neck; FS: Femoral shaft; GRF: Ground reaction force; HSA: Hip-structural analysis; IBS: Index of bone structural strength; I_{max}: Maximum second moment of area; I_{min}: Minimum second moment of area; IT: Intertrochanteric region; LS: Lumbar spine; LS3: Third lumbar vertebrae; NN: Narrow neck; NS: Not significant; PF: Proximal femur; pQCT: Peripheral quantitative computed tomography; RCT: Randomized, control trial; SPW: Sub-periosteal width; SSIp: Polar strength–strain index; TB: Total body; ToA: Total bone cross-sectional area; ToD: Total bone mineral density; TR: Trochanter; Z: Section modulus.

Table 1. Randomized, controlled and controlled exercise intervention studies in boys and girls with bone geometry and strength outcomes.

Study	Subjects	Subjects & study design	Intervention	Results (% difference EX vs CON)	Ref.
DXA with HSA (cont.)					
Alwis *et al.* (2008)	Boys: n = 127; Caucasian; prepubertal Mean age: EX: 7.8 ± 0.6 years CON: 8.0 ± 0.6 years	2-year controlled trial Group allocation: not randomized EX: n = 76 CON: n = 51 Imaging: DXA with HSA analysis Compliance: 95%	Program: Increased curricular time for physical education; indoor and outdoor activities, including ball games, running, jumping and climbing Frequency and duration: 40 min, five times per week for 24 months Progression: None stated	TB BMC: NS LS3 BMC: +6% ($p < 0.01$) FN BMC: NS LS3 width: +2.6% ($p < 0.01$) FN width: NS FN CSA: NS FN CSMI: NS FN bone strength (Z): NS	[43]
pQCT					
Heinonen *et al.* (2000)	Girls: n = 130; Caucasian; pre- and postmenarcheal Mean age: Premenarcheal: 11.7 ± 0.3 years (EX), 11.0 ± 0.9 years (CON) Postmenarcheal: 13.7 ± 0.9 years (EX), 13.1 ± 1.0 years (CON)	9-month controlled trial Group allocation: not randomized EX: n = 64 (25 premenarcheal, 39 postmenarcheal) CON: n = 66 (33 premenarcheal, 33 postmenarcheal) Imaging: DXA: LS, FN and TR pQCT: tibial midshaft Compliance: 65% (average of 1.3 exercise sessions per week) in the training group	Program: Jump training sessions, two- and one-foot jumps, used jump boxes and also did aerobic exercises Frequency and duration: 50 min (20 min jumping), twice per week for 9 months Progression: Month 1: 100 two-leg jumps, no box Months 2–3: box jumps incorporated and the number of box jumps gradually increased over this period Months 4–6: 125 two-leg and 25 one-leg box jumps Months 7–9: 150 two-leg and 50 one-leg box jumps (multidirectional)	Premenarcheal: LS BMC: +3.3% FN BMC: +4.0% TR BMC: NS Tibial midshaft: CoD and CoA: NS Bone strength (BSI): NS Postmenarcheal: No significant difference between EX and CON for change in any bone outcome	[45]

BA: Bone area; BMAD: Bone mineral apparent density; BMC: Bone mineral content; BSI: Bone strength index; BUA: Broadband ultrasound attenuation; BW: Body weight; CoA: Cortical bone area; CoD: Cortical bone density; CON: Control; CSA: Cross-sectional area; CSMI: Cross-sectional moment of inertia; C.Th: Cortical thickness; DXA: Dual energy x-ray absorptiometry; ED: Endosteal diameter; EX: Exercise group; FN: Femoral neck; FS: Femoral shaft; GRF: Ground reaction force; HSA: Hip-structural analysis; IBS: Index of bone structural strength; I_{max}: Maximum second moment of area; I_{min}: Minimum second moment of area; IT: Intertrochanteric region; LS: Lumbar spine; LS3: Third lumbar vertebrae; NN: Narrow neck; NS: Not significant; PF: Proximal femur; pQCT: Peripheral quantitative computed tomography; RCT: Randomized, control trial; SPW: Sub-periosteal width; SSIp: Polar strength–strain index; TB: Total body; ToA: Total bone cross-sectional area; ToD: Total bone mineral density; TR: Trochanter; Z: Section modulus.

Table 1. Randomized, controlled and controlled exercise intervention studies in boys and girls with bone geometry and strength outcomes.

Study	Subjects	Subjects & study design	Intervention	Results (% difference EX vs CON)	Ref.
pQCT (cont.)					
Johannsen *et al.* (2003)	Boys and girls: n = 54; pre-, peri- and postpubertal Mean age: EX: 10.3 ± 5.3 years CON: 10.0 ± 5.1 years	12-week RCT Group allocation: Randomized (blocks of two) by gender and age group EX: n = 28 (17 girls, 11 boys, 13 pre-, 5 peri- and 10 postpubertal) CON: n = 26 (14 girls, 12 boys, 13 pre-, 7 peri- and 6 postpubertal) Imaging: DXA pQCT: distal tibia Compliance: 76 ± 18% (range: 11–96%) of the total possible jumps completed by the intervention group	Program: High-impact jumping program conducted in schools and childcare centers. Children jumped off a 45 cm high box, GRF = 4–5 times that of BW Frequency and duration: 25 jumps per day, five times per week for 12 weeks Progression: None stated	Main effects: TB BMC: EX > CON (~1%) Leg BMC: EX > CON (~1.5%) pQCT: NS Interaction effects (group times maturity): Tib BMC (4% site): p = 0.04 LS BMC: p = 0.10 ToD (4% site): p = 0.03 Intervention effect in pubertal group only (Tanner stage 4 or 5)	[34]

BA: Bone area; BMAD: Bone mineral apparent density; BMC: Bone mineral content; BSI: Bone strength index; BUA: Broadband ultrasound attenuation; BW: Body weight; CoA: Cortical bone area; CoD: Cortical bone density; CON: Control; CSA: Cross-sectional area; CSMI: Cross-sectional moment of inertia; C.Th: Cortical thickness; DXA: Dual energy x-ray absorptiometry; ED: Endosteal diameter; EX: Exercise group; FN: Femoral neck; FS: Femoral shaft; GRF: Ground reaction force; HSA: Hip-structural analysis; IBS: Index of bone structural strength; I_{max}: Maximum second moment of area; I_{min}: Minimum second moment of area; IT: Intertrochanteric region; LS: Lumbar spine; LS3: Third lumbar vertebrae; NN: Narrow neck; NS: Not significant; PF: Proximal femur; pQCT: Peripheral quantitative computed tomography; RCT: Randomized, control trial; SPW: Sub-periosteal width; SSIp: Polar strength–strain index; TB: Total body; ToA: Total bone cross-sectional area; ToD: Total bone mineral density; TR: Trochanter; Z: Section modulus.

Table 1. Randomized, controlled and controlled exercise intervention studies in boys and girls with bone geometry and strength outcomes.

Study	Subjects	Subjects & study design	Intervention	Results (% difference EX vs CON)	Ref.
pQCT					
Macdonald *et al.* (2007) Macdonald *et al.* (2009)	Boys and girls: n = 410; 35% Caucasian, 53% Asian and 12% mixed ethnicity	16-month RCT Group allocation: (randomized by school, stratified by school size): EX: n = 281 (145 boys, 136 girls) CON: n = 126 (64 boys, 65 girls) Imaging: pQCT: distal and midshaft tibia with ImageJ and MomentMacro analysis Compliance: 74% with 'Bounce at the Bell'	Program: Action Schools! BC program (Classroom Action) and Bounce at the Bell; 5–12 countermovement or side-to-side jumps per session performed in the classroom GRF = 3.5–5 times that of BW Frequency and duration: Classroom Action – 15 min, five times per week for 16 months; Bounce at the Bell – 3 min, three times per day, four times per week for 16 months Progression: Number of jumps increased every month up to a maximum of 36 jumps per day	Analysis 1 [36] (boys and girls): Boys: p-value for group times maturity interaction Distal Tibia: ToA: NS ToD: +2.3% ($p = 0.07$) Bone strength (BSI): +5% ($p = 0.03$) (prepubertal boys) Midshaft tibia: CoA and CoD: NS Bone strength (SSIp): +2.3%, NS (prepubertal boys) Girls: no significant between group differences for change in pQCT outcomes Analysis 2 [40] (boys only): I_{max}: +3% ($p = 0.03$) I_{min}: +2%, NS CoA and C.Th by quadrant: +1–1.4%, NS	[36,40]

BA: Bone area; BMAD: Bone mineral apparent density; BMC: Bone mineral content; BSI: Bone strength index; BUA: Broadband ultrasound attenuation; BW: Body weight; CoA: Cortical bone area; CoD: Cortical bone density; CON: Control; CSA: Cross-sectional area; CSMI: Cross-sectional moment of inertia; C.Th: Cortical thickness; DXA: Dual energy x-ray absorptiometry; ED: Endosteal diameter; EX: Exercise group; FN: Femoral neck; FS: Femoral shaft; GRF: Ground reaction force; HSA: Hip-structural analysis; IBS: Index of bone structural strength; I_{max}: Maximum second moment of area; I_{min}: Minimum second moment of area; IT: Intertrochanteric region; LS: Lumbar spine; LS3: Third lumbar vertebrae; NN: Narrow neck; NS: Not significant; PF: Proximal femur; pQCT: Peripheral quantitative computed tomography; RCT: Randomized, control trial; SPW: Sub-periosteal width; SSIp: Polar strength–strain index; TB: Total body; ToA: Total bone cross-sectional area; ToD: Total bone mineral density; TR: Trochanter; Z: Section modulus.

3% greater gain in the biomechanically relevant maximum second moment of area. In addition, changes in cortical area and thickness in the anterior, medial and posterior quadrants of the bone cross-section tended to be greater in intervention boys (Figure 3), reflecting the predominantly anterior–posterior bending loads at the tibial shaft [48]. These region-specific adaptations were consistent with those reported in animal studies [41] and highlight how three-dimensional imaging techniques advance our understanding of bone structural adaptations to physical activity.

Although jumping programs appear to enhance tibial bone strength in boys, it is not clear whether girls benefit to the same extent. Neither the Action Schools! BC [36], nor a more intensive drop-jumping program [45], resulted in significant structural adaptations at the tibia in peripubertal girls. The lack of an osteogenic effect at the tibia in girls may be related to increased estrogen levels that are thought to modulate the bone response to physical loads by: increasing bone stiffness (via increases in cortical vBMD) [49] which, in turn, leads to a decrease in the amount of deformation for a given load; or inhibiting periosteal apposition [50]. Thus, it is possible that in girls, the window of opportunity for bone strength gains at the tibia occurs during prepuberty or earlier.

Together, the aforementioned studies provide convincing evidence that physical activity positively influences the normal trajectory of bone-mass accrual in children, although the bone response appears to be sex, maturity and site specific. In addition to intervention trials, results from well-designed prospective, observational studies also highlight the important role of physical activity in ensuring optimal skeletal development during childhood [51–53]. By contrast, bone structural adaptations to weight-bearing activity during adolescence and young adulthood are understood to a lesser degree. In a recent school-based RCT, Weeks *et al.* [37] found that 8 months of a classroom-based jumping program did not significantly augment DXA estimates of FN bone strength (CSMI and BSI) in adolescent girls and boys (13.8 years of age at baseline). It is not clear whether the lack of an intervention effect was due to an insufficient stimulus, limitations associated with the two-dimensional estimates of bone geometry and strength or the more advanced maturity status of the participants. Results from athlete studies indicate that the latter two explanations may be most appropriate in this adolescent cohort.

In female racquet-sport athletes, side-to-side differences in pQCT-estimated bone strength (BSI) of the mid-humerus were 14% greater in women who began their training prior to, or at, menarche ('young starters') compared with women who began training after menarche ('old starters') [14]. This result provides further support for the window of opportunity occuring during pre- and early puberty when the skeleton is most responsive to loading. Furthermore, it is possible that structural adaptations to weight-bearing activity during the later stages of puberty may differ from those observed during the early pubertal years. In the study of racquet-sport athletes, the bone strength advantage in the young starters was due to a larger cortical area that is likely to result from greater periosteal expansion than in the old starters [14]. By contrast, Bass *et al.* [54] reported that exercise initiated after puberty was associated with endocortical apposition at the mid-humerus that would confer little benefit to bone bending strength. As discussed, rising estrogen levels in girls are likely to mediate these geometric modifications and the resultant changes in bone strength. Further study is required to determine the optimal timing during puberty when exercise-related gains in bone strength are maximized in both boys and girls.

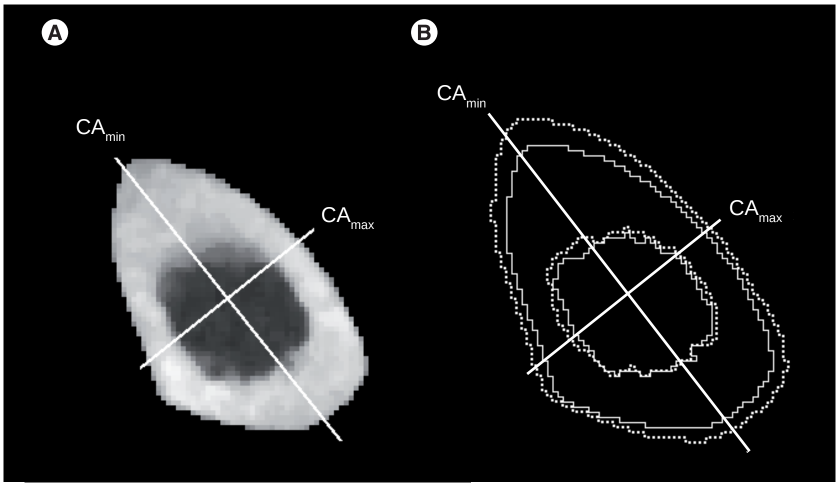


Figure 3. Peripheral quantitative computed tomography images of the tibial midshaft from the Action Schools! BC study. (A) Representative baseline pQCT image of an intervention boy's left tibia with the CA_{max} and CA_{min} superimposed. **(B)** Superimposition of the baseline (solid) and follow-up (dashed) bone surfaces demonstrates the primary anatomic sites where bone was formed in response to the intervention. The alignment of these images was based upon minimization of pixel greyscale differences. The apparent trend for greater periosteal apposition on the anterior and posterior surfaces lead to a significantly greater gain in bone bending strength (I_{max}) in intervention boys compared with controls.
CA_{max}: Maximum centroidal axis; CA_{min}: Minimum centroidal axis; I_{max}: Maximum second moment of area; pQCT: Peripheral quantitative computed tomography
Adapted from [40] with permission from Springer.

Whether these activity-related gains in bone mass and strength are maintained into adulthood and lead to reduced fracture risk is unknown. Owing to methodological challenges, no long-term prospective trials have been (and may never be) conducted, with fracture as an outcome, that demonstrate a definitive link between childhood and adolescent bone mass and strength and decreased fracture risk. However, athlete studies and observational studies of leisure-time activity suggest that bone gains achieved from weight-bearing activity during childhood are maintained into young adulthood [55,56] and may reduce fracture-risk later in life [57]. In addition, the longest follow-up study of a school-based intervention [58] found that almost 8 years after cessation of the jumping program, children from the intervention group maintained a 1.4% benefit in total-hip BMC compared with the control group. Thus, children should be encouraged to adopt and maintain a physically active lifestyle during growth and adolescence and into adulthood.

Physical activity & bone health in adults

The role of physical activity in adult bone health is primarily to conserve bone mass and strength and in later life, to diminish bone loss. In this section we highlight evidence that addresses the relationship between physical activity and bone strength in pre- and postmenopausal women and men.

Premenopausal women

The effects of physical activity on bone health in premenopausal women are less studied than in postmenopausal women [59]. Despite this, meta-analyses of RCTs highlight a small, protective role of impact and nonimpact exercise [59] and resistance training for lumbar spine aBMD assessed by DXA [60]. High-impact exercise and resistance training may also conserve bone mass at the FN; however, further study of premenopausal women is required to confirm the benefits of exercise on bone mass at this site [59,60].

Questions also remain regarding the influence of impact exercise or resistance training on bone structure and strength at the FN in premenopausal women. In a recent 10-year prospective observational study, premenopausal women who reported more physical activity at baseline maintained greater BMC at the trochanter than their inactive peers over the entire study period [61]. Despite the greater bone mass, FN bone strength, estimated using HSA (section modulus), was not significantly different in active versus inactive women. By contrast, bone mass and strength (section modulus) at the FN was 6–10% greater in active compared with inactive postmenopausal women [61]. Thus, it is possible that the benefits of physical activity on proximal femur bone strength may not become apparent until older age when the rate of decline in FN bone strength is greater [61].

As discussed above, the inherent limitations of HSA may not permit us to clearly identify relationships between physical activity and bone structure. However, only one RCT evaluated the effects of an exercise intervention on bone structure and strength in premenopausal women using a three-dimensional imaging tool. Vainionpää and colleagues in Finland [62] randomized women aged 35–40 years to carry out either 12 months of bone loading activities (step patterns, jumping, running, walking etc.) or normal daily activity (control group). Upon completion of the intervention, the bone structural response (by spiral QCT) to the intervention varied by skeletal site. At the mid-femur, the exercise group demonstrated a small, but significant, increase in bone circumference compared with the control group [62]. Although bone strength (assessed as CSMI) was not significantly impacted by the intervention, it is possible that with a longer intervention, further changes in bone circumference may translate into gains in bone bending strength at this site [62]. By contrast, at the proximal tibia, positive changes in bone geometry were only apparent in those women who were more compliant with the exercise program. Specifically, a 1.2% improvement in bone circumference was achieved in the most compliant group as well as a 0.5% increase in cortical cross-sectional area. These structural adaptations resulted in a 2.5% increase in estimated bone strength (CSMI) [63]. Thus, structural adaptations to weight-bearing physical activity enhanced bone strength in premenopausal women. However, as in all exercise intervention trials, there is a need to ensure good compliance if strength gains are to be achieved.

The Vainionpää *et al.* study was also unique in that they used accelerometry to capture physical activity patterns across the 1-year study [62]. Most commonly, adult studies use subjective physical activity measurement techniques such as self-report questionnaires. It is a clear advance that these researchers used accelerometers to objectively measure exercise intensity. In addition, they estimated the number of daily impacts from acceleration data to describe the level of impact loading associated with common physical activities [62]. Pooled control and intervention accelerometry data demonstrated that 12-month changes in the CSMI at the mid-femur were positively associated with acceleration levels of 1.1 g or more (i.e., stepping). Changes in cortical thickness were associated with acceleration levels of 3.9 g or more (i.e., jumping and running) [62]. Furthermore, in multiple regression analyses, the number and intensity of impacts accumulated over the study were significant predictors of change in mid-femur bone geometry. These data suggest that even relatively low-impact exercise (1.1 g) may be associated with improved bone structure in premenopausal women. They also highlight that accelerometry may be an important tool to determine the intensity of activity that stimulates bone strength adaptation.

Based on available evidence, we do not yet know the specific (or optimal) exercise prescription to enhance bone strength in premenopausal women. Further study is required to determine whether resistance training or a combination of resistance training and impact exercise preserves or enhances bone strength at the clinically relevant FN, lumbar spine or the peripheral skeleton. In addition, we need to better understand how changes in muscle mass, strength and power as a result of exercise relate to bone structural adaptations in premenopausal women. This new knowledge would serve to guide the design of effective exercise programs for this population.

Postmenopausal women

Several systematic reviews [60,64–66] summarize the considerable body of evidence that supports a protective effect of physical activity on bone mass (assessed by DXA) at clinically relevant sites in postmenopausal women. Specifically, resistance training and impact activities, alone or in combination, effectively prevented bone loss at the proximal femur and lumbar spine in older women. In the most recent systematic review [66], the largest intervention-related effect sizes for aBMD at both the lumbar spine and FN were associated with exercise protocols that combined jogging with low-impact activities such as walking and stair-climbing. Exercise programs that combined diverse and high-impact activities, such as running and aerobics, with high-intensity resistance training were effective at the lumbar spine only [66]. Together, these findings suggest that effective exercise programs for bone health in postmenopausal women should include a mixed-loading regimen [67].

More recent studies have assessed bone structure, vBMD and bone strength in postmenopausal women and, together, they support the beneficial effects of physical activity on bone strength in this population (TABLE 2) [18,68–72]. Karinkanta and colleagues assessed bone strength at the tibial shaft (BSI by pQCT) in postmenopausal women of 70–79 years of age who trained at least 2 days per week [71]. They found that a combination of resistance training and balance–jump training maintained tibial bone strength in those women who trained at least two times per week. This was a function of a smaller decrease in cortical area in the exercise group compared with controls. The combined exercise program may have maintained cortical thickness, either through reduced bone resorption on the endocortical surface, or increased periosteal apposition. Notably, approximately 50% of the bone strength advantage was maintained in the training group 12 months after study completion [73]. Exercise-related adaptations in cortical bone properties were also observed at the distal tibia following 12 months of a high-impact jumping intervention in early postmenopausal women [68], and at the tibial midshaft after 25 weeks of agility training in women aged 75–85 years [69]. In addition, a recent cross-sectional study of postmenopausal women aged 45–65 years found that leisure-time physical activity was positively associated with cortical bone area and thickness at the femoral midshaft [74]. Future studies that undertake a region-specific analysis of cortical bone across bone quadrants or sectors would better represent the structural adaptation in the plane of bending related to the loading intervention [75,76]. Furthermore, analysis techniques that identify the polar distribution of bone mass would determine whether exercise-related maintenance of bone strength is a result of the redistribution of bone mass. This structural adaptation was reported following 12 months of resistance training in early postmenopausal women [18].

It would be ideal if maintenance of bone strength owing to exercise training in postmenopausal women was also evident at the clinically relevant proximal femur and lumbar spine. However, in the relatively few studies conducted, data were equivocal. A RCT that reported change in bone structure at the FN (by HSA) following resistance training suggested that this regimen may benefit bone strength (section modulus) in older postmenopausal women [71]. Conversely, high-impact jump training did not maintain FN bone strength (section modulus, by HSA) in early postmenopausal women [68]. It is possible that the loads associated with jump training were insufficient to elicit osteogenesis at the FN whereas resistance training that involves large muscle groups may be a more effective means to enhance proximal femur bone strength. That said, much less

Table 2. Randomized, controlled exercise intervention studies in pre- and postmenopausal women with bone geometry and strength outcomes.

Study	Subjects	Study design	Intervention	Results	Ref.
Vainionpää *et al.* (2007)	Premenopausal: 120 women, 35–40 years of age Mean age: 38 ± 2 years	12-month RCT Group allocation: EX: n = 60 CON: n = 60 Imaging: Spiral QCT: femur (50% site); tibia (5 and 67% sites) Compliance: Average of 0.9 classes per week, 2.2 home sessions per week	Program: Supervised high-intensity/-impact activities (stepping, stamping, jumping, running and walking) and home sessions of similar activities Frequency/duration: Supervised class: 60 min, three times per week for 12 months Home sessions: 10 min, seven days per week for 12 months Progression: Program modified bimonthly to include higher jumps and drops	Mid-femur (50% site): Intent-to-treat analysis Bone circumference: EX > CON, +0.2%, p = 0.03 Cortical CSA, BMD and C.Th: NS Bone strength (maximum and minimum CSMI): NS Proximal tibia (67% site): Subgroup analysis (most compliant > least compliant) Bone circumference: +1.2%, p = 0.03 Cortical CSA: +0.5%, p = 0.04 Bone strength (maximum CSMI): +2.5%, p = 0.05	[62]
Uusi-Rasi *et al.* (2003)	Postmenopausal: 164 women Mean age: 54 ± 2 years	12-month RCT Group allocation: EX: n = 41 AL: n = 41 EX + AL: n = 41 CON: n = 41 Imaging: pQCT: tibia (distal and midshaft) DXA and HSA: proximal femur and lumbar spine Compliance: Average of 1.6 ± 0.9 sessions per week	Program: Supervised sessions of multidirectional jumping exercises (aerobic jump program or step program) and calisthenics (nonimpact) AL: 5 mg daily Frequency/duration: 60 min, three times per week for 12 months Progression: Magnitude of jumps increased from 10–25 cm	Intent-to-treat analysis (results similar for efficacy analysis) Distal tibia: TrD and ToA: NS CoA/ToA: EX > CON, +3.7% (95% CI: 0.1–7.3) Bone strength (BSI): EX > CON, 3.6% (95% CI: 0.3–7.1%) Tibial midshaft: CoA and CoD: NS Bone strength (BSI): NS FN BMC: NS FN bone strength (Z): NS LS BMC: NS	[68]

aBMD: Areal bone mineral density; AL: Alendronate; AT: Agility training; BAL: Balance jump training; BMC: Bone mineral content; BMD: Bone mineral density; BSI: Bone strength index; CoA: Cortical bone area; CoD: Cortical density; CSA: Cross-sectional area; CSMI: Cross-sectional moment of inertia; C.Th: Cortical thickness; DXA: Dual energy x-ray absorptiometry; FN: Femoral neck; HAS: Hip structure analysis; HRT: Hormone-replacement therapy; I_{max}: Maximum second moment of area; I_{min}: Minimum second moment of area; Ip: Polar moment of inertia; LS: Lumbar spine; NS: Not statistically significant; PF: Proximal femur; pQCT: Peripheral quantitative computed tomography; QCT: Quantitative computed tomography; RCT: Randomized, controlled trial; RES: Resistance training; RM: Repetition maximum; SSIp: Polar strength–strain index; ToA: Total bone cross-sectional area; TrD: Trabecular density; vBMD: Volumetric bone mineral density; Z: Section modulus.

Table 2. Randomized, controlled exercise intervention studies in pre- and postmenopausal women with bone geometry and strength outcomes.

Study	Subjects	Study design	Intervention	Results	Ref.
Cheng *et al.* (2002)	Postmenopausal: 80 women, 50–57 years of age	12-month RCT Group allocation: EX: n = 20 HRT: n = 20 EX + HRT: n = 20 CON: n = 20 Imaging: QCT: femur and tibia (proximal and midshaft sites) Compliance: Mean attendance was 1.2–1.3 sessions per week for EX plus HRT group and one session per week for EX group	Program: Supervised circuit-training sessions of high-impact activities (skipping, bounding, drop-jumping and hopping) and upper body resistance training; home-based circuit-training Frequency/duration: Supervised class: two times per week for 12 months Home-based training: four times per week for 12 months Progression: Height of jumps increased over the training period	Efficacy analysis (12 women excluded owing to poor compliance with either HRT or placebo pill-taking or inadequate participation in exercise program) Mid-femur: vBMD: NS CSA: NS Bone strength (I_{max}, I_{min}, Ip): EX plus HRT > CON, $p < 0.05$ Proximal femur: vBMD: EX plus HRT > CON, $p < 0.05$ CSA: NS Bone strength (I_{min}, Ip): EX plus HRT > CON, $p < 0.05$ Tibial shaft: vBMD: EX plus HRT > CON, $p < 0.05$ CSA: NS Bone strength (I_{max}, I_{min}, Ip): NS Proximal tibia: vBMD CSA: NS Bone strength (I_{max}, Ip): EX and EX plus HRT > CON, $p < 0.05$	[18]

aBMD: Areal bone mineral density; AL: Alendronate; AT: Agility training; BAL: Balance jump training; BMC: Bone mineral content; BMD: Bone mineral density; BSI: Bone strength index; CoA: Cortical bone area; CoD: Cortical density; CSA: Cross-sectional area; CSMI: Cross-sectional moment of inertia; C.Th: Cortical thickness; DXA: Dual energy x-ray absorptiometry; FN: Femoral neck; HAS: Hip structure analysis; HRT: Hormone-replacement therapy; I_{max}: Maximum second moment of area; I_{min}: Minimum second moment of area; Ip: Polar moment of inertia; LS: Lumbar spine; NS: Not statistically significant; PF: Proximal femur; pQCT: Peripheral quantitative computed tomography; QCT: Quantitative computed tomography; RCT: Randomized, controlled trial; RES: Resistance training; RM: Repetition maximum; SSIp: Polar strength–strain index; ToA: Total bone cross-sectional area; TrD: Trabecular density; vBMD: Volumetric bone mineral density; Z: Section modulus.

Table 2. Randomized, controlled exercise intervention studies in pre- and postmenopausal women with bone geometry and strength outcomes.

Study	Subjects	Study design	Intervention	Results	Ref.
Liu-Ambrose *et al.* (2004)	Postmenopausal: 98 women; 75–85 years of age Mean age: 79 ± 3 years	25-week RCT Group allocation: RES: n = 32 AT: n = 34 Stretching (CON: n = 32) Imaging: pQCT: tibia (10%, 50%) and radius (10%, 30%) DXA: proximal femur Compliance: 79–87%	Program: RES: Nine key exercises using Kaiser air pressure equipment AT: Balance and coordination activities and exercises to improve reaction time Frequency/duration: 50 min, two times per week for 25 weeks. Progression: Intensity of RES increased from 50–60% of 1 RM to 75–85% of 1RM. AT progressed by increasing the challenge to the sensory system and the number of stimuli and decreasing the predictability of the tasks	Intent-to-treat analysis Distal tibia & radius: No significant between-group differences for change in any pQCT outcome Tibia shaft: CoD: AT +0.5%, CON -0.4%, p = 0.03 CoA and BMC: NS Bone strength (SSIp): NS Radius shaft: CoD: RES +1.4%, AT -0.4%, p = 0.05 CoA and BMC: NS Bone strength (SSIp): NS FN and PF aBMD: NS	[69]
Engelke *et al.* (2006)	Postmenopausal: 78 women Mean age: 55 years	3-year RCT Group allocation: EX: n = 48 with 3-year data CON: n = 30 with 3-year data Imaging: Spiral QCT: lumbar spine (L1–L3) DXA: lumbar spine, proximal femur and forearm Compliance: Not described, women who attended less than two sessions per week (n = 15) were excluded from the analysis	Program: Group sessions: walk/run program, jump training, resistance training and flexibility training Home sessions: rope skipping, isometric and belt exercise and stretching Frequency/duration: Group sessions: 60–70 min, two times per week for 3 years Home sessions: 25 min, two times per week for 3 years Progression: After first 3 months, high-impact aerobics was added to the group sessions and RES was periodized	Efficacy analysis (15 women excluded from training group due to poor compliance) QCT: Cortical BMD: EX > CON, 7.9%, p < 0.001 Trabecular BMD: EX > CON, 8.8%, p < 0.001 DXA: LS aBMD: EX > CON, 4.1%, p < 0.001 PF aBMD: EX > CON, 1.9%, p < 0.001	[70]

aBMD: Areal bone mineral density; AL: Alendronate; AT: Agility training; BAL: Balance jump training; BMC: Bone mineral content; BMD: Bone mineral density; BSI: Bone strength index; CoA: Cortical bone area; CoD: Cortical density; CSA: Cross-sectional area; CSMI: Cross-sectional moment of inertia; C.Th: Cortical thickness; DXA: Dual energy x-ray absorptiometry; FN: Femoral neck; HAS: Hip structure analysis; HRT: Hormone-replacement therapy; I_{max}: Maximum second moment of area; I_{min}: Minimum second moment of area; Ip: Polar moment of inertia; LS: Lumbar spine; NS: Not statistically significant; PF: Proximal femur; pQCT: Peripheral quantitative computed tomography; QCT: Quantitative computed tomography; RCT: Randomized, controlled trial; RES: Resistance training; RM: Repetition maximum; SSIp: Polar strength–strain index; ToA: Total bone cross-sectional area; TrD: Trabecular density; vBMD: Volumetric bone mineral density; Z: Section modulus.

Table 2. Randomized, controlled exercise intervention studies in pre- and postmenopausal women with bone geometry and strength outcomes.

Study	Subjects	Study design	Intervention	Results	Ref.
Karinkanta *et al.* (2007)	Postmenopausal: 149 women, 70–78 years of age Mean age: 72 years	12-month RCT Group allocation: RES: n = 37 BAL: n = 35 Combination of RES plus BAL; n = 36 Nontraining (CON: n = 36) Imaging: pQCT: tibia and radius (distal and midshaft) DXA and HSA: proximal femur Compliance: 67% (range: 0–100%). Across the three training groups 59–78% of women trained at least 2 days per week	Program: Supervised classes of large muscle group exercises (RES) and balance, agility and impact exercises (BAL). The RES plus BAL group alternated weeks of RES and BAL Frequency/duration: 50 min, three times per week for 12 months Progression: Intensity of RES increased from 50–60% of 1 RM, two sets, 10–15 repetitions for first few weeks to 75–80% of 1 RM, three sets, 8–10 repetitions thereafter. Number of jumps and impacts in BAL increased gradually	FN BMC: NS FN width: NS FN bone strength (Z): RES > RES plus BAL, +5% (95% CI: 0–9%) Tibia & radius: No significant between group differences at any site in an intent-to-treat analysis Efficacy analysis (included women who trained at least two times per week): tibia shaft bone strength (BSI) decreased less (2%, p = 0.03) in the RES plus BAL group than CON group	[71]

aBMD: Areal bone mineral density; AL: Alendronate; AT: Agility training; BAL: Balance jump training; BMC: Bone mineral content; BMD: Bone mineral density; BSI: Bone strength index; CoA: Cortical bone area; CoD: Cortical density; CSA: Cross-sectional area; CSMI: Cross-sectional moment of inertia; C.Th: Cortical thickness; DXA: Dual energy x-ray absorptiometry; FN: Femoral neck; HAS: Hip structure analysis; HRT: Hormone-replacement therapy; I_{max}: Maximum second moment of area; I_{min}: Minimum second moment of area; Ip: Polar moment of inertia; LS: Lumbar spine; NS: Not statistically significant; PF: Proximal femur; pQCT: Peripheral quantitative computed tomography; QCT: Quantitative computed tomography; RCT: Randomized, controlled trial; RES: Resistance training; RM: Repetition maximum; SSIp: Polar strength–strain index; ToA: Total bone cross-sectional area; TrD: Trabecular density; vBMD: Volumetric bone mineral density; Z: Section modulus.

intense exercise (general LTPA) was positively associated with FN bone strength (section modulus) in a large population-based prospective cohort and cross-sectional studies of older women [77,78].

Very little research has been conducted regarding bone structural adaptations to exercise at the lumbar spine. This is, in part, due to the imaging tools most commonly used in research and the challenges associated with assessing vertebral bone structure without a significant dose of ionizing radiation from QCT. In the Erlangen Fitness Osteoporosis Prevention Study (EFOPS) [70], 3 years of low-volume, high-magnitude resistance training with high-impact aerobics was an effective means to increase lumbar spine cortical vBMD and maintain trabecular vBMD (by spiral QCT) in early postmenopausal women who demonstrated acceptable compliance with the intervention (less than two exercise sessions per week) (Figure 4). Owing to the spatial resolution of spiral QCT, it was not possible to determine whether the increase in cortical BMD was due to a change in cortical thickness [70]. However, it is likely that the adaptations in both the cortical and trabecular bone compartments contribute to enhanced bone strength at the lumbar spine, which may become evident with the application of finite element modeling to QCT scans.

In summary, exercise protocols that combine resistance training with impact activity may be our best strategy for maintaining bone mass and strength in postmenopausal women. We have yet to clearly define the effect of a mixed loading program on bone strength at various skeletal sites. That said, the evidence to date suggests that physical activity preserves bone strength in older women at both the weight-bearing proximal femur and tibia. Importantly, exercise programs that positively affect bone structure and strength may also benefit muscle function and balance [71,79] and in turn, reduce the risk of falls in postmenopausal women [80]. The challenging question for future investigations is whether any bone strength advantage associated with exercise in older women reduces fracture risk. In addressing this question, investigators must consider the wide variation in age, but more importantly, factors such as physical condition, presence of disease and life history among postmenopausal (and perhaps all) women. The considerable variability in these factors may influence the outcome of intervention trials. For example, an exercise protocol that has been proven effective in maintaining bone strength in healthy, early postmenopausal women may not be effective in an older and/or frailer population. Therefore, a 'one size fits all' approach to exercise prescription for bone health in postmenopausal women may be inappropriate and more customized prescription models that are suited to the unique needs and characteristics of the population should be considered.

Men

By contrast to the extensive literature on the benefit of exercise for bone health in women, very few exercise intervention studies have evaluated this relationship in men only. In a meta-analysis that included eight studies, Kelley and colleagues [81] concluded that site-specific exercise may improve or maintain aBMD in men. The average treatment effect for aBMD was 2.6%. Although the specific exercise prescription that might enhance bone mass and strength in older men is not known, resistance training interventions are most commonly administered [67]. Resistance training programs were undertaken for 3–12 months and the exercise intensity was moderate-to-high [67]. Overall, bone mass in exercising men was either maintained or improved, most notably, at the proximal femur. The positive bone-mass response to training was of similar magnitude to the response observed in women of the same age [67]. To our knowledge, no study has, as yet, evaluated bone structural adaptations to exercise in men.

A few prospective observation studies provide additional evidence that habitually active elderly men (and women) have a decreased rate of bone loss compared with inactive elderly individuals [82]. Furthermore, older adults who maintained a moderate level of physical activity over 10 years demonstrated better preservation of balance than inactive adults. Despite these apparent benefits, Daly *et al.* did not find that a physically active lifestyle was protective against fractures [82]. However, as with the majority of exercise intervention trials, this study was not adequately powered to evaluate group differences in fracture incidence.

Results from cross-sectional and retrospective studies demonstrate that both current and past physical activity levels are associated with bone strength in men. Among men (and women) over the age of 50 years, current participation in strenuous (or 'heavy') physical activity was associated with a significantly greater FN bone strength (section modulus) and cross-sectional area (by HSA) than adults who reported participating in only light activity levels [77]. Furthermore, lifetime (15–50 years) physical activity was positively associated with a greater sub-periosteal diameter at the intertrochanteric and shaft regions of the proximal femur. Although the difference in bone diameter between groups was relatively small (1.5–3%), it translates into a more substantial bone bending strength since resistance to bending forces increases exponentially as bone is distributed further from the centre of mass [83]. More recently, Daly and Bass reported a similar relationship between men's lifetime physical activity and mid-femur bone strength (polar moment of inertia, by QCT) [84]. They categorized long-term participation (13–50 or more years) in sport and leisure activities based on an osteogenic index (OI); lifetime OI was a significant determinant of bone area and estimated strength at the mid-femur (Figure 5). Importantly, lifetime OI was not significantly associated with aBMD by DXA at the mid-femur or other measured sites. This finding highlights the possibility that bone strength advantages may not be adequately represented by aBMD (by DXA) and emphasizes the need to also assess the geometric and structural properties that contribute to bone strength.

The role of physical activity in the prevention of falls

The propensity to fall is the strongest predictor of fracture at any site [85]. Thus, there is a need, in seniors or other vulnerable populations, to integrate an evaluation of falls and fall risk with an assessment of bone health or bone fragility. Furthermore, fall prevention should be a key element of any prevention strategy that aims to reduce fracture [86]. A third of seniors experience a fall each year and the proportion increases with age [87]. Fall-related injuries are significant – 1% of all falls result in a proximal femur fracture [87] and 90% of all proximal femur fractures are the result of a fall [88]. There is compelling evidence from RCTs, systematic reviews and meta-analyses that exercise, and in particular balance training, reduces fall risk by 15–50% in older, community-dwelling adults [85,89,90]. For example, the home-based Otago Exercise Program introduced balance training that was feasible and safe for elderly men and women (aged 65–97 years) to perform at home. The program effectively reduced falls and fall-related injury by up to 35% [91]. Importantly, falls are complex events with multiple risk factors (including balance, muscle strength, coordination, proprioception and cognition) that are positively affected by regular physical activity [92,93]. Ultimately, the key question is whether fall reduction results in fracture prevention. To date, fall prevention studies have not been adequately powered to detect an effect on fracture rates. However, several RCTs that evaluated fall prevention also reported a reduction in the number of fractures [94,95]. There is an urgent need for large, multicentre RCTs to determine whether fall prevention strategies also reduce fractures.

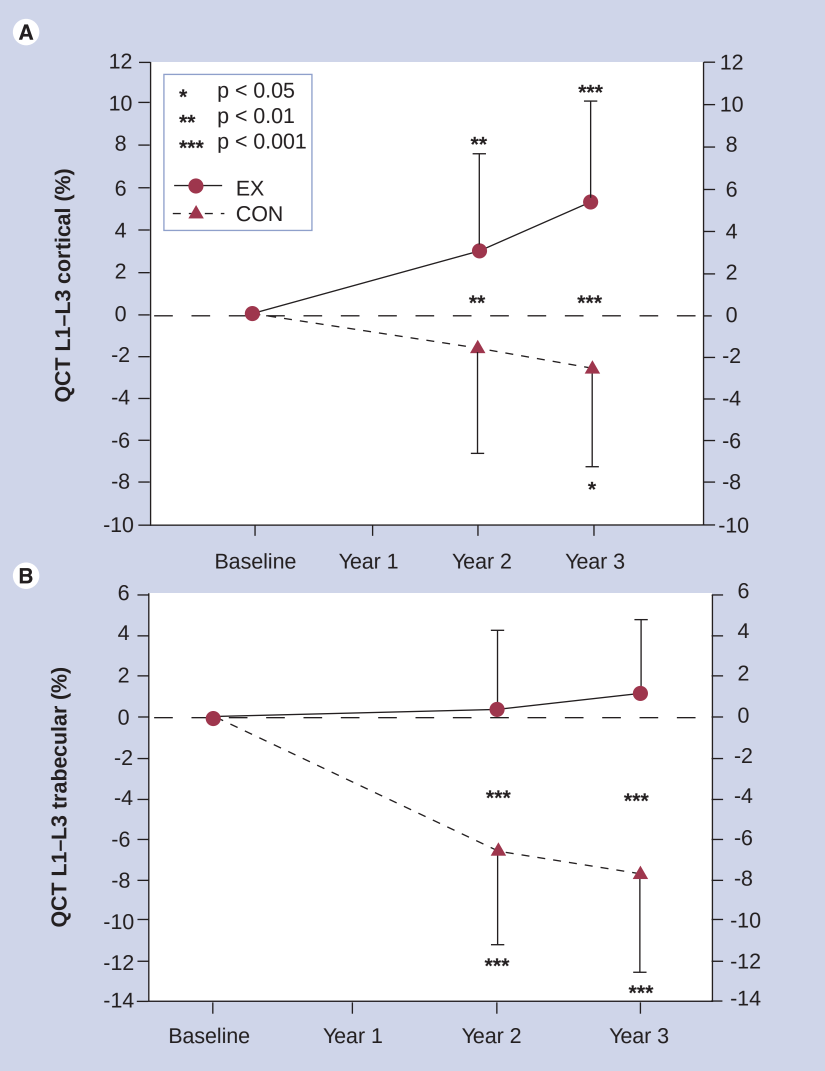


Figure 4. Quantitative computed tomography results of the lumbar spine from the Erlangen Fitness Osteoporosis Prevention Study. The exercise group (solid line and circle, n = 48) demonstrated a significantly greater percentage change from baseline in **(A)** cortical and **(B)** trabecular (volumetric) bone mineral density of the lumbar spine (L1–L3) compared with the control group (dashed line and triangle, n = 30). The exercise group includes those women who attended two or more exercise sessions per week averaged over the entire study period. Significance levels are indicated for within-group differences relative to baseline and for between-group differences at year 2 and year 3. QCT scans were not acquired at year 1.
CON: Control group; EX: Excercise group; QCT: Quantitative computed tomography.
Adapted from [70] with permission from Springer.

Does physical activity reduce fracture risk?

Despite the well-documented beneficial effects of physical activity on bone mass and strength and also on fall risk, we do not have sufficient proof that physical activity reduces the risk of

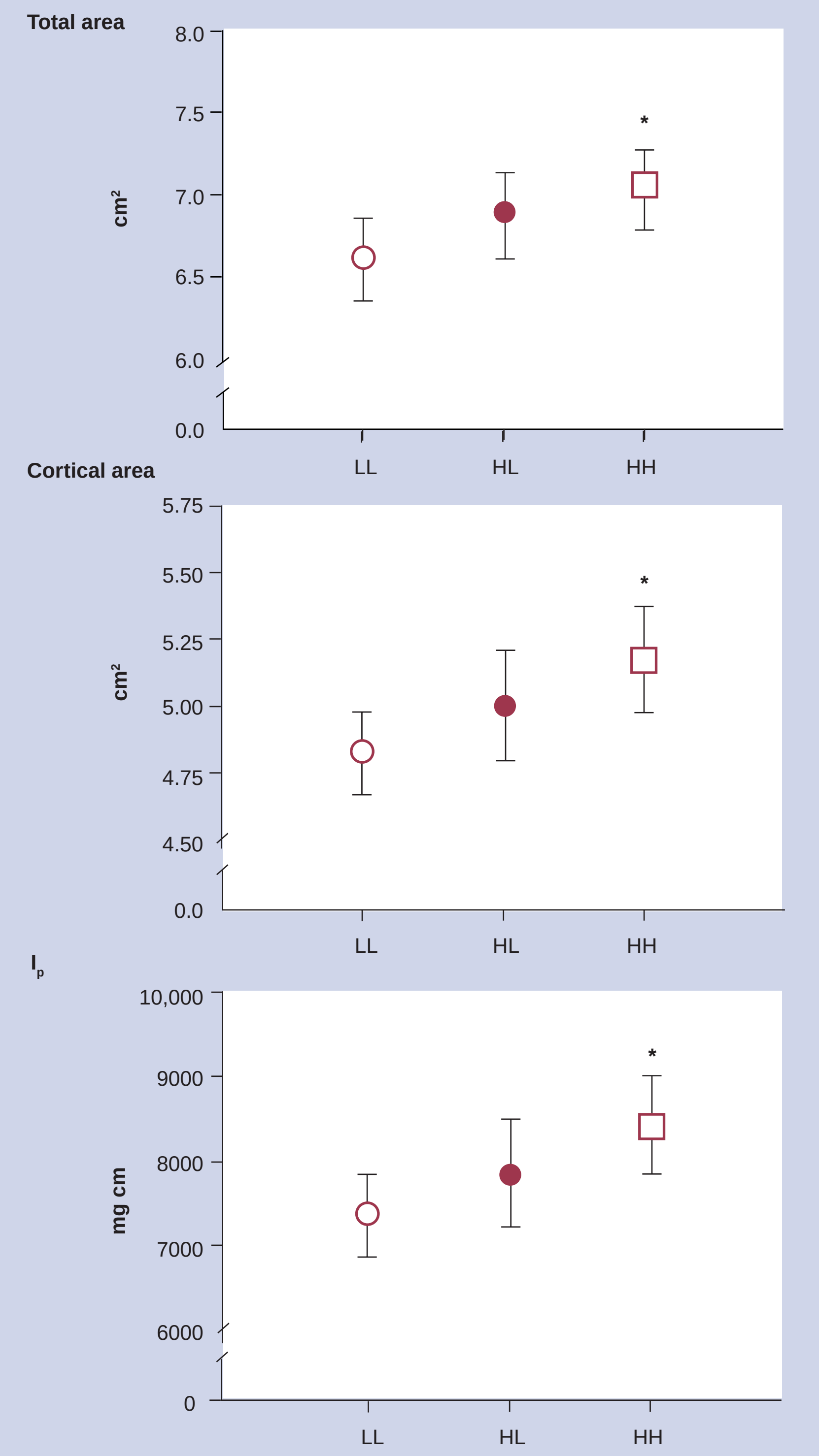


Figure 5. Positive adaptations in mid-femur bone geometry (total and cortical area) and estimated bone strength (Ip) by quantitative computed tomography in consistently highly active men aged 50 years and older. Each plot compares men by lifetime-loading history: LL (low impact during adolescence, low impact during adulthood), HL (high impact during adolescence, low impact during adulthood) and HH (high impact during adolescence and adulthood). Values represent means with 95% CI.
$^*p < 0.05$, HH greater than LL.
HH: High-to-high impact; HL: High-to-low impact; I_p: Polar moment of inertia; LL: Low-to-low impact.
Adapted from [84] with permission from Springer.

fractures. This is largely due to methodological challenges associated with conducting RCTs with fracture as the primary end point. In particular, the required sample size for such a study is substantial owing to the low incidence of hip fractures in the population (i.e., in a RCT of high-risk women, 7000 subjects in two groups would be required assuming a hip fracture-rate ratio of 75%) [96]. The challenges of fracture-based studies have prompted some to raise the issue of surrogate end points [97], similar to those used in other areas of medicine such as cardiovascular disease [98]. Examples of surrogate end points for fracture include trabecular microarchitecture by high-resolution pQCT, bone strength estimated with finite element analysis and vBMD by QCT, among others [97]. However, further study is required to determine whether these outcomes explain a significant proportion of the antifracture efficacy of specific treatments, including physical activity. There are no RCTs that have specifically addressed whether physical activity decreases fractures in older adults. We then look to evidence from large, well-designed prospective cohort studies that investigated the association between physical activity and fracture risk. In a recent meta-analysis of 13 cohort studies with proximal femur fracture as an end point, Moayyeri [96] found that moderate-to-vigorous physical activity was associated with a 38 and 45% reduction in proximal femur fracture risk in men and women, respectively. Even a relatively low level of physical activity (2–4 h per week) was associated with a 25% reduction in proximal femur fracture risk [99]. Conversely, older adults who became more inactive with age approximately doubled their risk of proximal femur fracture compared with those who remained moderately active [100].

Fewer cohort studies have investigated the relationship between physical activity and vertebral fracture risk. However, both the European Vertebral Osteoporosis Study (EVOS) [100] and the Study of Osteoporotic Fractures (SOF) [101] found that daily physical activity reduced vertebral fracture risk by 20–33%. Thus, the strength of the association between physical activity and fracture risk, particularly for fractures at the proximal femur, suggests that older adults should be encouraged to maintain a physically active lifestyle.

Conclusion & future perspective

In summary, there is a wealth of evidence to support an important role of physical activity in enhancing bone-mass and strength accrual during growth and to maintain bone health with aging. However, numerous questions remain. For example, what specific exercise prescription is most effective to augment bone strength? How does this vary at different critical time points across the lifespan, across skeletal sites and with varying doses of exercise? What is the response in bone sectors to weight-bearing physical activity? Does a program of weight-bearing physical activity prevent fractures in older populations? Clearly, there is much to do and these questions provide exciting avenues for future investigations.

There have been tremendous advances in imaging tools that are able to define the specific geometric, structural and microstructural bone properties that adapt to weight-bearing physical activity. It is likely that the next decade will further advance imaging technologies so as to extend our understanding of the complex nature of bone's response to physical activity across the lifespan. In addition, advances in finite element modeling and more powerful computers will provide an increased opportunity to model bone morphology and bone adaptations in three-dimensions.

Although prevalent in the cardiovascular literature, assessing physical activity using accelerometry is uncommon in the bone health field. In the future, more advanced accelerometers will be able to represent more intricate measures of physical activity such as intensity, frequency and daily impacts. These tools can then be used in intervention trials to customize physical activity based on the desired load. Accelerometers may serve a dual purpose and may be developed to also capture an individual's loss of balance or a fall.

There is likely to be not just one physical activity intervention to promote bone strength across the lifespan, but a host of programs specific to the sex, age, maturity or fragility of the population being studied. Thus, there is still a great need for well-designed randomized, controlled, physical activity trials to address this. Ideally, these trials would also evaluate the influence of mediating factors such as nutrition, hormones and pharmaceutical therapies. Finally, exercise intervention trials often suffer from high attrition rates – up to 30% in studies of postmenopausal women [18,68]. Studies of behavioral strategies and incentives that could potentially enhance compliance and sustain an individual's participation in physical activity programs would be of great benefit.

Researchers should be encouraged to continue to investigate the specific role of physical activity in bone health across the lifespan using novel tools, approaches and rigorous study designs. However, given the positive relationship between physical activity and the health of many biological systems, including bone, individuals of all ages should be encouraged to adopt and maintain an active lifestyle.

Executive summary

Three-dimensional imaging technologies provide accurate & reliable estimates of bone strength

- Two-dimensional dual energy x-ray absorptiometry measures of bone mass do not capture exercise-related modifications to bone geometry, volumetric bone mineral density or bone microarchitecture.
- Future studies would benefit from using three-dimensional imaging tools, such as peripheral quantitative computed tomography, high-resolution peripheral quantitative computed tomography and MRI, to investigate bone structural adaptations to physical activity across the lifespan.

Short bouts of high-impact exercise enhance bone strength accrual in children

- School-based programs that include short bouts of high-impact jumping or circuit programs are effective for optimizing bone strength accrual in pre- and early pubertal children.
- Bone structural adaptations to weight-bearing physical activity vary according to sex, maturity status and skeletal site.

Exercise is an effective means to maintain bone mass & strength in adults

- High-impact exercise and resistance training, alone or in combination, are effective for maintaining bone mass at the femoral neck and lumbar spine in postmenopausal women.
- Well-designed randomized, controlled trials using imaging technologies other than dual energy x-ray absorptiometry are needed to determine the optimal exercise prescription for bone strength in pre- and postmenopausal women and men.

Physical activity reduces fall risk in older adults & may reduce the risk of hip fracture

- Balance training reduces fall risk in community-dwelling, older adults by 15–50%.
- Moderate-to-vigorous physical activity is associated with a significant reduction in hip fracture risk in men and women.
- There is a need for randomized, controlled exercise intervention trials with fracture, or fracture surrogates, as the primary end point.

Conclusion

- Weight-bearing physical activity enhances bone mass and strength accrual during growth and maintains bone health with aging.
- Further study, using three-dimensional imaging technology, is required to determine the optimal exercise prescription to enhance bone strength across the lifespan.

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MedscapeCME Physical activity and bone strength across the lifespan

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Activity evaluation: where 1 is strongly disagree and 5 is strongly agree.	1	2	3	4	5
The activity supported the learning objectives.					
The material was organized clearly for learning to occur.					
The content learned from this activity will impact my practice.					
The activity was presented objectively and free of commercial bias.					

1. Which of the following statements about bone changes over different life stages and their assessment is most accurate?

- ☐ **A** Nutrition is the primary variable determining the skeleton's ability to respond to strain
- ☐ **B** Adult skeletons adapt to strain primarily through periosteal apposition
- ☐ **C** Dual-energy x-ray absorptiometry (DXA) is unable to assess bone geometry and microarchitecture
- ☐ **D** High-resolution peripheral quantitative computed tomography (pQCT) is limited to the assessment of bone strength at the hip in adults

2. Which of the following statements about physical activity and bone strength in children is most accurate?

- ☐ **A** Sustained, long-duration exercise is more osteogenic than short bouts of exercise
- ☐ **B** Jumping programs may be more effective in increasing bone strength among boys vs girls
- ☐ **C** The best results from exercise training occur in late adolescence
- ☐ **D** The optimal exercise prescription for increasing bone strength in children involves low-impact physical activity for at least 60 min per day

3. Which of the following statements about physical activity and bone health in adults is most accurate?

- ☐ **A** Exercise clearly increases bone strength at the femoral neck among premenopausal women
- ☐ **B** High-impact aerobic exercise alone appears most effective at increasing bone mineral density among postmenopausal women
- ☐ **C** Exercise preserves bone strength in the proximal femur and tibia among postmenopausal women
- ☐ **D** Exercise has not been demonstrated to affect bone mass among men

4. All of the following statements about research into physical activity and the risks for falls and fracture are accurate, *except*:

- ☐ **A** Randomized trials have demonstrated that exercise can reduce the risk for falls among older adults
- ☐ **B** Randomized trials have demonstrated that exercise can reduce the risk for fracture among older adults
- ☐ **C** Cohort studies have found that exercise can reduce the risk for proximal femur fractures
- ☐ **D** Cohort studies have found that exercise can reduce the risk for vertebral fractures