

Bone health and back pain: What do we know and where should we go?

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Abstract

Summary Bone health is generally not considered in patients who present with chronic back pain. Nonetheless, bone health and back pain share common genetic and environmental correlates suggesting a co-dependence. Evidence exists for a relationship between back pain and impaired bone health. Here we present the evidence, theoretic framework and clinical relevance.

Bone health and back pain are important determinants of musculoskeletal health. Back pain experienced in youth is a risk factor for future back pain, while suboptimal bone health during development increases the risk of skeletal fragility in later life. Generally, bone health is not considered in patients with chronic back pain who do not demonstrate other well-recognised bone health risk factors or associated conditions. Nonetheless, evidence suggests that back pain and impaired bone health share common environmental and genetic correlates, indicating that bone health ought to be considered in the context of back pain in otherwise healthy individuals. This review describes the likely mechanisms explaining the relationship between back pain and impaired bone health, evidence concerning the relationship and suggestions for future research. A narrative literature search was conducted using CINAHL, Medline,

PubMed and Web of Science electronic databases. A history of back pain is associated with decreased bone mineral density in adults, yet this tends to be site-specific. No studies were identified examining this association in youth, yet the negative effects of childhood skeletal trauma and obesity on bone and spinal health provide indirect evidence for an association. Further research is required to clarify the impact of back pain on bone health at different lifespan stages using prospective cohort designs.

Keywords Back pain · Behaviour · Bone health · Bone mineral density · Genetics · Review

Introduction

Bone health and back pain are two important and likely correlated aspects of musculoskeletal health across the life span. An association between bone health and back pain is plausible given the environmental and genetic correlates which are common to both.

Bone health relates to maintenance of the structural integrity of the skeleton throughout life, encompassing both bone accrual and bone loss. Several indices of bone health are available, yet arguably, the most clinically relevant is bone mineral density (BMD) [1] as measured by dual energy X-ray absorptiometry (DXA). BMD is a surrogate clinical measure of bone strength and therefore the resistance to fracture [2], reflecting peak bone mass and extent of bone loss. Ensuring optimal bone health in childhood, adolescence and adulthood through adequate physical activity, nutrition and healthy lifestyle habits is important since these environmental factors minimise the impact of bone loss later in life [3–6]. However, a large component of bone health is also determined by genetic

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factors [7, 8]. Prevention of bone conditions common in late adulthood, such as osteoporosis, remains a major public health priority considering the burden this disorder imposes on the individual as well as the health care system [9]. Consequently, a large amount of research has been directed towards optimising bone health, predominantly in the context of post-menopausal and age-related osteoporosis, through pharmacological [10], physical activity [11, 12], lifestyle modification [13] and nutritional [14, 15] interventions. Although these interventions are aimed at minimising bone loss, enhancement of bone accrual *prior* to late adulthood, is now recognised as being equally, if not more, important from a developmental perspective [16].

Back pain is one of the most prevalent musculoskeletal disorders experienced throughout life and places a significant burden on the individual and the community [9, 17]. The lifetime community prevalence of low back pain in adults has been reported to be as high as 85.5%, and significant activity limitation occurs in about one in ten adults with back pain [18–20]. Back pain imposes the greatest burden during middle age [9], thus interventions are important for this age group, while preventative strategies are indicated earlier in life. Importantly, back pain is *not* trivial in youth [21]. International epidemiologic studies report a low point prevalence for back pain among children (1–6%) which rises sharply during adolescence (18–50%), approaching adult rates [21–25], while the lifetime prevalence of back pain experienced by adolescents is reported to be up to 84% in the lumbar spine and 72% in the thoracic spine [26]. Of concern is that back pain experienced by children and adolescents is associated with disability in up to 94% of cases [27] and that back pain is becoming more common in adolescents, suggesting a growing disease burden in adulthood [28] due to the higher prevalence of back pain sequelae, one of which may be impaired bone health.

Bone health and back pain are both determined through a developmental trajectory, and the risk for a disruption to normal trajectories seems to be high in youth. For example, during youth, there is a narrow window of opportunity for optimising peak bone mass, which is around the time of peak height velocity [29]. Moreover, it has been estimated that between a quarter to half of adult calcium is deposited at this time [30, 31]. Interruptions to the attainment of peak bone mass during youth may lead to severe skeletal consequences in later life [16], specifically inadequate bone mass in middle age and increased bone fragility in late adulthood. Similarly, back pain experienced in childhood is a strong predictor for back pain later in adolescence [32] and in middle age [33–35]. Therefore, attempts to optimise bone and spinal health in youth and middle age are important. Moreover, it may also be important to minimise the impact of any dependent relationship between back pain and impaired bone health.

A relationship between impaired bone health and back pain is readily apparent in conditions such as osteoporosis and during late adulthood. In these contexts, episodes of back pain are commonly mediated by vertebral fractures [36] and hyper-kyphosis [37] and the association between back pain and bone health, and mechanisms leading to impaired bone health, are well recognised. However, it is still difficult to establish a definitive relationship between bone health and back pain in the contexts of osteoporosis or old age due to potentially confounding variables such as the increased prevalence of spinal degenerative and structural changes, accelerated bone loss due to decreasing levels of circulating oestrogen, and difficulty in diagnosing vertebral fractures [38]. It may be, for these and other reasons, that previous studies have not established a strong negative relationship between BMD and back pain in elderly populations [39–41]. The relationship between bone health and back pain is much less clear for populations where recognised risk factors for, or conditions associated with, impaired bone health are absent.

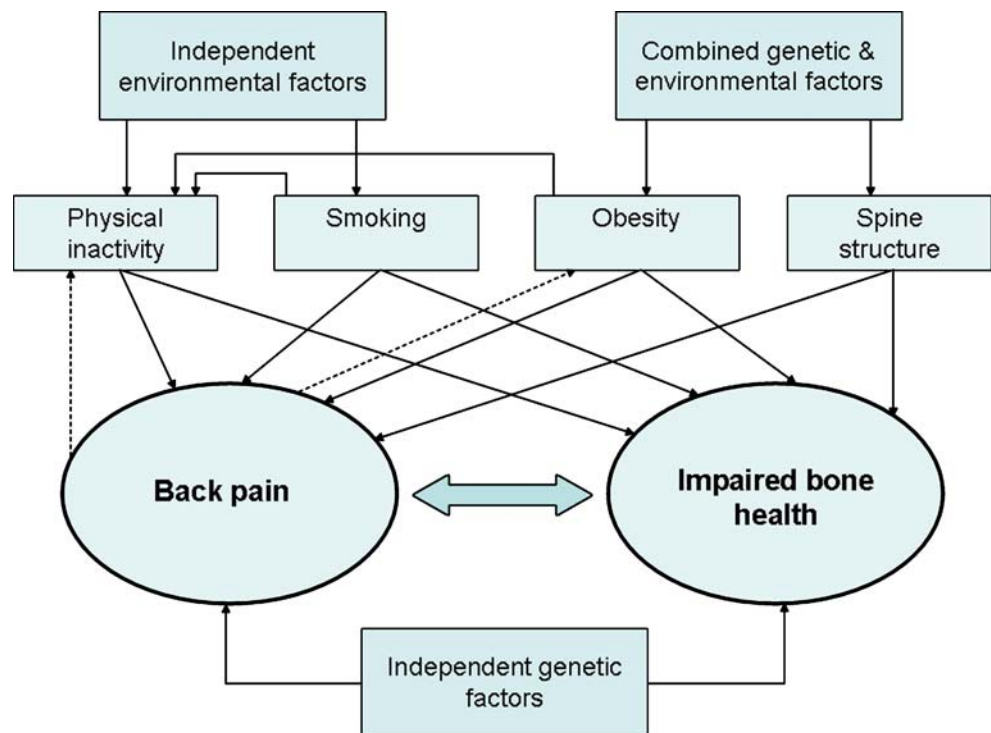
The aim of this review is to consider plausible mechanisms for a potential relationship between bone health and back pain (outside the contexts of osteoporosis and late adulthood) and present the evidence concerning this relationship. Furthermore, we aim to highlight to clinicians the potential importance of considering bone health in the context of chronic back pain in youth and middle age, given the individual and community significance of back pain and its implications for impaired bone health in later life. This may be particularly important for current clinical practice where bone health is not routinely investigated in patients who present with chronic back pain [42, 43] and who do not demonstrate risk factors for comorbidities such as endocrinopathies, rheumatic disease, malignancy, vascular disease, metabolic bone disease or skeletal trauma. Finally, we aim to highlight areas where future research should be focussed.

A literature search was performed using CINAHL, Medline, PubMed and Web of Science electronic databases from inception to December 2007 as well as cross-searching reference lists of relevant papers. Given the limited literature, we chose to present a narrative review rather than a systematic review to avoid the possibility of excluding studies with a low level of evidence but which were nonetheless of clinical importance.

Plausible mechanisms for an association between bone health and back pain

Both environmental and genetic factors impact upon bone health and the development of back pain. Figure 1 represents the plausible links between bone health, back pain and shared risk factors.

Fig. 1 Model illustrating the environmental and genetic factors which impact on back pain and bone health



Independent environmental factors impacting on bone health and back pain

Bone health is likely to be affected most significantly by a reduction in physical activity related to the onset of back pain. Bone responds to mechanical load and the response tends to be U-shaped, where both reduced physical activity and very high levels of physical activity are associated with bone loss [44]. The nature of severe and disabling back pain is such that vigorous physical activities which load the spine and/or lower limbs are limited or avoided, leading to reduced physical fitness [45, 46], yet physical capacity to perform non-vigorous activities of daily living often remains unaffected [47]. Individuals with severe back pain tend to stiffen the trunk and limit normal movement at the intervertebral joints [48–51]. This altered neuromuscular strategy decreases the opportunity for normal physiologic stresses, necessary for the maintenance of skeletal integrity, to be transferred through the vertebrae.

Smoking has been associated with back pain in epidemiologic studies [52, 53], yet due to the predominance of cross-sectional studies, causation cannot yet be established. Nonetheless, animal models confirm smoking causes intervertebral disc degeneration [54]. Whether these smoking-induced changes are associated with pain in humans is uncertain. Smoking is also an independent risk factor for bone loss and fractures, and the likely mechanisms have been reviewed previously [13]. The negative cardiopulmonary effects of smoking also limit the ability of

individuals to engage in vigorous physical (osteogenic) activity.

Combined genetic and environmental factors impacting on bone health and back pain

In addition to physical inactivity, other factors which are mediated by both environmental and genetic influences also mediate back pain and bone health, for example, obesity and spinal structural changes. Obesity has been associated with back pain in adolescents and adults, yet causation remains uncertain [55]. The association between obesity and bone health is complex. Although a positive relationship has been reported between body fat mass and bone mineral measures in middle-aged women [56], there is evidence to suggest that obesity is not protective against bone loss [57]. Whereas high body mass may have positive effects on bone density due to mechanical loading effects and the conversion of androgens to oestrogen in adipose tissue, there are several observations which point to a negative effect of obesity on bone health. Preliminary evidence suggests that extreme obesity is associated with reduced BMD in post-menopausal women possibly due to high leptin levels [58], while obese children and adolescents appear to have inadequate bone mass and bone size in proportion to their weight [59, 60]. A recent study also highlighted that obesity may accelerate bone loss [61]. The authors reported that increased fat mass was associated with decreased bone mass when effects of mechanical loading

from body weight were adjusted for. Furthermore, the same genetic determinants of obesity also appear to influence bone health [62], and obesity is a risk factor for vitamin D deficiency, which is also an important mediator of bone health [63]. Similar to individuals who smoke, the capacity of obese individuals to perform vigorous physical activity is often reduced. Obesity, especially during youth, has also been shown to significantly increase the risk of intervertebral disc degeneration in the lumbar spine [64].

Spinal structural changes, such as intervertebral disc degeneration and endplate lesions, impact on bone health and back pain. Intervertebral disc degeneration is implicated in both bone health [65] and back pain [66] and is determined largely by genetics [67] and to a lesser extent (in the range of 5%) by environmental factors [68], such as physical inactivity and nightshift work [69]. Vertebral bone structure is also influenced by genetics [7] and the environment, such as repetitive lifting leading to endplate micro- and macro-trauma [70]. Increasingly, attention is being directed towards the relationship between back pain and vertebral bone structural changes characterised by bone marrow lesions adjacent to the vertebral endplate, known as Modic changes. These are MRI-detected abnormalities in vertebral subchondral bone extending from the vertebral endplate involving hypervascularisation as a result of inflammation (type 1), replacement of vertebral haematopoietic elements with fat (type 2) and bone sclerosis (type 3) [71]. These changes are strongly associated with disc degeneration [71, 72] and adult back pain [66, 72–74]. These studies highlight that both bone health and back pain can be influenced by spinal structural integrity which in turn is determined by a complex interaction between environment and genetics. These associations suggest a possible direct genetic link between bone health and back pain or an indirect link due to a predisposition in behaviour [68]. However, it is also important to consider that there is generally poor correspondence between pathoanatomical signs, e.g., disc degeneration and back pain [75]. This highlights the need for sub-classification in chronic back pain conditions and identification of groups where a link between pathoanatomy and pain is established, for example, individuals who present with Modic changes.

Independent genetic factors impacting on bone health and back pain

In the context of back pain, the heritability component appears to be dependent on age. At young adolescence (age 11), genetics appears to play a very minor role in the expression of back pain with 59% and 41% of variance in back pain attributed to non-shared and shared environmental factors, respectively, in Finnish twins [76]. Similar results have been reported for young Danish twins, yet in

later adolescence and middle adulthood, the genetic contribution to back pain is more significant (40–44%) [77]. In mid- to late adulthood, the genetic contribution to back pain is greater (30–68%), with more severe presentations of back pain having higher heritability [68, 78, 79], while in old age (70 years and older), the genetic contribution to back pain reduces to only a modest level in men and disappears for women [80]. Although genes and the environment exert a combined effect on bone health and back pain, it is important to recognise the potential for an independent effect of genetic factors common to each condition (see Fig. 1). For example, the vitamin D receptor (VDR) gene impacts on bone health and affects the predisposition to osteoporosis [16]. In addition to their association with low bone density, polymorphisms of the VDR gene have also been associated with degenerative lumbar disc disease in a single cohort, suggesting that such polymorphisms impact on both mineralized and non-mineralized tissue [81]. Although this does not provide primary evidence for heritability of disc degeneration, it points to a common genetic influence between bone health and back pain. Furthermore, haplotype data analysis in Caucasian families provided evidence for the RANK gene to be associated with obesity and osteoclastogenesis [82], while other quantitative trait loci shared between body fat mass and BMD have been identified [62], again suggesting shared genetic pathways between obesity and bone health.

Genetic factors have also been shown to account for a modest proportion of variance in spinal kinematics [83], endplate lesions such as Schmorl's nodes [84], intervertebral disc health [67, 68] and the back pain experience [68, 79, 80], all of which are likely to have implications on bone health through structural mechanisms as well as through behaviour, for example, the propensity to engage in physical activity [68, 78]. Although an association between back pain and psychological distress is well established, MacGregor et al. [78] demonstrated that this relationship is predominantly mediated by genetic rather than environmental factors. Notably, depression and anxiety have also been linked to reduced bone density and reduced bone turnover [85–88], highlighting another common genetic link between back pain and bone health. While the relationship between depression and reduced BMD is largely mediated by cortisol [86], which can contribute to reduced bone metabolism and alterations in bone architecture [89], the psychological sequelae and/or antecedents of back pain including stress, anxiety and depression contribute to a cycle of fear, avoidance, altered motor control and physical inactivity, thus contributing to the potentially negative impact on bone health. Although the importance of genetics in determining the aetiology of many health conditions is becoming increasingly recognised, it is difficult to speculate on a direct genetic link between

impaired bone health and back pain; nonetheless, there is some evidence to suggest this is plausible.

Evidence for the relationship between bone health and back pain

Relatively few studies have been conducted which specifically examine the relationship between bone health and back pain. Inconsistencies in the literature with respect to the relationship may be due to differences in cohort characteristics, particularly regarding the duration, severity and associated disability of back pain experienced. Inconsistencies may also be due to small sample sizes and variability in the bone densitometry methods used in the studies. These differences may cloud the relationship between bone health and back pain. Here we report the evidence for a relationship between bone health and back pain in middle age and youth.

Healthy adults

Manabe et al. [90] reported a positive relationship between BMD and back pain in middle-aged Japanese women (odds ratio [95% CI] 1.4 [1.14–1.73]), when adjusted for age and body mass index. The authors concluded that higher BMD was a predictive factor for an increasing prevalence of LBP. Although the investigators reported a large cross-sectional study ($n=2,244$) with adequate control for confounding lifestyle (smoking, alcohol, nutrition, physical activity) and medical characteristics, some design caveats should be considered.

First, BMD in that study was measured using DXA at the distal one third of the radius rather than the lumbar spine or hip. The radius is a non-weight-bearing bone, and thus, the biological significance of BMD measures at this site would largely depend on its correspondence to BMD measured at load-bearing sites such as the lumbar spine or hip. Notably, the group with significantly increased radial BMD in the study also demonstrated significantly decreased exercise, although the nature and mode of this exercise were not reported. Intuitively, a large component of the exercise regime would be lower limb weight-bearing, and thus, it would be expected that lumbar and hip BMD would be reduced, with little to no effect observed at the radius. A previous study established a significant association between physical activity and BMD at the hip and spine but not at the forearm [6] and suggested this was due to the fact that the radius is a non-weight-bearing bone. The distal third of the radius contains more cortical bone, rather than the metabolically active trabecular bone of interest [91], so the effect of back pain on trabecular bone would not be easily identified using forearm BMD.

Second, the authors reported the association between 'current' back pain and BMD, with no indication about the

pain duration, severity or associated disability. The combination of such a broad operational definition for back pain and focussing only on point prevalence may significantly affect the heterogeneity of the groups being compared. The potentially negative effects of back pain on BMD may not be evident in a point-prevalence investigation. Instead, severe back pain of 3–6 months duration or more may be required before BMD might be affected and changes identified [92]. An earlier study failed to establish a relationship between bone mineral content (BMC) measured at the forearm and back pain in a Scandinavian population of working adults ($n=575$) [93] and this is likely due to the same limitations as those discussed above. Finally, Haara et al. [94] reported no relationship (OR=1.03, 95% CI 0.95–1.13) between chronic back pain and a metacarpal index (MCI) among healthy Finnish adults. Similar to the aforementioned studies, this study failed to measure bone integrity in the lumbar spine, but instead measured a surrogate of BMD in the hand (MCI), which is unlikely to have any association with back pain for the reasons discussed above, or indeed any association to vertebral bone integrity. Moreover, the definition of chronic back pain was based only on 1 month prevalence and a physical examination consisting of range of motion and posture. Impairments in these physical parameters may not be evident if chronic back pain was caused predominantly by a motor control or psychosocial disorder [95].

Gaber et al. [96] examined the relationship between bone density and back pain in a moderately disabled (mean [SD] Oswestry 48 [17.2]%, range 18–78%), mixed gender sample ($n=25$) with protracted pain (mean [SD] 9 [7.8] years). The authors reported significantly lower Z scores for BMD measures taken at the lumbar spine compared to a Hologic age-matched reference database (admittedly, sub-optimal control data). Importantly, there was no significant difference in Z-scores between the subjects with back pain and age-matched scores for the forearm and hip, potentially indicating the importance of site-specific densitometry measures. In addition, 52% of the sample was classified as osteoporotic or osteopenic based on World Health Organisation (WHO) criteria. Although the age range was 25–63 years, the mean [SD] age was 45 [9.1] years, suggesting a low proportion of the cohort having post-menopausal osteoporosis. The lack of association between disability or duration of pain and BMD may be attributable to the small sample size. Although a pilot study, the findings provide some evidence for the negative effects of chronic back pain on bone health in a middle-aged population. Similarly, Ho et al. [97] reported a significantly greater loss in vertebral BMD among middle-aged Chinese women who experienced back pain ($n=27$) compared to women with no history of back pain ($n=56$) in the preceding 9 months after adjustment for body fat (mean

[SD] percentage change in BMD 3.2% [2.0] compared to 2.1% [3.1]). The BMD change at 24 months was similar, yet did not reach statistical significance (6.3% [3.4] compared to 5.7% [4.3]).

Discrete clinical groups (adults)

Findings from discrete clinical adult groups indirectly support a negative relationship between BMD and back pain. Transient bone loss is common during pregnancy and lactation [98], yet a recent study reported that although no association was observed between bone loss over a 23-week period of pregnancy (weeks 12–35) and back/pelvic pain, a subgroup of women who continued to experience back/pelvic pain at 5 months postpartum demonstrated significantly greater bone loss than other postpartum women who were pain-free at 5 months postpartum [99]. That study was limited by a small sample size ($n=48$); nonetheless, it points to a possible link between back pain and bone loss due to inactivity. Similarly, women who were prescribed bed rest during pregnancy experienced significantly greater trabecular bone loss, measured at the ultra-distal forearm (a site containing more trabecular than cortical bone), compared to those who were not prescribed bed rest, independent of preeclampsia and gestational hypertension [100]. Due to pregnancy, DXA scans were performed at forearm regions in both the aforementioned studies. Notably, the authors argued, as we do, that BMD assessment at the hip or spine would be more clinically meaningful.

Trauma and chronic injuries are known to affect bone health negatively. This is likely attributable to reduced physical activity associated with the condition when other confounding factors are controlled [101]. Reduced physical activity probably also contributes to bone loss in a range of musculoskeletal and neuropathic disorders. Adults with fibromyalgia [102] or rheumatoid arthritis [103] demonstrate lower BMD than healthy adults, while individuals with upper or lower extremity reflex sympathetic dystrophy demonstrate lower BMD in the affected limb [104] and unaffected limb [105]. Notably, data from animal models suggest that BMD deficits observed in the context of neuropathic pain is a consequence of disruptions in bone–nerve signalling rather than reduced mechanical loading [106]. Bogdanffy et al. [107] described a systematic decrease in areal BMD in the lumbar spine measured by DXA in patients who had undergone lumbar spinal fusion surgery due to intractable back pain. BMD measured by lateral projection DXA postoperatively decreased on average by 10.1% and 12.7% at 3 and 6 months, respectively. The deficit in BMD measured by AP-projection DXA was less (4.0–4.3%). The authors argued that the bone loss was likely due to altered mechanical loads imposed on the

lumbar spine and possibly related to reduced physical activity postoperatively.

Youth

We were unable to identify any studies examining the impact of back pain on bone health in healthy youth. However, musculoskeletal injury or pain sustained during childhood has been shown to negatively affect local and/or systemic bone accretion in later life even when physical activity, maturational, medication and nutritional factors were accounted for [108–110]. In cases of skeletal trauma, bone loss may be related to immobilisation or grossly reduced physical activity [101]. However, in a study of distal forearm fractures, where significant skeletal immobilisation is not practiced, the rate of bone accrual was less in the fracture group [108]. Whether this is a cause or effect of the fracture is uncertain. These studies provide some evidence for sustained negative effects of skeletal trauma on bone health in youth. Similar consequences may be observed with episodes of back pain in children or adolescents. In addition to trauma, childhood obesity is now recognised as an important negative factor in skeletal development. Obese children demonstrate reduced total body and vertebral bone mass for their mass, potentially leading to spinal overload and ultimately back pain [59, 60]. While the implications of obesity for bone accrual are uncertain, the association between childhood obesity and forearm fractures is well-established [111]. Coupled with back pain and the tendency towards reduced physical activity associated with back pain [21], childhood obesity appears likely to have an impact on bone health generally and may well lead to other musculoskeletal disorders.

Issues related to the evidence presented and recommendations for future directions

There is evidence in the literature suggesting a negative relationship between back pain and bone health. However, the scientific level of this evidence is low owing to study design limitations, particularly with respect to bone densitometry methods and the quality and extent of information collected with respect to back pain symptoms and outcomes, leading to heterogeneity among samples.

The impact of back pain on bone health is likely to be site-specific and therefore BMD should be measured at the lumbar spine wherever possible. As highlighted above, measurement of BMD at the distal radius may not provide an adequate or even valid representation of the effect of back pain on BMD since physiologic load, an osteogenic stimulus, would be reduced to a far greater extent at sites

other than the upper limb in a population disabled due to back pain. However, it is recognised that in circumstances such as pregnancy, measurement of hip and vertebral BMD is not appropriate.

Conversely, Manabe et al. [90] argued that BMD measured from the forearm was a better site for bone densitometry in their study population (middle-aged Japanese women) given that vertebral BMD measured by DXA may be artificially elevated due to degenerative changes in the spine [38]. A recent study also established a positive association between back pain and vertebral BMD in elderly males and attributed this to spinal degenerative changes [41]. Therefore, AP-DXA may not provide a valid representation of the impact of back pain on vertebral trabecular bone mass in adults due to the over-riding influence of spinal degenerative conditions. Indeed, some densitometry units choose not to use AP-DXA because of this limitation and instead rely on BMD measures taken from the hip or the lumbar spine through lateral projection DXA [112]. However, the impact of spinal degenerative changes on AP-DXA accuracy would be less significant in adolescents and young adults. Although considered less precise than AP-DXA, lateral projection DXA offers potential advantages with respect to diagnostic sensitivity, since the over-riding influences of degenerative conditions rich in dense cortical bone such as osteophytosis, facet joint osteoarthritis and aortic calcification are largely eliminated [36, 113, 114], and more precise measures of vertebral depth are possible. Lateral DXA has been used previously for these reasons when examining BMD changes after spinal fusion surgery performed for back pain, and the observed deficit in BMD was greater when measured by lateral DXA compared to AP-DXA [107]. Lateral DXA also provides an opportunity to measure subregional vertebral BMD. This technique has been shown previously to be precise [115] and demonstrates greater diagnostic sensitivity than AP-DXA [36, 116] due to the heterogeneous distribution of bone mineral content in the lumbar and thoracic spine [117]. Given that subregional bone mass has been shown to be modulated by intervertebral disc degeneration [65], and this is an important factor for back pain, and potentially the impact of painful back conditions on vertebral bone properties, lateral DXA may provide greater sensitivity for identifying the impact of back pain on bone health. It is important to note that DXA is unable to provide a true measure of volumetric BMD. Often, only areal BMD (BMC divided by projected bone area) is reported, which does not adequately account for variability in bone size. Instead, it has been argued that BMC and bone area or body size be used as outcome measures or be included in multivariate models in prospective clinical studies of bone densitometry, unless bone size is expected to remain constant across time [112].

A limitation of many of the studies presented in this review relates to the amount of information collected with respect to back pain. Only Gaber et al. [96] reported a mean [SD] duration of pain and associated disability. Without such information, it is difficult to interpret the impact of back pain on a population and homogeneity of the sample. Approximately 10% of adults who suffer from back pain experience significant activity limitation [18, 19], and it is this subgroup who are most likely to experience a negative bone health outcome. The association of vertebral BMC measures with back pain and disability was weak in a postmenopausal population with a mean [SD] Oswestry score of 20.5 [12.8] [39], while Gaber et al. [96] studied a more disabled population (Oswestry: 48 [17.2]) and observed a significant difference in *Z* scores compared with reference data. In addition to quantifying back pain severity and disability, the duration of pain is also an important variable. Studies which do not report a negative association between back pain and bone health [90, 93, 94] investigated only point prevalence of back pain and have not reported any duration, severity or disability information associated with the pain. It may be for these reasons and the fact that BMD was measured at the forearm that their findings conflict with those of Gaber et al. [96] and Ho et al. [97]. Finally, most studies presented in this review have been cross-sectional in design, limiting conclusions to associations between bone health and back pain rather than causation.

Considering these limitations, we recommend future studies should adopt a prospective cohort design to define more clearly the relationship between back pain and bone health. Cohorts should include children, adolescents and adults to identify the impact of chronic back pain on skeletal health during the transition to adulthood and late adulthood, respectively. Adequate adjustment for potentially confounding factors such as smoking, alcohol intake, nutrition, medical conditions, medication history, maturation and physical activity (vigorous and routine) is important for interpreting results. Detailed information about the experience of back pain including severity, duration and disability is important to ensure adequate homogeneity of the sample and to ensure that trivial pain episodes with little biological and public health importance are not over-estimated [19]. Recently, an international working party of expert researchers agreed on a minimum set of criteria that should be included in epidemiologic research into low back pain in an effort to introduce some standardisation into the field [118]. Equally important is to avoid diagnosing back disorders based solely on pathoanatomical signs or limited physical assessments, given the poor association between pain and radiographic signs and spinal range of motion, particularly in the context of motor control disorders. Finally, the relationship between bone

health and back pain should be explored throughout the lifecourse as risk profiles are likely to differ according to age and stage of life. The trajectory followed by risk factors is likely to vary, and these factors may be modifiable at different stages of the lifecourse. This developmental health concept is embraced by the WHO as the Lifecourse Approach to Health and Functional Capacity [119]. Models within this WHO framework suggest that there are critical periods of growth and development as well as sensitive developmental stages from infancy to late adolescence which influence health and functional capacity trajectories and risk profiles in later life. This concept is well recognised in the development of chronic conditions. For example, smoking history is a risk factor for cancer, heart disease and respiratory disease, while inadequate peak bone mass in youth is a risk factor for increased bone fragility in later life. We suggest a similar framework be used to study the impact of back pain on bone health.

In addition to epidemiologic studies, research efforts should also be directed towards medical imaging, for example, optimising methods for the measurement of subregional vertebral BMD and investigating Modic changes more closely. The clinical course and pathophysiological sequelae of Modic changes are relatively uncertain at the present time. In particular, the effects of chronic inflammatory processes, fatty degeneration of bone marrow and bone sclerosis in vertebral subchondral bone, coupled with the effects of back pain, may have important consequences for vertebral bone quality and bone strength.

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Conflicts of interest None.

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