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Review Article

Exercise Protects Bone after Stroke, or Does It? A Narrative Review of the Evidence

Karen Borschmann

Florey Neuroscience Institutes, 245 Burgundy Street, Heidelberg VIC 3084, Australia

Correspondence should be addressed to Karen Borschmann, karenb@unimelb.edu.au

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Physical inactivity contributes to accelerated bone loss after stroke, leading to heightened fracture risk, increased mortality, and reduced independence. This paper sought to summarise the evidence for the use of physical activity to protect bone in healthy adults and adults with stroke, and to identify international recommendations regarding any means of bone protection after stroke, in order to guide rehabilitation practice and future research. A search was undertaken, which identified 12 systematic reviews of controlled trials which investigated the effect of physical activity on bone outcomes in adults. Nine reviews included healthy adults and three included adults with stroke. Twenty-five current international stroke management guidelines were identified. High-impact loading exercise appears to have a site-specific effect on the microarchitecture of healthy postmenopausal women, and physical activity has a small effect on enhancing or maintaining bone mineral density in chronic stroke patients. It is not known whether this translates to reduce fracture risk. Most guidelines included recommendations for early mobilisation after stroke and falls prevention. Two recommendations were identified which advocated exercise for the prevention bone loss after stroke, but supporting evidence was limited. Research is required to determine whether targeted physical activity can protect bone from early after stroke, and whether this can reduce fracture risk.

1. Introduction

Stroke-related impairments and inactivity contribute to the accelerated development of osteoporosis [1–3]. Combined with a high rate of falls [4–6], stroke survivors are particularly vulnerable to fall-related injuries, especially fractures. The risk of fracture after stroke is 1.5- to fourfold compared to age-matched controls [7], and fractures after stroke reduce the ability to regain independent walking and increase mortality [8].

Bone maintains its strength through the modulation of its remodelling activity (bone turnover), adapting its structural and material properties in response to its loading environment [9]. Loads on bone are generated by ground reaction forces and muscle activity. Immobility from hemiplegia or extended bed rest decreases loads and thus contributes to increased removal of bone [10]. Conversely, during adulthood, mechanical loading of bone can contribute to maintenance of bone strength by maintaining bone mass, and vigorous high-impact loading may have a small capacity to increase bone mass [10].

Physical activity levels are often very low among acute stroke patients [11, 12], who may spend over half of the day (8 am to 5 pm) resting in bed [12]. Prolonged bed rest, however, leads to rapid loss of bone [13]. Urinary markers of bone resorption (C-telopeptide and N-telopeptide), which can be used to predict hip fracture in older women [14], were elevated by 17.8% and 28.7%, respectively, after one day of bed-rest in healthy men aged 25.5 years (SD 2.9) [13]. In addition, reductions in bone mineral density (BMD) at the tibia of up to 3% have been observed in a similar group of young men after five weeks of bed rest [15]. In comparison, the normal rate of bone loss in healthy men and women aged over 60 years is approximately 1% per year [16–18].

The period of immobility after stroke appears to strongly influence the amount of bone which is lost. People who remained nonambulant for one year after stroke lost up to 13% of femoral neck BMD of the paretic limb [19]. In contrast, people who relearned to walk within two months, and people who walked from the first week after stroke showed losses of 8% and 3%, respectively [19]. Other stroke-induced impairments also appear to contribute to the amount of bone loss: severity of impairment [20, 21], disuse of paretic limbs [22], reduction in weight bearing [20], reduced muscle mass [23], muscle weakness [24], and reduced cardio-respiratory fitness [23].

Evidence supports the role of targeted physical activity for maintaining or improving BMD in healthy women and men aged over 60 years, in whom bone loss is occurring [25, 33]. High-impact loading exercise has a modest, positive, and site-specific effect in healthy postmenopausal women, primarily enhancing cortical, rather than trabecular, bone mass and geometry [29]. National guidelines recommend physical activity for the prevention of osteoporosis in the healthy adult population [36]. Moreover, physical activity is recommended to improve mobility and function [37], muscle strength [38, 39], and fitness [40] after stroke, and early and frequent mobilisation is recommended for the prevention of complications in acute stroke patients [41]. In addition, some evidence suggests that physical activity may maintain or improve bone density in chronic stroke [42]. However, despite the prevalence and detrimental effects of bone loss after stroke, and the potential for physical activity to modulate bone structure and density, recently updated Australian clinical guidelines for stroke management [41] did not mention bone loss. Evidence from healthy adults contributes to our understanding of bone loss after stroke; however, separate evaluations are warranted, since the generalisability of results from healthy adults to adults with stroke may be limited due to stroke-related impairments and neurovascular changes. The aims of this paper were to summarise the evidence for the use of physical activity to protect bone in both healthy adults and adults with stroke. A secondary aim was to summarise international recommendations regarding any means of bone protection after stroke.

2. Method

A search was undertaken in order to retrieve all systematic reviews, of controlled trials that investigated physical activity interventions and contained bone-related outcomes in healthy adult or adult stroke populations. The following electronic databases were searched from 2001 on 31 May 2011: Ageline, Allied and Complimentary Medicine (AMED), Cochrane Library, Cumulative Index to Nursing and Allied Health Literature (CINAHL), Embase, Medline, Physiotherapy Evidence Database (PEDro), PsycINFO, SPORTDiscus, and Web of Knowledge. Keywords used to identify reviews included "bone, bone loss, fracture, or osteoporosis" combined with "physical activity, exercise or loading." International stroke management guidelines were identified in these databases using terms "stroke" and "management, guideline, or consensus statement." Additionally, stroke association websites and colleagues with content knowledge were consulted to identify systematic reviews and clinical guidelines. Non-English language guidelines were identified in the described search and were included in subsequent drafts of the manuscript once colleagues were available to translate.

The identified systematic reviews were summarised for included trials, conclusions, and recommendations for future research, and this information is contained on Table 1. The identified stroke management guidelines were searched for key terms of "bone, fracture, or osteoporosis," and recommendations were reviewed for content regarding bone protection, physical activity, exercise, and falls prevention. Summaries of these recommendations and their levels of evidence are recorded on Table 2. Appendices A and B contain descriptions of classifications of levels of evidence and grades of recommendations.

3. Results

3.1. Physical Activity for the Prevention of Bone Loss in Healthy Adult Populations. Nine systematic reviews of controlled trials which investigated the use of exercise as an intervention against bone loss in healthy adults were identified. One review investigated adults with low bone mineral density [30], one investigated premenopausal women [68], five studied postmenopausal women [25, 26, 28, 29, 31], and two [32, 33] included adults of all age groups. Interventions were based on various forms of physical activity which were hypothesised to reduce bone loss through weight bearing and muscular action on bone. Outcomes were two dimensional measurement of bone mass of spine, hip, wrist, or total body, using dual-energy X-ray absorptiometry (DXA), or three-dimensional bone mass and bone architecture, measured with peripheral quantitative computerised tomography (pQCT).

There were mixed results regarding the effect of impact (weight bearing) and nonimpact (resistance training, aerobics) exercises on BMD of pre- and postmenopausal women's lumbar spine [25, 26, 28, 31, 68], femoral neck [26, 31], whole hip [25, 28, 68], and wrist [25]. Bone mineral density was reported to be improved by weight-bearing aerobic exercise with or without muscle strengthening exercise, when the duration of the intervention was at least a year [30]. Exercise appeared to positively influence site-specific bone mass and geometry in postmenopausal women, with the most prominent changes being in response to high-impact loading exercise. Exercise was reported to be able to reduce falls, fall-related fractures, and several risk factors for falls in individuals with low BMD [30]. Most authors commented on the heterogeneity of interventions and research quality. Recommendations were made for the design of future studies including high-quality methodology, larger sample sizes, periods of intervention greater than one year, targeted exercise programs, and consistent methods and sites of outcome measurement. It was reported that research was needed to determine whether improvements in bone mass and geometry were capable of preventing fractures.

Table 1: Summary of systematic reviews of exercise interventions for the prevention of adult bone loss.

Reference	Objectives and number of included studies	Conclusions and recommendations
Bonaiuti et al. [25]	To examine the effectiveness of exercise in preventing bone loss and fractures in postmenopausal women 18 RCTs; $n = 1423$	(i) Aerobics, weight bearing, and resistance exercises are effective in increasing BMD of the spine in postmenopausal women. Aerobic exercise is effective in increasing BMD of the wrist. Walking is effective on the hip. (ii) The quality of the reporting of the trials in the meta-analysis was low, in particular, in allocation concealment and blinding.
Martyn-St James and Carroll [26]	To evaluate effects of progressive, high-intensity resistance training on postmenopausal BMD. 15 RCTs; $n = 585$	(i) Significant increase in BMD of the lumbar spine following high-intensity resistance training. (ii) Methodological quality of studies was low, and a reporting bias towards studies with positive BMD outcomes was evident
Myint et al. [27]	Critical review of recent studies on strategies to prevent bone loss and fractures after stroke. 1 RCT of exercise in chronic stroke patients, $n = 63$	(i) Emerging evidence that exercise can improve bone health in chronic stroke. Further work is necessary to evaluate early physiotherapy and exercise interventions in acute stroke patients (ii) Prevention of falls is important in preventing hip fractures. Studies of falls prevention for stroke populations are needed.
Marsden et al. [1]	158 papers focusing on risk factors or interventions to prevent bone loss or fractures after stroke. 1 RCT of exercise intervention, $n = 63$	(i) Early mobilisation may reduce bone loss & avoid fracture, but evidence is needed. Large, prospective studies are needed to clarify optimum treatments to reduce poststroke bone loss, and test the effects on clinical outcomes.
Martyn-St James and Carroll [28]	To assess the effects of prescribed walking programmes on BMD at the hip and spine in postmenopausal women. 5 RCTs, 3 non-RCTs, $n = 621$	(i) Regular walking has no significant effect on preservation of BMD at lumbar spine in postmenopausal women. Inconsistent results observed on BMD of femoral neck. (ii) Diverse methodological and reporting discrepancies in published trials. Other forms of exercise that provide greater targeted skeletal loading may be required to preserve BMD in this population.
Hamilton et al. [29]	To determine the effects of exercise on bone mass and geometry in postmenopausal women 4 RCTs, 1 non-RCTs, 3 cross-sectional & 4 longitudinal studies, $n = 905$	(i) Exercise appears to positively influence bone mass and geometry in postmenopausal women, with the most prominent changes in response to high-impact loading exercise. Exercise effects appear to be modest, site-specific, and preferentially influence cortical rather than trabecular components of bone. (ii) Research is needed to determine the types and amounts of exercise required to optimise improvements in bone mass and geometry in postmenopausal women & determine whether these improvements are capable of preventing fractures.
De Kam et al. [30]	To investigate efficacy of exercise interventions in individuals with low BMD in reducing (1) falls & fractures (2) risk factors for falls & fractures 28 RCTs, $n = 1592$	(i) Exercise can reduce falls, fall-related fractures, and several risk factors for falls in individuals with low BMD. Bone strength was improved by weight-bearing aerobic exercise with or without muscle strengthening when interventions were at least a year long. (ii) Exercise for patients with low BMD or osteoporosis should include weightbearing, balance, and strength training to reduce falls & fracture risk

Table 1: Continued.

Reference	Objectives and number of included studies	Conclusions and recommendations
Martyn-St James and Carroll [31]	To assess the effects of impact exercise on postmenopausal bone loss at the hip and spine 10 RCTs & 5 nonrandomised controlled trials, $n = 1358$	(i) Mixed loading exercise programmes combining jogging with other low-impact loading activity (walking and stair climbing) and programmes mixing impact activity with high-magnitude resistance training appear effective in reducing postmenopausal bone loss at the hip and spine. (ii) High-impact only and odd-impact only protocols were ineffective in increasing BMD at any site in this population. (iii) Diverse methodological and reporting discrepancies are evident in published trials.
Guadalupe-Grau et al. [32]	To review relevant studies in adults and animals, highlighting variables like mode of exercise, intensity, duration, endocrine and metabolic factors, and sex differences in the osteogenic response to training.Young men: 4 cross-sectional studies, $n = 442$; 4 longitudinal, $n = 161$ Middle-aged men: 2 longitudinal, $n = 158$ Older men: 3 longitudinal, $n = 194$ Young women: 4 cross-sectional studies, $n = 381$, 9 longitudinal, $n = 4$ Premenopausal women: 4 longitudinal, $n = 293$ Older women: 8 longitudinal, $n = 221$	(i) Participation in high impact sports, especially before puberty, is important for maximising bone mass and achieving a greater peak bone mass in men and women. Continuing sport practice is associated with fewer fragility fractures in older men and women (ii) A mix of high impact and weight-lifting exercises may be the best method for enhancing bone mass and preventing OP. Unloaded exercise (swimming and cycling) has no impact on bone mass. Walking & running has limited positive effect. (iii) For those with OP, WB exercise in general, and resistance exercise in particular, along with balance, mobility and posture exercise should be recommended to reduce the likelihood of falling. (iv) Older men respond better to osteogenic training than women, but RCTs on the effect of exercise on bone mass in older people are lacking.
Nikander et al. [33]	To evaluate the effects of long-term supervised exercise on estimates of lower-extremity bone strength from childhood to older age. 5 RCTs of children/adolescents, $n = 1160$ 1 RCT of premenopausal women, $n = 80$ 4 RCTs of postmenopausal women, $n = 369$	(i) Exercise can enhance bone strength at loaded sites in children but not in adults. In premenopausal women with high exercise compliance, improvements of 0.5% to 2.5% have been reported. (ii) There is a need for further well-designed, long-term (>2 year) RCTs with adequate sample sizes to quantify the effects of exercise on whole bone strength and its structural determinants throughout life.
Martyn-St James and Carroll [34]	To assess the effects of impact exercise on BMD at the hip and spine in premenopausal women. 6 RCTs, 3 non-RCTs, $n = 735$	(i) Combining odd- or high-impact activity with high magnitude resistance training appears effective in augmenting BMD in premenopausal women at the hip and spine. High-impact-only protocols are effective only on hip BMD in this group. (ii) Diverse methodological and reporting discrepancies are evident.
Borschmann et al. [35]	To investigate the skeletal effects of physical activity in adults affected by stroke. 1 RCT, 1 non-randomized CT, 1 quasirandomized CT ($n = 95$)	(i) Small effect size of physical activity in maintaining of improving bone density and bone structure on paretic side for chronic stroke patients. (ii) Quality studies are required to investigate the effect of targeted physical activity from early after stroke.

BMD: bone mineral density, OP: osteoporosis, RCT: randomised controlled trial, SCI: spinal cord injury, WB: weight bearing.

Table 2: Summary of current guidelines regarding bone protection, mobilisation and rehabilitation, and falls prevention after stroke.

Reference	Keyword* or bone protection included (level of evidence)	Mobilisation and rehabilitation (level of evidence)	Falls prevention (level of evidence)
American Heart Association *Physical activity recommendations for stroke survivors*. [43]	Decreased activity after stroke leads to secondary complications including osteoporosis.	Rehab goals include preventing complications of prolonged inactivity. Initiate regimens to regain prestroke level of activity as soon as possible.	Not included
American Heart Association *...Rehabilitation care for stroke survivors* [44]	Not included	It is reasonable to provide a comprehensive interdisciplinary assessment of mobility.	Consider all people with stroke as having increased falls risk. Work with patient & carers, to minimise falls.
Beijing Neurological Club [45] (English summary only available)	Not included	Rehab should occur as early as possible: 48 hours after stabilisation of vital signs and symptoms in ischemic strokes. Delay rehab until 10–14 days after haemorrhage.	Not included
Belgian Stroke Council [46, 47]	Not included	Mobilise on stroke unit as soon as possible to prevent complications including aspiration pneumonia, DVT, decubitus ulcers.	Not included
Canadian Stroke Network and the Heart and Stroke Foundation of Canada [48]	Not included	Early consultation with rehab professionals can reduce risk of complications from stroke-related immobility such as joint contracture, falls, aspiration pneumonia, & DVT.	Multifactorial community interventions including individualised exercise programs may prevent or reduce falls number & severity. (Level A)
Chinese Stroke Management Guidelines [49] (English summary only available)	Not included	Recommend stroke unit (I, A).	Not included.
Croatian Stroke Society [50]	Not included	Recommend early mobilisation unless intracerebral hypertension is present, to help prevent complications including aspiration pneumonia, DVT, & ulcers (IV).	Not included
European Stroke Organization [51]	Exercise, calcium supplements, & bisphosphonates improve bone strength & decrease post stroke fracture rates. Bisphosphonates for women with previous fractures (II, B).	Early mobilisation is recommended to prevent complications such as aspiration pneumonia, DVT, and pressure ulcers (IV, GCP).	Assessment of falls risk is recommended for every stroke patient (IV, GCP).Vitamin D/calcium for patients at risk of falls (II, B).
Italian SPREAD Collaboration [52]	Not included	Early mobilisation for acute stroke patients, unless clinically contraindicated (C).	Evaluate falls risk on admission and periodically during hospitalisation (C).

Table 2: Continued.

Reference	Keyword* or bone protection included (level of evidence)	Mobilisation and rehabilitation (level of evidence)	Falls prevention (level of evidence)
Japan Stroke Guidelines Committee [53]	Not included	Aggressive rehab can reduce incidence of pneumonia & other complications (B). Stroke unit for acute patients, except sub-arachnoid haemorrhage, lacunar infarction, deep coma, or patients with poor premorbid ADL (A).	Not included
National Collaborating Centre for Chronic Conditions (UK) [54]	Not included	People with acute stroke should be mobilised as soon as possible (when their clinical condition permits) on a specialist stroke unit.	Not included
National Stroke Foundation (Australia) [41]	Not included	Patients should be mobilised as early and as frequently as possible (B). Rehab should provide as much practice as possible within the first 6 months after stroke (A), minimum of one hour active practice per day at least five days a week (GCP).	Falls risk assessment should be undertaken using a valid tool on admission to hospital. Management plans should be initiated for people at risk of falls (GCP). Provide multi factorial community interventions, including individually prescribed exercises for people at falls risk (B).
Norwegian Stroke Guidelines [55]	"Fracture" mentioned twice.	Comprehensive stroke unit for all patients. Multidisciplinary team to contribute to patients' mobilisation out of bed, as early and frequently as possible (B).	Give patients with falls risk multi factorial intervention targeting individual and contextual risk factors, including individually prescribed exercise (C).
Nova Scotia Health [56]	Prevention & management of medical complications including osteoporosis is required in stroke rehabilitation.	All patients with stroke should begin rehab early, once medically stable (1). Patients should be mobilised as early and as frequently as possible (III-3). As much therapy as patients are willing & able to tolerate (A).	All patients should be assessed for fall risk (III-2). Patients at risk of falls should have a management plan formulated and documented in collaboration with the patient and caregiver(s) (III).
Ottawa Panel [57]	Not included	147 recommendations for 13 rehab treatments including gait & exercise.	Balance training is essential in preventing falls
Royal Dutch Society for Physical Therapy [58]	Not included	Starting rehabilitation as soon as possible (within 72 hours of stroke), preferably in a stroke unit, may accelerate & enhance recovery. If possible, mobilise immediately to reduce DVT risk.	It is plausible that the positive effects on postural symmetry & speed of symmetric standing up & sitting down reduce falls while standing up and sitting down.
Scottish Intercollegiate Guidelines Network (SIGN) [59]	Not included	Where safe, every opportunity to increase the intensity of therapy for improving gait should be pursued (B).	Not included
Scottish National Advisory Committee for Stroke [60]	Risks from exercise include cardiac events, falls and fractures.	Community programs: should be mostly aerobic walking, also functional strength & balance exercises. Frequency: 3x per weekDuration: 1 hour per sessionIntensity: moderate if possible	Individuals' history of falls, balance, osteoporosis & psychoactive medications need to be considered in tailoring of exercise interventions..

Table 2: Continued.

Reference	Keyword* or bone protection included (level of evidence)	Mobilisation and rehabilitation (level of evidence)	Falls prevention (level of evidence)
Singapore Ministry of Health [61]	Not included	Early mobilisation for all stroke patients to reduce DVT & pulmonary embolism (D, 2+)	Long-term anticoagulation is contraindicated in elderly patients at high risk of falls.
South African Stroke Society [62]	Not included	Early mobilisation is recommended to prevent complications: aspiration pneumonia, DVT, & pressure ulcers (IV, GCP).	Recommend assessment of falls risk for every stroke patient (IV, GCP). Patient safety & prevention of falls and injury are of paramount importance.
Stroke Foundation of New Zealand [63]	Not included	Early mobilisation for all acute stroke patients to prevent DVT and PE (IV).Rehab should provide as much practice as possible within 6 months of stroke (A), a minimum of 1 hour active rehab per day (IV).	Falls risk assessment should occur on hospital admission, and a management plan initiated (IV).Multifactorial community intervention, including tailored exercises for people at falls risk (B)
Stroke Society of the Philippines [64]	Not included	Major rehab goals for stroke patients are to (1) prevent complications of prolonged inactivity, (2) decrease recurrent stroke and cardiovascular events and (3) increase aerobic fitness.	Stroke survivors are often deconditioned & predisposed to sedentary lifestyle that limits performance of ADLs, increases falls risk, and may contribute to increased risk for recurrent stroke & cardio-vascular disease.
Swedish Stroke Guidelines [65]	Training of balance, safe transfers, and education are important measures to prevent falls and related fractures.	Stroke units are strongly recommended, and mobilisation from early after stroke is of highest importance. Patients should not have unnecessary heart monitoring if it interferes with early mobilisation.	Some evidence supports assessment and prevention of falls for stroke patients, including balance training, patient/ carer information, home hazard reduction, and discontinuation of psychotropic drugs.
UK National Guidelines [66]	Not included	Mobilise people with stroke as soon as their clinical condition permits, on a specialist stroke unit.	Any patient with significant balance impairment should be given intensive progressive balance training.
Veteran's Affairs/Department of Defence (U.S.) [67]	Early mobilisation & paretic limb movement reduces fracture risk (II-1, A). Consider medications to reduce bone loss (II-1, B), including vitamin D (I, B). Consider assessing bone density for patients with osteoporosis who have been mobilised (sic) for 4 weeks.	All patients should be mobilised, as soon as possible, for prevention of DVT.	Not included

*Keyword: bone, fracture or osteoporosis, ADL: activity of daily living, DVT: deep vein thrombosis, GCP: Good clinical practice, PE: pulmonary embolism. Class A–D and levels I–V; see appendices for classifications of levels of evidence.

3.2. Physical Activity for the Prevention of Bone Loss in Adults with Stroke. Three systematic reviews of controlled trials which investigated the use of physical activity as an intervention against poststroke bone loss were identified [1, 27, 35], and these reviews described three controlled trials. One trial [42, 69] investigated people who were approximately 5 years after stroke. This study found beneficial effects on tibial bone architecture, and maintenance of paretic hip BMD, as a result of a 19-week exercise intervention. Marsden et al. [1] reported that although the study was level "A" evidence due to its being a randomised trial, the sample size was small ($n = 63$) and was biased toward a younger male population. Marsden et al. [1] concluded "*...early mobilization may reduce bone loss and avoid fracture, but evidence is needed...,*" *which reflects the conclusion of Myint et al. [27] "Further work is necessary to evaluate early physiotherapy and exercise interventions in acute stroke patients....*" Two further trials which included chronic stroke patients were identified by Borschmann et al. [35]. One was a low-quality trial [70] which found no effect on upper limb BMD with an intervention of ball squeezing for a duration of one-to-three years. The other trial [71] observed a small positive on enhancing tibial bone cortical thickness with six months of twice weekly body-weight supported treadmill training. Borschmann et al. concluded that although the number of studies was limited, results demonstrated a small effect of physical activity in maintaining or improving bone density and bone structure on the paretic side in chronic stroke patients. Quality studies are required to investigate the effect of targeted physical activity interventions to minimize bone loss after stroke.

3.3. International Recommendations Regarding Bone Protection after Stroke. Twenty-five international stroke management guidelines were identified [41, 43–60, 62, 64–67, 72]. Seven guidelines [43, 51, 55, 56, 60, 65, 67] contained one or more keywords "bone, fracture, or osteoporosis." Almost all guidelines included recommendations for physical activity after stroke, and most contained recommendations for falls prevention. Two guidelines [51, 67] contained comments regarding the use of physical activity for bone protection after stroke, one [67] which contained a chapter regarding poststroke osteoporosis.

The European Stroke Organisation's stroke management guideline [51] contained the statement "*Exercise, calcium supplements, and bisphosphonates improve bone strength and decrease fracture rates in stroke patients...*" However, the supporting reference [73] did not provide evidence for the use of exercise to improve bone strength or decrease fracture rates. The US Veteran's Affairs guideline [48] contained a chapter on osteoporosis after stroke, including the recommendation "*Early mobilization and movement of the paretic limbs will reduce the risk of bone fracture after stroke....*" Three supporting references were supplied for this recommendation. Two references were the literature reviews previously described [1, 27], and the third reference was a narrative review by Beaupre and Lew [74] which included 18 longitudinal or cross-sectional studies which investigated bone density changes after stroke. Beaupre et al [74] reported that "*...it is beginning to be recognized that improvements in performing the activities of daily living...will also benefit the patient by helping to preserve bone mass and thereby reducing the risk of hip fracture...,*" in reference to a drug trial by Ikai et al. [75]. In the control group of this trial, people who had higher activity of daily living (ADL) function were observed to experience less bone loss over three months, compared to people who had lower ADL. Although the trial did not use an intervention based on ADL training, Ikai et al. concluded "*ADL is related to the progression of osteoporosis for women with hemiplegia and that increasing the level of ADL (will) lead to decrease the progression of osteoporosis ....*"

4. Discussion

Despite well-documented bone loss, increased fracture risk, and poor outcomes after fracture in people with stroke [19, 77], only seven of the 25 international stroke management guidelines identified in this search contained a keyword "bone, fracture, or osteoporosis." Many of the guidelines provided information on falls prevention, which is likely to reduce fracture rate, and the use of pharmacological bone protection was advocated. Targetted exercise appears to enhance site-specific bone architecture in healthy postmenopausal women, and there is limited evidence to support the use of physical activity to enhance bone mineralisation and architecture in chronic stroke patients. If physical activity from early after stroke can prevent bone loss, then current recommendations for early mobilisation may provide skeletal benefits. However, the safety of early mobilisation is still being investigated. Recommendations should take this into consideration, given their potential to change practice.

Although more research is required, it appears that physical activity has the capacity to maintain or improve bone-related outcomes in both the healthy and stroke adult populations. Healthy adults have an approximate annual bone loss of 1%. Healthy adult participants without reported activity limitations, who were included in the trials reported in this paper, were observed to have enhanced BMD when the intervention duration was at least a year. Moreover, exercise appears to positively influence site-specific bone geometry in postmenopausal women, with the most prominent changes in response to high-impact loading exercise. In contrast, in the trials which included people with chronic stroke who were able to walk at least 10 m, and who had potentially lost 15% of BMD in the first year after stroke, small effect sizes were observed in hip BMD, with just 23 weeks of physical activity intervention. It is possible that in people with higher rates of bone loss (stroke patients compared to healthy adults), a shorter duration of intervention is required to observe the effects of interventions. However, it is not clear whether these skeletal improvements (bone mineralisation and bone geometry) reduce fracture risk.

Coupled with bone fragility, falls are an important component of fracture risk for people with stroke [27]. De Kam et al. (2009) reported that exercise for people with low BMD or osteoporosis should include weight-bearing,

Table 3: Principles of exercise to maximise bone adaptation.

Exercise principle	More effective	Less effective
Weight bearing	(i) High impact (jogging, jumping) (ii) Bursts of activity (iii) Rapid movement	(i) Low impact (walking) (ii) Sustained activity (iii) Slow movement (iv) Non-weight-bearing aerobic (swimming or cycling) does not enhance bone density
Resistance training	(i) Heavy weight (ii) Rapid lifting (power training)	(i) Light weight (ii) Slow lift (traditional resistance training)
Muscle groups	(i) Target muscle connected to bones at risk of osteoporotic fracture (hip, wrist, spine)	(i) Non-specific-muscle groups
Length of training	(i) Short bouts interspersed with rest breaks	(i) Continuous movement
Direction of force	(i) Novel force patterns (change in direction or height of jumps)	(i) Repetitive force patterns (jogging in one direction, consistent height jumps)

Adapted from http://www.osteoporosis.org.au/images/stories/documents/internal/oa_exercise_gphp.pdf.

Table 4: Levels of evidence for intervention studies.

Level of evidence	Type of evidence
1++	High-quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias.
1+	Well-conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias.
1−	Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias.*
2++	High-quality systematic reviews of case-control or cohort studies. High-quality case-control or cohort studies with a very low risk of confounding, bias orchance and a high probability that the relationship is causal.
2+	Well-conducted case-control or cohort studies with a low risk of confounding, bias orChance, and a moderate probability that the relationship is causal.
2−	Case control or cohort studies with a high risk of confounding, bias or chance, and asignificant risk that the relationship is not causal.*
3	Nonanalytic studies (e.g., case reports and case series).
4	Expert opinion, formal consensus.

* Studies with a level of evidence "–" are not used as a basis for making a recommendation.
RCT, randomised controlled trial.
National Institute for Health and Clinical Excellence, *The guidelines manual 2007*, ed. NICE. 2007, London [76].

balance, and strength training to reduce falls and fracture risk. Most stroke management guidelines identified in this review recommended falls risk assessment and individualised management for all stroke patients. Level A evidence was presented in the guidelines to recommend mobility training for people with stroke who have difficulty walking [41] and individually tailored exercise programs for community-based falls prevention [44, 48]. Multifactorial falls prevention programs were recommended within the hospital environment, but supporting evidence for this was low [41, 59].

Until further research into poststroke bone loss is undertaken to guide the ongoing development of recommendations for protection of bone, it would be prudent to incorporate principles of bone adaptation into individually tailored stroke rehabilitation programs. Individual tailoring of programs for people with stroke should consider falls risk, mobility, potential low bone mass, ability to follow commands, and other stroke impairments. High impact exercises may not be practical or safe for people with stroke impairments and possible osteoporosis, but any weight-bearing activity provides greater loading on bone than bed rest. Guidelines for healthy adults [36] report that although there is a lack of evidence regarding the optimal prescription of exercise to prevent fracture, evidence-based principles of exercise to maximise bone adaptation have been developed (Table 3).

The body of literature regarding the use of exercise to modulate bone loss in adults demonstrates the large international interest in this important area of research. However, there are many gaps in the literature regarding the skeletal effect of physical activity, particularly in the stroke population. Only three intervention trials [42, 69, 71] which investigated the skeletal effects of physical activity in people with stroke were reported in any of the 25 international stroke guidelines and 12 systematic reviews identified in this review. There is an urgent need to develop the international research agenda regarding bone loss after stroke, in order to reduce fracture risk and its devastating outcomes after stroke.

Table 5: Gradings of recommendations.

Grade	Description
Level A	Body of evidence can be trusted to guide practice
Level B	Body of evidence can be trusted to guide practice in most situations
Level C	Body of evidence provides some support for recommendations(s), but care should be taken in its application
Level D	Body of evidence is weak, and recommendation must be applied with caution
Good clinical practice (GCP) points	Recommended best practice based on clinical experience and expert opinion

National Health and Medical Research Council, *NHMRC additional levels of evidence and grades for recommendations for developers of guidelines*. 2008–2010 [78].

5. Conclusion

Weight-bearing exercise and avoidance of bed rest have the potential to prevent bone loss after stroke. Bone loss appears to be rapid after stroke, but evidence regarding the timing and magnitude of bone loss is required, in order to determine the most beneficial timing of interventions. High-quality studies of over two year's duration, with adequate sample sizes and consistent outcome measurement, are required to determine whether targeted skeletal loading exercise, mobilisation, and avoidance of bed rest, from early after stroke are able to reduce bone loss and fracture risk. This information will support the ongoing development of international stroke management guidelines to guide rehabilitation practice and improve outcomes for people with stroke.

Appendices

A.

For more details, see Table 4.

B.

For more details, see Table 5.

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