Risk Assessment and Interventions for Individuals at Risk of Osteoporotic Fractures

by

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Author's Declaration

This thesis consists of material all of which I authored or co-authored: see Statement of Contributions included in the thesis. This is a true copy of the thesis, including any required final revisions, as accepted by my examiners. I understand that my thesis may be made electronically available to the public.

Statement of Contributions

Matteo Ponzano was the sole author for Chapters 1 and 6, which were written under the supervision of Dr. Lora Giangregorio and were not written for publication. This thesis consists in part of six manuscripts written for publication. Exceptions to sole authorship of material are as follows:

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The research presented in this chapter was conducted at the University of Waterloo and at KITE Toronto Rehabilitation Institute (at Lyndhurst Centre) by Matteo Ponzano under the supervision of Dr. Lora Giangregorio and Dr. B. Cathy Craven. Matteo Ponzano, Miss Lindsie Blencowe, Dr. Julio Furlan, Dr. Sivakumar Gulasingam, and, Dr. Hany Kasani are co-authors on the publications related to the work presented in this chapter.

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Abstract

Older adults, especially with low bone mass, hyperkyphosis or vertebral fractures (OVF), and individual with spinal cord injury (SCI) are at increased risk of fragility fractures. Individuals with SCI and OVFs are subgroups of people with osteoporosis that are at high risk of fractures and present unique impairments, limitations, and restrictions that require population-specific and individually tailored and interventions.

The **objectives** of this thesis were: 1) to explore potential sources of error during LS bone densitometry and trabecular bone score (TBS) values in individuals with SCI, and the applicability of TBS in fracture risk assessment; 2) to assess the effects of PRT on health-related outcomes in people with low bone mass or hyperkyphosis; 3) to establish recommendations for the non-pharmacological management of osteoporotic vertebral fractures; 4) to co-develop a virtually delivered education and training program on safe movement, pain management, nutrition, and exercise among people with osteoporotic vertebral fractures, and to test its acceptability and usability.

Chapter one consists of a review of the literature on the epidemiology of fragility fractures, their consequences in the populations at greater risk, and the knowledge gaps in terms of risk assessment and non-pharmacological management. **Chapter two** presents the findings from two observational studies. Study 1 explored potential sources of error during LS densitometry in people with chronic SCI. Facet sclerosis and osteophytes and challenges in detecting bone edges are the most common sources of error, and most of the scans presented vertebrae with outlier BMD values. Study 2 described lumbar spine TBS values in a cohort of people with chronic SCI, whether they change over a two-year period, and how TBS affects fracture risk assessment in people with SCI. Individuals with chronic SCI on this cohort presented with normal bone microarchitecture based on TBS. TBS was not different between sexes, people with motor complete and motor incomplete injury or with and without previous fragility fracture. Clinical decisions regarding fracture prevention should not be based on TBS or FRAX® in people with chronic SCI at this time. The **third chapter** reports the protocols of two systematic reviews. One systematic review investigated the effects of PRT interventions on health-related outcomes in people with low bone mass, while the second investigated the effects of exercise interventions on improving postural and health-

related outcomes in people with hyperkyphosis. The **fourth chapter** reports the outcomes of an International Modified Delphi Consensus process, which established recommendations on the non-pharmacological management of osteoporotic vertebral fractures. We generated recommendations on pain management (e.g., educate on pain expectation; assess pain-related psychological factors; limit prolonged sitting; lying supine with feet flat on surface and knees bent), nutrition (e.g., educating on recommended daily intake of protein, calcium, and vitamin D; refer to dietitian in presence of poor appetite or weight loss), safe movement (e.g., avoid heavy physical exertion, lifting, or activities that exacerbate pain for the first 12 weeks; bend at hip and knees; step to turn; hold objects close to body), and exercise (e.g., timing, intensity, example exercises, goals including improving back extensor endurance, spinal mobility, physical functioning, and balance). There was consensus on limiting bed rest, and on prescribing orthoses only to select patients. The **fifth chapter** presents the co-development of a virtual intervention for the non-pharmacological management of OVF (VIVA) and its acceptability and usability testing among people with OVF. VIVA has been co-developed to provide education and training on safe movement and pain management techniques, nutrition, and exercise, and involves seven 1-on-1 virtual sessions delivered by a physiotherapist over five weeks. We delivered VIVA to 8 individuals with vertebral fractures, to evaluate acceptability and usability. Participants perceived improvements in pain and felt more confident during the activities of daily living and in self-managing their OVF. All the participants believed that VIVA was very useful and were very satisfied with the 1-on-1 sessions. Three participants found the information received very easy to practice, four participants believed they were easy to practice, and one participant found them somewhat difficult. Four participants were very satisfied and four were satisfied with the supporting resources delivered throughout the program. Participants found accessing the resources easy, but think that logging in and out to access videos and resources, or to track adherence, was cumbersome. **Chapter six** provides a general discussion of how the present dissertation improved the knowledge in fracture risk assessment and non-pharmacological interventions in people at risk of fractures, and what the next steps to address the knowledge-to-action gaps in populations at high risk of fracture should be.

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Dedication

To my parents.
Who taught me everything.
To whom I owe everything.

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List of Abbreviations

aBMD: areal Bone Mineral Density
BMD: Bone Mineral Density
vBMD: volumetric Bone Mineral Density
BCW: Behavior Change Wheel
CAMOS: Canadian Multicentre Osteoporosis Study
CFS: Rockwood's Clinical Frailty Scale
CI: Confidence Interval
CT: Computed Tomography
EFS: Edmonton Frailty Scale
HCP: Healthcare Professional
HR: Hazard Ratio
HRpQCT: High-resolution Peripheral QCT
HRQoL: Health-Related Quality of Life
HU: Hounsfield units
IANA: International Association of Nutrition and Ageing
ICC: Intraclass Correlation Coefficient
IKT: Integrated Knowledge Translation
ISNCSCI: International Standards for Neurological Classification of SCI
IRR: Incidence Rate Ratio
ISCD: International Society for Clinical Densitometry
LS: Lumbar Spine
MCID: Minimum Clinically Important Difference
MD: Mean Difference
MRI: Magnetic resonance imaging
OVF: Osteoporotic Vertebral Fracture
OWD: Occiput-wall Distance
PRT: Progressive Resistance Training
RCT: Randomized Controlled Trial
ROI: Region Of Interest
pQCT: Peripheral QCT
QCT: Quantitative Computed Tomography
RR: Risk Ratios
SCI: Spinal Cord Injury
SMD: Standardized Mean Difference
TbN: Trabecular Number
TBS: Trabecular Bone Score
TbTh: Trabecular Thickness
TbSp: Trabecular Spacing
TbSpSD: Trabecular Spacing Standard Deviation
TDF: Theoretical Domains Framework

TUG: Timed Up and Go
VFA: Vertebral Fracture Assessment
VIVA: Virtual Intervention for Vertebral frActures
VOI: Volume Of Interest

Chapter 1
Introduction

1.1 Fragility factures: epidemiology and populations at greater risk

Fragility fractures are defined as fractures that occur in a low trauma event that would be insufficient to fracture healthy bones, such as a fall from standing height or less.[1] Fractures represent an important cause of morbidity and mortality: the risk of death is five- to eightfold increased in the first three months after hip fractures,[2,3] while 18% of people die within a year following an osteoporotic vertebral fracture (OVF).[4] The Kellogg International Working Group on the Prevention of Falls by the Elderly defined a fall as "an event which results in a person coming to rest inadvertently on the ground or other lower level and other than as a consequence of the following: sustaining a violent blow, loss of consciousness, sudden onset of paralysis, as in a stroke, an epileptic seizure".[5] The prevalence of falls among older adults is high, with 30-40% of individuals over the age of 65 experience at least one fall per year.[6] However, fragility fractures can occur without any trauma. Older age, female sex, low bone mineral density (BMD), previous fractures, parental history of hip fracture, smoking, and use of glucocorticoids are common risk factors for fractures.[7]

Older adults, especially with low bone mass, hyperkyphosis or OVF, and individuals with spinal cord injury are at high risk of fragility fractures. Specifically, individual with spinal cord injury (SCI) or OVFs are at high risk of sustaining a new fracture, but existing fracture risk assessment tools may not be applicable in people with SCI. The chances of having a subsequent OVF after the first one are high, and there is a need for improvements in the assessment of the risk of experiencing an OVF as well as assessment of OVF-related impairments or activity limitations, and interventions to prevent or manage them. Individuals with SCI and OVFs are subgroups of people with osteoporosis that are at high risk of fractures and present unique impairments, limitations, and restrictions that require population-specific and individually tailored and interventions. The studies included in the present dissertation provide novel insights on the assessment and management of two groups at high risk of fracture: individuals with SCI, and individuals with OVFs, living in the community.

1.1.1 Aging and osteoporosis

Aging is a physiological process that involves declines in neuromuscular function and performance, along with several comorbidities. Cardiovascular disease, diabetes, dyslipidemia and obesity are common during aging, and 70% of older adults have hypertension, which increases the odds of major cardiac conditions.[8,9] Aging may lead to frailty, a state of clinically recognizable vulnerability resulting in declines of physiological function across multiple organ systems.[10,11] The frailty phenotype proposed by Fried et al[10] includes five criteria (shrinking, weakness, poor endurance and energy, slowness and low physical activity level), and the presence of at least three criteria indicates frailty, while individuals with one or two criteria are identified as prefrail. The Clinical Practice Guidelines for the Identification and Management of Frailty recommend the Rockwood's Clinical Frailty Scale (CFS),[12] the International Association of Nutrition and Ageing (IANA)'s FRAIL scale,[13] and the Edmonton Frailty Scale (EFS) as screening tools for frailty.[14]

Aging is also characterized by a loss of both muscle and bone tissue. Sarcopenia is the term used to define the age-related loss of muscle mass, resulting from alterations of neural system, hormonal status and nutritional intake, that can result in physical disability, poor quality of life and death.[15–17] Muscle cross-sectional area decreases up to 40% between the age of 20 and 80 years,[18] while type II fibers are subjected to a greater atrophy compared to type I,[18] thus explaining the decrements in muscle strength with aging. During aging, BMD declines at a rate of 0.5% per year,[19] with peaks up to 2-4% within the first 5-10 years after menopause in females.[20] Osteoporosis is a bone disease characterized by low bone mass and microarchitectural deterioration of bone tissue, which leads to bone fragility and an increased risk of fractures.[21] Osteoporosis affects 9.9 million Americans and 1.5 million Canadians, and one in two Caucasian women and one in five Caucasian men will experience an osteoporosis-related fracture during their life.[22] Many people with osteoporosis live with fear of fractures, or with pain and impairments in physical function from prior fractures, which can result in reduced activity levels and community participation.[23] Age-related changes and osteoporosis result in a high susceptibility to injuries that, combined with the high incidence of falls, represents a life-threatening risk for older adults.

1.1.2 Osteoporotic vertebral fractures

OVFs are the most common type of fractures in individuals with osteoporosis,[24–26] and are associated with several morbidities and decreased survival.[27,28] An observational study in 2725 women showed that 20% of the 381 participants who developed an incident OVF will experience another one within one year,[29] and the risk of death is nine times higher after an OVF.[3] OVFs may cause pain, loss of height and progressive thoracic kyphosis, which may lead to difficulties in performing daily activities.[24,30] OVFs are associated with thoracic hyperkyphosis; indeed, the degree of kyphosis increases with the number of OVFs, especially anterior wedge thoracic fractures, while women without OVFs but with hyperkyphosis are more likely to experience a subsequent OVF.[31–33] However, only about one third of OVFs come to clinical attention, after self-reported pain or height loss prompt physicians to order a spine radiography,[34] but many fractures are not reported even when present on X-ray.[35] Data from the Canadian Multicentre Osteoporosis Study (CaMos) show that 21.5% of men and 23.5% of women aged 50 years or older have at least one vertebral compression deformity,[36] and approximately 50% of OVFs occur in people with a T-score greater than -2.5.[37] OVFs are typically diagnosed by lateral radiography of the vertebral column, with or without anteroposterior views.[38] Magnetic resonance imaging (MRI) or computed tomography (CT) are useful to identify suspected retropulsion, expansion of the fracture to the posterior column, involvement of the spinal cord or the timing of the fracture, as recent fractures have edema.[38,39] Furthermore, vertebral fracture assessment (VFA) is an application of new DXA fan-array scans, which permit accurate lateral projections of the spine from T4-T5. Indeed, fan-array machines do not cause parallax, since vertebral dimensions are not altered by the angle of the beams as happens with pencil-beam machine (see chapter 2.2 for a description of fan-array and pencil beam machines).[40] VFA can be performed with a quantitative or semiquantitative technique. The quantitative technique consists in the apposition of six landmarks, four on the corners and two on the endplate's midpoints, by the operator to identify the anterior, mid-, and posterior heights of the vertebra and quantify their reduction. Different thresholds have been proposed to diagnose OVFs. Prevalent OVFs[§] should be diagnosed if there is at least a 15% reduction in the ratio

[§] Prevalent fractures are those fracture identified at a baseline scan, as opposed to incident fractures, that were not present at the baseline and are detected for the first time during follow up scans.

between the anterior or the mid-height and the posterior height of the vertebra, or between the posterior height and the posterior height of an adjacent vertebra compared to a mean value for the normal population.[41–43] Other authors proposed a diagnosis of prevalent OVFs if a three-standard deviations reduction in the ratio between the anterior or the mid-height and the posterior height of the vertebra compared to normative data is present.[44,45] Incident OVFs are diagnosed in the presence of a 20-25% decrease of one of the vertebral heights compared to the baseline scan.[46] The semi-quantitative technique developed by Harry Genant[47] is based on the visual recognition of three types of vertebral deformities (wedge, biconcave or crush) whose gravity is assessed on a 4-point scale: grade 0 = no deformity, grade 1 = mild deformity (reduction in vertebral area of approximately 10-20%), grade 2 = moderate deformity (reduction in vertebral area of approximately 20-40%), grade 3 = severe deformity (reduction in vertebral area >40%). Even though Genant's technique relies on the experience of the observer in the detection of changes in vertebral shape, the apparent objectivity of the semiquantitative technique is debatable. Indeed, landmark placement is a subjective process that may also be affected by confounders and patient positioning. On the other hand, the Algorithm-Based Qualitative methodology[48] aims to distinguish OVFs from non-osteoporotic or non-fracture deformities based on the visual analysis of the endplates. The combination of quantitative and semi-quantitative techniques is suggested over the use of either one alone.[40] In the thesis, we will define and classify OVFs according to the semi-quantitative technique by Harry Genant.[47]

1.1.3 Hyperkyphosis

The physiologic thoracic spine curvature averages between 20º and 29° in the childhood and through the third decade of life,[49] while values over 40º define hyperkyphosis.[50,51] It has been estimated that 20%-40% of older adults have hyperkyphosis.[50,51] with several consequences in terms of musculoskeletal health, physical functioning and quality of life. Forward head posture, shoulder protraction, flattening of lumbar lordosis are common changes after hyperkyphosis,[52] and people with hyperkyphosis are at high risk of future fractures independent of age and previous

fractures.[33,53,54] Morphological alterations can impair pulmonary function[55–59] and physical functioning, as people with hyperkyphosis have impaired balance and reduced gait speed, which put them at risk of falls.[52] Consequently, quality of life is affected, with general fear and low satisfaction in perceived health, relationships, economic conditions and life in general.[51,60] Furthermore, hyperkyphosis and its severity are associated with mortality independent of BMD and OVFs.[50,61,62]

Hyperkyphosis is also present in many individuals with spinal cord injury (SCI). Indeed, muscles like rectus femoris, glutei, tensor fasciae latae, iliopsoas, erector spinae and abdominal muscles are responsible for the control of the center of pressure in able-bodied individuals in a sitting position, but people living with SCI are totally or partially lacking motor control of the aforementioned muscles, therefore their ability of maintaining sitting balance is reduced. The most relevant postural alteration caused by the impaired trunk control is a posterior tilting of the pelvis, which results in flattened lumbar spine, thoracic hyperkyphosis, and hyper-extension of the cervical spine.[63] The resulting hunched posture provides biomechanical stability, allowing shifting the body weight more backward to improve balance while sitting in the wheelchair, and enables activities of daily living and wheelchair propulsion.[64] Consequently, people with SCI assume a "c-shaped" sitting posture caused by a 15-degrees posterior tilting of the pelvis compared to non-injured individuals.[65] Furthermore, pelvic angle and the forward head posture increase with age and duration of spinal cord injury independent of kyphosis,[66] and this may result in anterior, posterior, or lateral spinal deformities, spasticity, increased risk of pressure ulcers, neck and shoulder pain and decreased respiratory function.[63,65]

The X-ray measured Cobb angle[67] is the gold standard to assess spine curvatures. Two lines perpendicular to the superior endplate of T4 and the inferior endplate of T12 are drawn, and two other lines are drawn perpendicularly to these two lines to from and angle that defines the degree of kyphosis.[68] Their poor visibility due to overlying structures represents the reason why of the first three thoracic vertebrae are not considered.[69] According to the original technique, lines are manually drawn on radiographic films to measure Cobb angle. However, measurement errors up to 5º may occur, resulting in spurious diagnoses of scoliosis curves progression.[70,71] Therefore, three methodological approaches (computer assisted, automatic and smartphone apps) have been

proposed to offset this measurement error. Findings from a systematic review[72] showed high reliability (intraclass correlation coefficient [ICC] 0.83-0.99) in all the included studies, with lower standard error and mean absolute difference in automatic compared to digital and manual procedures. The authors also noticed that only mobile apps that automatically calculate the Cobb angle have higher intra- and inter-observer agreement than manual procedures. Furthermore, the radiation exposure and the high costs support the development of alternative tools that are more easily usable in clinical practice. The flexicurve is a flexible ruler that must be pressed onto the thoracic and lumbar spine, and the obtained conformation is reported on a paper to calculate the kyphosis index[31] or angle.[73] One study found a high correlation between Cobb angle and kyphosis index (ICC 0.88-0.99),[68] but two studies with larger sample size revealed only a moderate correlation (ICC 0.68-0.69).[73,74] Despite the moderate-to-high correlation, values obtained with the flexicurve are, on average, 20º smaller than the Cobb angle;[73,75] therefore, caution is recommended before making inferences. Manual inclinometers demonstrated high correlation and agreement with Cobb angle[75] and high intra-rater reliability[76,77] thus representing a valid tool to assess kyphosis in clinical practice. Similar results were obtained by using digital inclinometers, which showed a high intra-rater reliability (ICC 0.83) when tested in healthy individuals between 20-35 years.[78] Occiput-wall distance (OWD) is a surrogate measure of kyphosis that is correlated with flexicurve angle (r = 0.90),[79] and provides indications regarding the necessity of performing spine X-rays. OWD is moderately correlated with kyphosis angle measured with inclinometer (r = 0.72), and thresholds of 5cm have been proposed to diagnose hyperkyphosis or suggest the need to perform a spine radiography.[80] The Blocks Method represents another surrogate measure of kyphosis: blocks with a height of 1.7cm are placed under the patient's head until a neutral position of the head (head neither hyperextended nor hyperflexed) was achieved and with the eyes directed toward the ceiling.[50,81] The Spinal Mouse, a wheeled accelerometer which rolls along the spine, is another non-radiographic tool to record distances and changes of inclination.[82] This device has high intra- and interrater reliability,[82–84] but the validity is low.[84] Finally, one study[85] demonstrated high validity of a manual goniometer, but further research is needed to test its reliability. Non-radiographic techniques offer several advantages in the clinical practice; however, they present some limitations. Indeed, skin-surfaced technique follow the spinous process and not the vertebral

bodies, as it happens during x-ray; furthermore, the amount of adipose tissue overlying the spine may represent a threat to the validity of the measurement.[82] The incorrect positioning of the landmarks is the most common source of error when using all the methods that rely on the identification of the beginning and the end of the curve.[73,86] Therefore, practitioners should base their choice on the available validity and reliability data, the cost-effectiveness of the method, the population being tested, the expertise of the evaluator(s).

1.1.4 Osteoporosis after spinal cord injury

In Canada, over 86,000 people live with spinal cord injury (SCI), with an estimated incidence of 3,675 new cases per year.[87] Spinal cord lesions can be either complete, when there is no sensory or motor function in the lowest sacral segment, or incomplete, when sensory and/or motor function is preserved to some extent below the neurological level (including the lowest sacral segments).[88] The level of lesion determines the distinction between tetraplegia, a lesion of the cervical elements of the spinal cord who results in impairments of the four extremities, trunk and pelvic muscles, and paraplegia, a lesion to the thoracic, lumbar or sacral spine who spares the functionality of the arm and of all the muscles above the level of lesion.[88]

After SCI, atrophy of the muscles below the level of the lesion, along with a switch from type I to type IIx muscle fibers, can be observed.[89] Biopsies from vastus lateralis showed that the greatest decrease in muscle fiber cross-sectional area (CSA) occurred 6 weeks after injury (-22%), followed by a less important reduction between 11 and 24 weeks (-10%).[90] The loss of muscle reaches a plateau 11 months after injury, and CSA of individuals with SCI is 45-80% of able-bodied individuals.[91,92] Similar declines are observed in bone tissue. In the acute phase, trabecular bone content is reduced by 4% per month,[93] resulting in tibial trabecular and cortical bone loss up to 80% and 30%, respectively.[94] Despite some evidence of a plateau of bone loss 3-5 years post injury,[95,96] a slight ongoing bone loss (0.45% per month) has been documented at the tibial epiphysis as late as 10 years from injury.[97] Consequently, fragility fractures are a common problem after SCI. Individuals with SCI have a fracture risk 5- to 23-fold higher than able-bodied individuals of similar age,[98] with a higher incidence of fractures compared to non-SCI individuals.[98,99] Twenty-five to forty-six percent of the people with chronic SCI will develop

fragility fractures,[98,100] and the first fracture occurs, on average, 9 years after the injury.[99,101] Low BMD, history of fractures, being female and older than 50 years of age, white race, complete or older injuries and use of opioid or anticonvulsants increase the risk of fractures in people with SCI.[102] Being paraplegic and having a high Charlson Comorbidity Indices represent additional risk factors for osteoporotic fractures.[98,103] The higher mobility of people with lower spinal cord lesions and the ability to take part in more dynamic activities may contribute to the higher incidence of fractures compared to individuals with tetraplegia. People with SCI usually fracture after low-energy traumas,[104] and transfers into or out of the wheelchair represent the main cause of fracture in people with SCI. A retrospective chart review of 140 people with SCI for at least 2 years revealed that 43% of the fractures in the lower extremities occurred while using a wheelchair, 24% of which occurred during transfers. Another retrospective study of 325 individuals with chronic SCI demonstrated that 59% of fractures were caused by a fall, but only 24% were falls from the wheelchair.[105] The discrepancy may be explained by the different methods used in the two studies. Indeed, Champs et al attributed the cause of a fracture to a transfer only if the fracture occurred during the transfer per se, while the cause was recognized as a fall if the individual fell during transfer. Moreover, many wheelchair-related fractures are unrelated to transfers.[104] The most common circumstances include collision with objects, trips or falls due to environmental hazard, equipment failure, bathing and toileting, and turning in bed, while 22% of fractures occur during transfers not involving wheelchairs.[104]

Traumatic etiology of SCI, longer duration of injury and being female older than 50 years are associated with an increased risk of femur and tibia/fibula fractures, but not hip fractures.[106] Age and sex do not affect the location of the fractures, but women with SCI experience fracture more often than men.[98,104,107] The distal femur and proximal tibia are the two most common locations of fractures in people with SCI, but further research is required to establish if there are any differences between ambulatory and wheelchair users. Akhigbe et al[104] analyzed charts from 138 wheelchair bound and two ambulatory individuals, and 54% of fractures occurred at tibia/fibula and 33% at femur. Conversely, Champs et al[105] observed an opposite trend, with ambulatory individuals fracturing more often the distal tibia/fibula compared to wheelchair users, who fracture more frequently the distal and proximal femur.[105] Similarly, a retrospective study of

107 individuals with SCI, of whom 92 were ASIA-A, reported that 61% of fractures occurred at femoral level and 39% at the lower leg.[108]

Thirty-four to seventy-five percent of people with SCI experience at least one fall in their life,[109–113] and most of them happen during walking;[113] therefore, interventions to prevent falls in ambulatory individuals with SCI do not differ to those for able-bodied individuals at risk of a fall. Falls remain a major concern among wheelchair users, but their dynamics is different. Kirby et al[114] administered a postal questionnaire to individuals with SCI living in Nova Scotia. Paraplegia or spina bifida, daily wheelchair use, male gender, younger age and propelling with both hands emerged as common factors associated with injurious wheelchair-related accidents. Among the 577 people who answered the questionnaire, 57.4% reported that they had tipped over or fallen from their wheelchairs at least once, and 66% reported they had partially tipped. Finally, tipping and falling are the most common forms of accidents, and are responsible for 68.5% and 73.2% of fatal and nonfatal injuries, respectively. Wheelchair user typically fall during transfers, while trying to reach something, operating a van lift or playing sports.[115,116] Wheelchair accidents occur mainly outdoors, and several environmental hazards, like uneven, wet or icy terrains, ramps and curbs, increase the risk of falls.[114,116–118] Tips and falls often result in fractures (45.5%), lacerations (22.3%), and contusions/abrasions (20.1%),[119] 59% of fractures after SCI happen as a consequence of a fall.[105] Therefore, prevention strategies for falls and fractures among individuals with SCI must consider the type of injury and daily habits of individuals, such as the amount of time spent on a wheelchair, especially outdoor, the modality of transfer, and the use of van lifts.

1.2 The assessment of fracture risk

1.2.1 Fracture risk calculators

The identification of people at greater risk for fracture is a key step in fracture prevention. Apart from low bone mineral density (BMD), several risk factors (i.e., obesity, smoking, alcohol ≥3 units/day, personal and/or family history of fragility and hip fractures, use of glucocorticoids, rheumatoid arthritis) have been associated with an increased risk of fragility fracture. FRAX®,[120] CAROC,[121] Garvan[122] and QFracture[123,124] are the most common fracture risk assessment tools

used in clinical practice. The FRAX® tool[120] was developed from nine population-studies (the Rotterdam Study, The European Vertebral Osteoporosis Study – later the European Prospective Osteoporosis Study (EVOS/EPOS), The Canadian Multicentre Osteoporosis Study (CaMos), Rochester, Sheffield, Dubbo, a cohort from Hiroshima and two cohorts from Gothenburg), and predicts the 10-year risk for hip and major osteoporotic fractures by combining clinical risk factors specific for a designated country with BMD at the femoral neck (however, the 10-year risk of injury can be also calculated without BMD). The Canadian Association of Radiologists and Osteoporosis Canada (CAROC) system for fracture risk assessment[121] takes into account BMD, sex, age, prior fragility fractures, and glucocorticoid use; CAROC categorizes 10-year major osteoporotic fracture risk as low (<10%), moderate (10–20%), or high (>20%) and does not require computer or web access. The Garvan algorithm[122] was created from baseline data of over 2,000 men and women 60 years or older enrolled in the Dubbo Osteoporosis Epidemiology Study, and the 5- or 10-year fracture risk is calculated based upon 5 clinical risk factors with or without BMD. Finally, the QFracture tool[123,124] was developed in the UK from a database of 3.7 million patients and can estimate the risk of fracture from 1 to 10 years including 25 clinical risk factors with or without BMD. However, even though these tools can estimate the fracture risk regardless of BMD, BMD alone has a higher gradient or risk (i.e., increase in fracture risk per each standard deviation decrease in BMD) compared to the clinical risk factors (excluding history of fracture);[125] therefore, where possible, the inclusion of BMD in the fracture risk calculation is recommended. However, fracture risk assessment tools have not been validated in the SCI population,[126] but different BMD fracture risk assessment methods or BMD thresholds have been proposed for people with SCI. Garland et al[127] estimated a fracture threshold with a BMD $\leq$0.78 g/cm^2 and a fracture breakpoint of $\leq$0.49 g/cm^2. Eser et al[128] identified fracture thresholds for femoral epiphysis trabecular vBMD (<114 mg/cm^3) and tibia epiphysis trabecular vBMD (<72 mg/cm^3), while, according to Lala et al[129] the fracture threshold for tibial epiphysis should be elevated to 84 mg/cm^3.

1.2.2 Assessment of areal bone mineral density (aBMD)

Dual-Energy X-ray Absorptiometry (DXA) is the gold standard to evaluate areal bone mineral density (aBMD). Indeed, it has been demonstrated that the sensitivity of standard x-rays is not adequate to diagnose osteoporosis before it becomes severe enough to result in fractures.[130] During DXA scans, energy beams of two different energies are produced by an x-ray tube and absorbed by the bone to an extent directly proportional to its density, and the beams that are not absorbed are detected on the other side of the body by a radiation detector. The energy of radiation absorbed by every pixel is converted into an areal density (g/cm^2), and the sum of the number of pixels in a certain region of interest (ROI) is used to calculate the bone density.[130–132] There are two different kinds of DXA machines: *pencil-beam scanners,* where a narrow pencil-shaped beam moves in tandem with a detector, and *fan-array scanners*, which consist on a broad fan-shaped beam and an array of detectors that allow an instantaneous quantification of the entire scan line with high precision and image resolution.[132] The studies performed to compare the two types of machines revealed no or very slight differences.[41,133,134] However, even though these discrepancies are not large enough to preclude the use of databases developed with pencil-beam scanners when using fan-array machines, this represents a potential source of error during longitudinal scans, that should not be performed without cross-calibrating the machine.[135]

According to the International Society for Clinical Densitometry (ISCD), osteoporosis in postmenopausal women and men 50 years or older is diagnosed with a T-score at the lumbar spine (anteroposterior projection L1-L4), total hip or femoral neck less than or equal to -2.5.[136] T-score corresponds to the number of standard deviations the patient's aBMD is lower than the average peak aBMD of young females. Lateral spine projection, Ward's triangle and greater trochanter should not be used for diagnosis because they tend to underestimate aBMD and may result in false diagnoses of osteoporosis.[136,137] Even though the lateral spine projection eliminates confounding effects like cortical posterior elements, its application is not recommended due to the overlap of L1-L2 with the ribs and of L4 with the hip. [138–140] The 2019 ISCD official position statement recommends that women and men undergo BMD testing if they are at least 65 and 70 years old, respectively.[136] People with SCI should have DXA scans of total hip, proximal tibia, and distal femur as soon as they are medically stable, and BMD at those sites is used to diagnose

osteoporosis, predict lower limb fractures and monitor treatments.[141] However, standardized protocols developed by DXA machine manufacturers to measure aBMD at the distal femur or proximal tibia, the two most common fracture sites in the SCI population, are not currently available. The Toronto Rehabilitation Institute created a protocol to assess aBMD at the knee region utilizing the lumbar spine software and a specific calculator for distal femur and proximal tibia (available at the following link: https://kite-uhn.com/clinical/tools/knee-dxa-protocol).[129]

DXA scanning tables have a weight limit of 136 kg, but abdominal width and thickness may be a source of errors also in obese adults and children weighting less than 136 kg.[131,132] In addition, 2D DXA imaging does not allow the distinction of the different bone components and, consequently, the understanding of the determinants of low bone mass. Furthermore, DXA images should be carefully reviewed due to several artifacts that may spuriously elevate – or, less frequently, lower – BMD. All the vertebrae affected by structural changes or artifacts must be excluded, and the ISCD recommends to base diagnoses on a different skeletal site if only one vertebra is eligible.[136] Moreover, vertebrae should be excluded if there is a T-score difference of at least -1 with an adjacent vertebra.[136]

1.2.3 Assessment of volumetric bone mineral density (vBMD)

Computed tomography (CT) provides a spatial distribution of an X-ray absorption coefficient that is normalized to the absorption of water and air, and is defined as CT value expressed as Hounsfield units (HU).[142] Quantitative computed tomography (QCT) is calibrated for BMD by means of a reference phantom located below the patient during the scan and provides 3D projections for the measurement of a volumetric BMD (vBMD) expressed as g/cm^3.[132,142] A series of axial CT images are reconstructed and transferred to an external computer, where a volume of interest (VOI) is identified. The ability of imaging a transverse slice through the abdomen that allows the distinct analysis of cortical and trabecular bone is the most relevant clinical application of QCT.[143] This feature is important because, although trabecular bone is the most metabolically active, cortical bone may play an important role in determining fracture risk.[144] On the other hand, the opportunity

to exclude the vertebral body cortical shell from the VOI, allows the quantification of LS trabecular BMD, whose variation are much higher than DXA LS BMD.[142,145]

The ISCD position statement affirms that QCT trabecular spine BMD predicts OVFs in postmenopausal women to the same extent that DXA LS BMD, but there are no data to make the same statement for men. Furthermore, total femur trabecular BMD but not trabecular spine BMD predicts hip fractures as well as DXA in both men and women.[136] The ISCD recommend using L1 and L2 for BMD analysis at the spine and from femoral neck to proximal shaft at the hip.[136] One of the greatest advantages of QCT technology is the high precision (1%-2%) in the assessment of BMD of spine, hip and radius with a scanning duration in the order of seconds or a few minutes.[145]

Peripheral QCT (pQCT) allows the assessment of muscle and bone at the proximal tibia, and it is particularly relevant in the SCI population, as the distal femur and proximal tibia are the sites where the greatest number of fractures occur. Furthermore, since radiosensitive organs are distant from the primarily exposed area, the radiation exposure associated with pQCT is similar to the ones associated with DXA and single-slice qCT.[146] pQCT scans are typically performed at 4% (ultradistal), 38% and 66% of the tibial length moving distal to proximal, with the latter being used to estimate muscle size and fat infiltration. Giangregorio et al provided a detailed description of the procedures of image acquisition and analysis in people with SCI.[147] CORTBD mode is used to calculate total, trabecular, cortical and subcortical bone densities and areas at the bone shaft, while CALCBD is used at the ultradistal tibia, and require the choice of a contour and a peel mode by the user. In line with a previous study,[148] the authors used a contour mode 3 and a peel mode 2 with inner and outer thresholds of 130 mg/cm^3 and 400 mg/cm^3, respectively, at the ultradistal tibia, and 710 mg/cm^3 threshold to define cortical bone at the bone shaft. However, given the considerable endocortical resorption that takes place in people with SCI, the authors recommend considering a lower threshold before beginning the analysis.

QCT technology presents some limitations. The angulation of the spine with reference to the scanner gantry and patient positioning across longitudinal scans are two significant challenges.[143] Similarly, the identification of the same volume of interest (VOI) during longitudinal scans represent another potential source of error. One of the main limitations of QCT is the low spatial resolution that causes blurring of the bone cortex, thus increasing its thickness

with a consequent underestimation of BMD.[145] High-resolution peripheral QCT (HRpQCT) offsets this issue thanks to an increased resolution that permits the imaging of single trabeculae.[149,150] HR-pQCT allows the quantification of several macro and microstructural parameters, such as trabecular number (TbN), thickness (TbTh), spacing (TbSp), trabecular spacing standard deviation (TbSpSD) and cortical thickness, with an elevated precision ranging from 0.9% to 4.4%.[150] However, this machine is currently available for distal radius and tibia, and the high doses of radiation represent the main drawback of this technique.

1.2.4 Trabecular Bone Score (TBS)

Trabecular bone score (TBS) is a textural index that estimates trabecular bone microarchitecture by evaluating pixel grey level variation in conventional DXA scans by using a specific software and without exposing patients to further radiations.[151] The TBS iNsight™ software (Medimaps Group SA, Geneva, Switzerland) works on most GE and Hologic DXA scanners, and automatically provides TBS values with new DXA scans or calculates TBS values retrospectively from scans previously performed. DXA machines do not have a sufficient resolution to identify individual trabeculae, but the fractal dimension allows the estimation of the complexity of bone tissue structure based on the surface irregularity.[152] Therefore, the tridimensional bone structure is projected onto a bidimensional plane, and a dense trabecular microstructure generates an image containing a large number of pixel-to-pixel grey-level variations of small amplitude, whereas a porous trabecular structure produces an image with a low number of pixel-to-pixel grey-level variations, but of much higher amplitude. The squared sum of the grey-level differences between pixels is used to calculate a variogram, which allows the user to estimate the tridimensional structure of the bone. TBS is calculated as the slope of the log-log transform of the variogram, where the slope is given by the amplitude of the grey-level variations. TBS is measured at the lumbar spine using the same ROI as the BMD measurement and, even though values are given for every single vertebra, the reported index is the average of the first four lumbar vertebrae. In clinical practice, a TBS index corresponding to or greater than 1.350 is considered normal, between 1.200 and 1.350 identifies a partially degraded bone microarchitecture, while an index lower than

1.200 indicates a degraded microarchitecture.[153] TBS is negatively associated with weight, BMI and age,[154–157] but it is not affected by sex after adjusting for abdominal and truncal soft tissue thickness[158]. The ISCD states that TBS can be used in association with FRAX® and BMD to adjust FRAX®-probability of fracture in post-menopausal women and older men.[136] Indeed, TBS, alone and combined with LS BMD, improves the prediction of hip and major osteoporotic fractures compared to BMD alone and independently of FRAX®.[159–162]

1.3 Rationale

Individuals with SCI and those who experienced an OVF are populations at high risk of fracture or of sustaining a subsequent one; however, several gaps in terms of both risk assessment and interventions to prevent and manage fractures persist. At the present time, there are no risk assessment tools validated in people with SCI. Furthermore, individuals with SCI most commonly experience fractures at the distal femur and the proximal tibia, but the existing fracture risk assessment tools have poor sensitivity when it comes to identify people with SCI at higher risk.

The ISCD states that people with SCI should have a DXA scan of the total hip, proximal tibia, and distal femur as soon as medically stable.[136] However, some complications (e.g., contractures, heterotopic ossification, orthopedic hardware) may interfere with the acquisition of DXA scans, thus not allowing the estimation of BMD at body sites prone to fracture. For such individuals, looking at the LS might be an option. However, LS BMD appears to be within the normal range in people with SCI, and it is not clear whether some artifacts cause a spurious elevation of the BMD. Testing whether outcomes that proved to be effective in fracture risk prediction in the general population, without being affected by osteoarthritic changes, can be useful to estimate fracture risk assessment in the SCI population.

Furthermore, individuals with SCI and OVFs are subgroups of people with osteoporosis that are at high risk of fractures and present unique impairments, limitations, and restrictions that require population-specific and individually tailored and interventions. People with SCI often assume a hyperkyphotic posture, and the consequences of hyperkyphosis, as well as the association between hyperkyphosis and OVFs, made us plan on reviewing the literature on exercise for

hyperkyphosis, and designing a study to test whether an exercise intervention would improve posture in this population. However, due to the Covid-19 pandemic we had to revise our plan. OVFs are probably overlooked in people with SCI, but are also difficult to diagnose in the non-SCI population, as two thirds of OVFs are asymptomatic and only one third come to clinical attention.[26,34,163] Given the high risk of experience another OVF after the first one, and considering that symptomatic OVFs cause excruciating acute pain that, sometimes, become chronic, there is a need for interventions to manage OVFs. A 2019 Cochrane review[164] of exercise trials in people with OVF could include only 9 studies, and the findings show that exercise may improve mobility, while the evidence on the effects on pain and health-related quality of life were inconclusive. Furthermore, people with OVFs present with physical, functional, psychological, and social impairments and there is very limited evidence as to how address such impairments. Therefore, the first step to address this gap was to establish recommendations for the non-pharmacological management of OVFs, and then test the usability of a virtual rehabilitation intervention implementing the recommendations. Before developing a large-scale RCT, smaller studies that assess acceptability, usability, and feasibility are required. Covid-19 pandemic, as well as common barriers experiences by individuals with OVFs, such as transportation, bad weather, or lack of options for rehabilitation, made us decide to develop a virtual intervention.

The present dissertation reports findings from my doctoral research, that was focused on providing clarity on fracture risk assessment and management in two sub-populations at high risk of fracture with unique impairments and activity limitations. Specifically, we studied factors influencing the validity of LS BMD in people with SCI (e.g., is it really within the normal range, or do other factors affect it? What are TBS values in people with SCI?). We also established consensus on the non-pharmacological management of OVFs, and then developed and evaluated the acceptability, and usability of a virtual intervention for the management of pain after OVF.

1.3.1 Limitations of fracture risk assessment in individuals with SCI

BMD is a predictor of future fractures; however, most osteoporotic fractures occur to people with BMD above the threshold for low bone mass.[37] Indeed, fractures are a result of the imbalance between the force applied to the bone and the bone strength, and not only a consequence of low

BMD; furthermore, the mechanical properties of bone, its elasticity and rigidity are determined by microstructural (e.g., trabecular thickness and connectivity, cortical thickness and porosity) and ultrastructural (e.g., bone collagen, presence of crosslinks, etc.) parameters.[165] The greatest bone loss after SCI occurs in the lower legs,[166] but most of the fractures happen at the distal femur and proximal tibia.[104,105,108] OVFs are rarely diagnosed in people with SCI, who have a lumbar spine aBMD within normal values.[166–168] However, only one third of OVFs come to clinical attention in the general population,[26,34,163] and this may happen also in the SCI population, where the absence of sensory function reduces the perception of pain,[169] thus explaining the low number of ascertained OVFs. Furthermore, several factors may spuriously elevate aBMD in people with SCI. Heterotopic ossification (HO), degenerative joint diseases and calcifications are common after SCI.[170–172] Preliminary data showed that HO leads to overestimation of total hip BMD,[172] but the effects of these conditions have not been investigated in the lumbar spine. People with SCI who also have degenerative joint diseases have T-scores at the lumbar spine above the normal range when measured with DXA, but values indicating low bone mass when assessed with QCT.[168] Similarly, another cross-sectional study in people with SCI demonstrated that LS BMD measured with QCT was more than 2 standard deviations (SD) below the mean, while LS BMD assessed with DXA in the same population was more than 1 SD above the mean.[173]

Fracture risk assessment tools have not been validated in the SCI population, and the CAROC and FRAX® tools demonstrated good agreement in postmenopausal women and men over 60 years of age and poor agreement in premenopausal women and young men in this population [126]. The fact that CAROC cannot be applied to individuals younger than 50 years may represent a first explanation, given that SCI occur earlier in the life compared to the age these assessment tools have been designed for. Moreover, CAROC does not account for risk factors that are relevant in SCI (Table 1). Finally, they rely on femoral neck BMD, while the distal femur and proximal tibia are the most common fracture sites in people with SCI.[104,105,108] Therefore, alternative solutions should be sought to assess risk of fractures in people with SCI. Considering that QCT and pQCT are not routinely performed in clinical practice, TBS may represent a valid, reliable, time- and cost-effective alternative to increase the accuracy of fracture risk assessment in people with SCI. In the healthy population, TBS, alone and combined with LS BMD, improves

the prediction of hip and major osteoporotic fractures,[159–162,174] and a TBS-adjusted version of the FRAX® tool (https://www.sheffield.ac.uk/TBS/) is now available. To date, only one study assessed TBS in people with SCI;[175] however, the authors applied an algorithm validated for the lumbar spine to the distal femur and proximal tibia, and the adoption of an incorrect methodological approach invalidates the results. Therefore, exploring the TBS values at the lumbar spine in people with SCI, the longitudinal changes in a 2-year period and the impact on the assessment of risk of fracture may be of clinical relevance.

Table 1. Risk factors for lower extremity fragility fractures in people with spinal cord injury.[98,107,127,176–182]

Risk Factors for Lower Extremity Fragility Fracture After SCI
Age > 50 years
White/Caucasian race
Alcohol intake > 5 servings per day
BMI < 19 kg/m^2
Female gender
Hip fracture in the last year or prior lower extremity fracture
Family history of fracture
Age at injury < 16 years or duration of SCI ≥ 10 years
Motor complete lesion (AIS A or B)
Paraplegia
Osteogenesis imperfecta
Routine use of benzodiazepines, anticonvulsants (i.e., carbamazepine, phenytoin), heparin, opioid analgesia (≥28 mg morphine for a 3-month period)

1.3.2 Progressive resistance training for people at risk of fracture: where are we at?

Exercise represents a non-pharmaceutical treatment for reducing the risk of falls and fracture, and to increase quality of life.[183–185] Clinical practice guidelines recommend exercise to prevent future fractures; however, several concerns still need to be addressed. Elderly patients are often provided generic suggestions such as to walk or get more active without considering different types of exercise.[23] This is a result of the lack of a systematic analysis of the literature regarding the effects of different kinds of exercise on health-related outcomes. Indeed, many trials have attempted to investigate the effects of different types of exercise, and the quality of the evidence and the risk of bias of those studies need to be assessed in a systematic review. Moreover, the target population of most of the studies are post-menopausal women, with or without osteoporosis and/or fractures.

Hence, there is a need to apprise and summarize with a systematic approach the findings from studies targeting older men and women at risk of or with low bone mass.

Two systematic reviews concluded that progressive resistance training (PRT) is an effective method to improve muscle mass and strength in frail adults or people with previous fractures.[186,187] However, these systematic reviews did not consider relevant outcomes such as fracture risk, falls and adverse events, physical performance and quality of life. There is evidence acknowledging positive effects of PRT in maintaining or increasing BMD.[188] A meta-analysis of 15 RCTs reported positive effects of resistance training on spine, hip and femoral neck BMD in post-menopausal women.[189] Similarly, a Cochrane review highlighted increments in spine and hip BMD after resistance training or combined resistance and aerobic training in post-menopausal women 45-70 years old.[190] On the other hand, a recent systematic review of 8 RCTs including PRT and multiple exercise interventions showed only modest effects on BMD in older men.[191] However, low BMD represents only one of the risk factors for fracture. It is important to also assess the effectiveness of PRT for improving mobility, functionality, reducing risk of falls, and improving quality of life. Therefore, a systematic approach to analyze the outcomes of these studies is needed to make recommendations.

Furthermore, there is no evidence on risk of fractures and/or serious adverse events during exercise, thus making clinicians uncomfortable when prescribing specific types of exercise. Potential adverse events occurring among people at high risk of fractures during physical activity and transfers must be considered when prescribing exercise programs, especially among older adults, who present a higher risk of falls and fractures. Therefore, safety of PRT training programs is another outcome that is worth investigation among the currently available literature, to encourage people to exercise but also making clinicians more comfortable when prescribing exercise. Exercise prescriptions aiming to prevent fracture must be individually tailored and specific regarding frequency, intensity, type and time of the training protocol. There is the need for a systematic review to establish the efficacy of PRT in reducing falls rate, fractures, adverse events, as well as improving mobility and quality of life in older adults with low bone mass or OVFs. Furthermore, in light of new PRT trials, a new systematic review was needed update the

upcoming Clinical Practice Guidelines for Management of Osteoporosis and Fracture Prevention in Canada.

1.3.3 The limited evidence on exercise for improving posture in people with hyperkyphosis

The evidence regarding the benefits of exercise on improving posture in adults with hyperkyphosis is scarce and conflicting, and systematic reviews could not demonstrate consistent improvements after different kinds of exercise programs. Three narrative reviews[192–194] highlight the need for further studies to assess the real efficacy of exercise in improving hyperkyphotic posture, as the available literature reports no-to-little improvements, and the heterogeneity of the studies does not allow to make inferences about the ideal frequency, intensity, type and duration of the exercise programs. A 2014 systematic review from our lab[195] could not perform a meta-analysis due to the limited number of available randomized controlled trials. The quality of the included studies was often low, with conflicting results: despite the modest improvements in posture observed after a few supervised exercise protocols, other studies showed no effect. A recent meta-analysis[196] showed modest improvement of kyphotic curvature after exercise programs, especially when only moderate or high-quality studies were pooled (standardized mean difference [SMD]: -3.56 degrees, 95% confidence intervals [CI]: -5.36, -1.79, 5 studies). However, the authors included studies with participants at least 18 years old, while osteoporosis-related hyperkyphosis typically has its onset after 40 years of age, and the evidence in the effects of exercise among people at least 40 years old with hyperkyphosis is still scarce. Furthermore, the authors included only RCTs and, given the limited number of available studies, the inclusion of non-randomized trials could substantiate the findings. Moreover, the exclusion of trials where physical therapy was part of the intervention can represent a limitation, as corrective programs for hyperkyphosis generally combine exercise and manual therapy. Finally, it is still unclear whether changes in back extensor strength affect spine curvature; therefore, including outcomes like back extensors strength and endurance may provide some insight.

Therefore, we decided to update the previous systematic review from Bansal et al[195] about the effects of exercise on improving hyperkyphotic posture in people at least 45 years old. Given the association between hyperkyphosis and risk of fracture,[32–34,54,197] the findings will inform the

upcoming Canadian Guidelines for Prevention and Management of Osteoporosis, providing evidence about the benefits and safety of exercise interventions for back extensor muscles in people at risk of fracture.

1.3.4 Challenges in delivering non-pharmacological interventions to people with osteoporotic vertebral fractures

Individuals with OVFs should be involved in management and preventative therapies, but the absence of specific exercise guidelines for people with OVFs[198] represents a barrier for healthcare providers to the prescription of exercise programs. Despite the paucity of the evidence available, exercise recommendations for people with OVFs encourage resistance, balance and aerobic exercise training after consultation with a physical therapist to ensure the adoption of spine sparing strategies.[183,199] In a 2019 Cochrane review[164] on the effects of exercise in people with OVFs, we reported that the number of studies is inadequate to determine the effects on falls, fractures, adverse events, pain and health-related quality of life (HRQoL), while the small improvement in the Timed Up and Go test was statistically significant but not clinically important. Accordingly, a recent multicentre pilot RCT (the B3E study) showed improvement in the 5-time sit-to-stand test after a 12-month home strength and balance exercise program, but no effects on pain, HRQoL and fear of falling.[200] However, fear of falling and dynamic balance improved in 76 Norwegian women with OVFs after a 12-week home multicomponent exercise program.[201] People with vertebral fractures have high fear of falling with consequent reductions in exercise self-efficacy;[202] therefore, future RCTs with adequate sample size should assess whether home exercise programs have beneficial effects on pain, fear of falling and HRQoL.

Adherence to exercise programs may be a concern among people with OVFs.[203] However, adherence to exercise was not influenced by fear of falling or exercise self-efficacy in the B3E study,[204] and sensitivity analyses including only individuals with adherence ≥ 80% did not show statistically significant effects.[203] A recent pilot study evaluated the feasibility and acceptability of a technology-based exercise program to improve posture among people with hyperkyphosis.[205] The authors delivered the exercise program via videoclip links prompted by text messages, and the adherence to video viewing was 100%, while the good practice of posture training at home was

71% (range 0-100). The feasibility and acceptability of the program, the promising results in posture improvement and physical activity levels,[205] and the association between hyperkyphosis and OVFs,[31–33,197] suggest testing the effects of the program on a larger scale and/or in other populations, such as people with OVFs. Moreover, attending in-person exercise programs during the COVID-19 pandemic is not possible, and as programs reopen, fear of in-person contact may still pose challenges. Exercise is recommended to prevent health complications due to a sedentary lifestyle but also to alleviate the psychological effects of the quarantine.[206] Exercise delivered remotely may represent a solution to offset the physiological and psychological consequences of the quarantine. Therefore, technology-based interventions need to be pilot tested and then implemented on a larger scale in different populations.

1.4 Thesis objectives

The objectives of this thesis were: 1) to describe potential sources of error during LS bone densitometry; 2) to explore trabecular bone score (TBS) values in individuals with SCI, and the applicability of TBS in fracture risk assessment; 3) to synthetize the evidence on the effects of PRT on health-related outcomes in people with low bone mass, with and without OVFs; 4) to synthetize the evidence of exercise on posture- and health-related outcomes in people with hyperkyphosis 5) to establish recommendations for the non-pharmacological management of osteoporotic vertebral fractures; 6) to co-develop a virtually delivered education and training program on safe movement, pain management, nutrition, and exercise among people with osteoporotic vertebral fractures, and to test its acceptability and usability.

Chapter 2
Novel insights on fracture risk assessment in individuals with spinal cord injury

The findings from this chapter will be disseminated as two manuscripts that are currently being prepared for submission.

2.1 Study 1. An exploration of potential sources of error during lumbar spine bone densitometry (DXA) in individuals with spinal cord injury

2.1.1 Introduction

People with spinal cord injury (SCI) experience a considerable loss of bone after the injury, which results in an increased risk of fracture.[94,101,207] Bone loss is greater in the lower extremities, and lumbar spine (LS) bone mineral density (BMD) in people with SCI has been reported to be within the normal range or even higher when assessed with DXA.[166–168] However, a cross-sectional study in people with SCI demonstrated that LS BMD measured with QCT was more than 2 standard deviations (SD) below the mean, while LS BMD assessed with DXA in the same population was more than 1 SD above the mean.[173] It is hypothesized that, among people with SCI, there are sources of error that lead to a spurious increase in LS BMD.

Several sources of errors in acquisition, analysis and interpretation of bone densitometry scans have been reported in the general population. A cross-sectional study reported that 75% of men and 61% of women had osteophytes, and 20% of men and 10% of women with osteoporosis were misdiagnosed.[208] On average, osteophytes spuriously increase LS BMD by 10%, with a range from +14% at L1 to +9% at L4.[209,210] Drinka et al developed a grading for facet sclerosis (from 0, indicating the absence of sclerosis, to 3, indicating marked sclerosis) and observed that grade 2 and 3 sclerosis resulted in false increases of LS BMD.[211] Furthermore, compression fractures falsely increase BMD and, if not excluded from analysis, could lead to erroneous BMD and fracture risk assessment.[212] Incorrect positioning of the patient during the scan, wrong labeling of vertebrae and variability in the identification of regions of interest in case of longitudinal follow ups are other commonly reported sources of error.[213] On the other hand, rotations of the spine for any reasons, such as roto-scoliosis, ascites, laminectomy and spina bifida generally decrease LS BMD.[137,212,214]

Heterotopic ossification, degenerative joint diseases and calcifications are common after SCI,[170–172] but their effect on spine densitometry has been poorly investigated. Findings from a cross-sectional study showed that heterotopic ossification falsely increased total hip BMD,[172] but the effects of heterotopic ossification on LS BMD was not an objective of the study. A cross-sectional study showed that people with SCI who also have degenerative joint diseases had T-scores at the lumbar spine above the normal range when measured with DXA but values indicating low bone mass when assessed with QCT.[168] However, the SCI sample size was limited, and the authors only focused on degenerative joint diseases without considering other potential confounders. Therefore, the aim of this study was to describe the prevalence of potential sources of error that may alter LS BMD measurement in a cohort of individuals with chronic SCI.

2.1.2 Methods

Participants and study design

We reviewed baseline and 2-year follow up DXA scans from a cohort of men and women with chronic SCI. Participants with chronic traumatic SCI were recruited from outpatient physiatry clinics at two tertiary SCI rehabilitation hospitals in Ontario (Canada) according to the following inclusion criteria: a) age ≥ 18 years; b) ability to communicate in English and to give informed consent; c) a spinal cord impairment (C2-T12) of sudden onset (< 24 hours) associated with a stable motor neuron, neurologic deficit of trauma-like etiology occurred at least 24 months prior the beginning of the study. Exclusion criteria were: a) current or prior known conditions other than paralysis that are known to influence bone metabolism including: oral glucocorticoid use for ≥ 3 months, malignancy, known liver or malabsorption condition; b) weight > 150 kg (maximum tolerance for bone density machines); c) contraindications to pQCT testing (e.g. bilateral metal implants, severe spasticity and allergy to Ativan); d) women who either are or are planning to become pregnant.

BMD and technical issues

Lumbar spine scans were performed using a Hologic DXA device (Hologic Inc., MA, USA) according to the standardized protocol provided by the manufacturer. Trained technologists performed the scans. Intra-class correlation coefficients for repeated distal femur and proximal tibia BMD measures in our lab are 0.99 and 0.97, respectively. Each scan was examined by two

independent physicians for the presence of potential sources of error in LS BMD measurement. The physicians commented on whether the scan is appropriate for BMD analysis, should be re-analyzed, or be removed from the dataset. Based on the literature available and on clinical experience, the following issues have been identified as potential confounders during BMD measurement: a) incorrect positioning, observable as the spine is not straight nor centered in the field of view due to improper positioning; b) problems with detection of bone edge due to low image quality or other reasons; c) errors in labeling vertebrae; d) inconsistent BMD across vertebrae, where there is a >1 T-score difference between a vertebra and the adjacent vertebra/ae;[215] e) less than three contiguous vertebrae are appropriate for analysis; f) OVFs, recognized as loss of height in the anterior, middle or posterior segment of a vertebra according to the Genant method (Grade 1: < 25%, Grade 2: 25-40%, Grade 3: >40%);[47] g) surgical procedures and orthopedic hardware that may alter BMD (e.g. disc replacement, spinal fusions, pedicle screws, laminectomy, vertebral augmentation, etc.); h) heterotopic ossification; i) evidence of degenerative joint diseases, such as osteophytes, loss of joint space, identified as pathological hardening of tissue, especially from overgrowth of fibrous tissue or increase in interstitial tissue, or facet sclerosis; j) extraneous calcified tissue (e.g., atherosclerotic or pancreatic calcifications, kidney stones, etc.). Furthermore, the raters reported on any other issues they observed and considered relevant. The study received ethics approval from the Clinical Research Ethics Board at the University of Toronto.

Statistical analysis

We used mean (standard deviation) to present continuous variables, and number (percent) to report categorical variables. We reported the prevalence of each issue and the level of severity, where relevant. The raters reported the observed issues on a form for each scan, and assessed the presence/absence of issues with three answer options: “YES”, if the issue was observable; “NO”, if the issue was not present; “UNCLEAR”, if the quality of the image did not allow to determine the presence/absence of the issue. We calculated the agreement between raters on the presence/absence of each issue using Cohen’s kappa. Kappa values <.20 indicate slight agreement, values between .21 and .40 fair agreement, values between .41 and .60 moderate agreement, values between .61 and .80 good agreement, and values between .81 and 1 indicate very good

agreement.[216] Statistical analysis was performed with SPSS Statistics version 28.0.1 (Armonk, NY, USA).

2.1.3 Results

We reviewed 115 lumbar spine DXA scans from 58 participants (Table 1), and 107 (93.0%) scans from 52 participants presented at least one source of error. At baseline, the average number of potential sources of error per scan was 5.5 ± 1.7 and 5.7 ± 1.5 according to rater 1 and rater 2, respectively. Follow up scans presented an average of 5.6 ± 1.6 and 5.7 ± 1.4 potential sources of error according to rater 1 and rater 2, respectively (Table 2). In addition, one rater reported that obesity was observable in 14 scans from 8 participants.

Table 2. Demographic and anthropometric characteristics of the participants.

	Total (n = 58)
Age (years) (mean ± SD, median)	48.5 ± 11.8, 28
Males (n, %)	42 (72.4%)
Females (n, %)	16 (27.6%)
Time from injury (years) (mean ± SD, median)	15.0 ± 10.3, 11
AIS A-B (n, %)	36 (62.1%)
AIS C-D (n, %)	22 (37.9%)
Tetraplegia (n, %)	32 (55.2%)
Paraplegia (n, %)	26 (44.8%
Height (cm) (mean ± SD)	176.6 ± 8.8
Weight (kg) (mean ± SD)	81.0 ± 18.0
BMI (kg/m^2) (mean ± SD)	25.9 ± 5.1
Femoral neck T-score	-2.0 ± 1.1
Lumbar spine T-score	-0.1 ± 1.5
History of fracture (n, %)	15 (25.9%)
Currently on bisphosphonate therapy (n, %)	45 (77.6%)
Currently on calcium supplementation (n, %)	49 (48%)
Currently on vitamin D supplementation (n, %)	52 (89.7%)

Table 3. Prevalence of potential sources of error in the DXA scans reviewed.

Potential sources of error (Number of scans, % of total number of scans)	Baseline			Follow up		
	Rater 1	Rater 2	Interrater agreement	Rater 1	Rater 2	Interrater agreement
DXA scan not appropriate for BMD analysis*	16, 27.6%	5, 8.6%	k = .799, p<.001	13, 23.2%	4, 6.8%	k = .807, p<.001
Incorrect positioning of the patient for the scan	4, 6.9%	11, 19.0%	k = .515, p<.001	4, 7.1.5%	9, 16.1%	k = .849, p<.001
Bone edges not clearly detectable	18, 31.0%	6, 10.3%	k = .678, p<.001	18, 32.1%	6, 10.7%	k = .659, p<.001
Errors in labelling vertebrae	1, 1.7%	5, 8.6%	k = .861, p<.001	1, 1.8%	3, 5.4%	k = .857, p<.001
Outlier BMD values in some regions or vertebrae	28, 48.3%	24, 41.4%	k = .609, p<.001	32, 57.1%	23, 41.1%	k = .667, p<.001
Less than three contiguous vertebrae appropriate for analysis	14, 24.1%	6, 10.3%	k = .800, p<.001	15, 26.8%	4, 7.1%	k = .795, p<.001
OVFs	3, 5.2%	1, 1.7%	k = .845, p<.001	3, 5.4%	0	k = .856, p<.001
Previous surgical procedures	4, 6.9%	4, 6.9%	k = .923, p<.001	3,5.4%	3, 5.4%	k = .937, p<.001
Facet sclerosis or osteophytes	21, 36.2%	30, 59.7%	k = .707, p<.001	20, 35.7%	35, 62.5%	k = .632, p<.001
Heterotopic ossification	2, 3.4%	3, 5.2%	k = .860, p<.001	2, 3.6%	2, 3.6%	k = .871, p<.001
Extraneous calcified tissue	0	0	k = .920, p<.001	0	0	k = .866, p<.001
Average number of issues per scan (mean ± SD)	5.4 ± 1.7	5.6 ± 1.5		5.6± 1.6	5.7 ± 1.4	

NOTE. The first three columns refer to baseline scans: two columns report the number and percentage of scans that presented each of the potential sources of error, while the third column reports the interrater agreement. The fourth and the fifth column reported the number and percentage of follow up scans that presented each of the potential sources of error; the sixth column reported the interrater agreement on the review of follow up scans. * DXA scan is not appropriate for BMD analysis if presents one of the following: only 1 vertebra is appropriate for analysis; ≥ 3 vertebrae with bone edges not clearly detectable; patent incorrectly positioned; heterotopic ossification across the first four lumbar vertebrae (L1-L4); extraneous calcified tissue interfering with BMD analysis at ≥ 3 vertebrae; degenerative joint disease ≥ 3 vertebrae; any other potential sources of error that make the scan ineligible for analysis. OVF = osteoporotic vertebral fracture.

2.1.4 Discussion

The present exploratory analysis showed that up to 27% of the LS DXA scans in people with chronic SCI may not be appropriate for BMD analysis, and 93% of the scans presented at least one potential source of error. Facet sclerosis or osteophytes, challenging in detecting bone edge, and outliers BMD values, that often do not allow to have three adjacent vertebrae appropriate for BMD analysis, were the most common potential sources of error. Interrater agreement was good overall; however, we noticed an interrater difference greater than 10% on six items, which warrants further exploration for the clinical interpretation of the results.

The findings from this study validate existing recommendation to not consider LS BMD for fracture risk assessment and management in people with SCI.[182,215] Facet sclerosis and osteophytes were the most prevalent issues in our cohort, and they have been reported to spuriously increase BMD by up to 24%.[217] The high percentage of degenerative changes most likely explains the high number of scans that presented vertebrae with outlier BMD values. Outlier BMD values among vertebrae may identify OVFs or degenerative changes, and BMD values that are not increasing from L1 to L3, or that are increasing from L3 to L4 should raise some concerns.[218] The International Society of Clinical Densitometry recommends that at least two adjacent vertebrae must be appropriate for BMD analysis.[136] We decided to report on how many scans presented at least three contiguous vertebrae, to be conservative in terms of statistical accuracy and precision.[136] Lateral scanning of the lumbar spine may allow to exclude degenerative changes from the ROI,[219] but the International Society for Clinical Densitometry guidelines do not support such variation in routine clinical practice.[136]

Our data showed good or very good interrater agreement on the detection of potential sources of error. Nonetheless, a great percentage differences between raters was observed six items, and differences in interpretation may lead to incorrect decisions in clinical practice. The identification of potential sources of errors is not straightforward; some artifacts may be suspected, but the quality of DXA images does not always allow the identification of specific issues. Furthermore, even though localized degenerative joint disease is relatively easy to detect, its identification becomes more challenging when present at multiple levels of the lumbar spine in a relatively homogeneous pattern.[220] However, DXA is not performed for diagnostic purposes with regards to any of the conditions considered in the present paper, and the reported prevalence of

potential sources of error deemed to have a larger effect on BMD (e.g., surgical hardware, heterotopic ossification) was very similar across raters.

This study presents some limitations. In bone densitometry, errors can happen during scan acquisition, analysis, or interpretation, but the quality of the images does not always allow to discern between positioning errors and presence of actual sources of error. Lateral spine scans or qCT imaging would have allowed to quantify the impact of sources of error on BMD; however, this study was a secondary data analysis from an established cohort, and neither lateral spine scans nor qCT were performed. Finally, the forms used by the raters to document the technical issues were designed by the authors. Even if a training session was scheduled before the beginning of the study, involving the raters in the design of the forms and in the choice of the answer options would have minimized discrepancies in the interpretation of the issues observed.

2.1.5 Conclusion

Facet sclerosis and osteophytes and challenges in detecting bone edges are the most common sources of error in LS DXA scans among people with SCI, and most of the scans presented vertebrae with outlier BMD values. The high prevalence of potential sources of error validates extant recommendations against the use of LS BMD for fracture risk assessment in people with SCI.

2.2 Study 2. Trabecular Bone Score as a Tool to Estimate Fracture Risk in Individuals with Chronic Spinal Cord Injury?

2.2.1 Introduction

Individuals with motor complete spinal cord injury (SCI) are at high risk for sublesional osteoporosis, with sizable declines in bone and muscle mass below the level of injury [94,101,207,221–223]. The proximal tibia and distal femur are the most common sites for fractures after SCI [94,101,107,207,221–224]. Fractures often lead to complications including delayed healing, pressure sores, cellulitis and pneumonia [169,225] and a five-year increase in mortality [226]. Prevention of fracture related morbidity and mortality necessitates reliable tools for detecting low bone mass and accurately estimating fracture risk.

Lumbar spine (LS) bone mineral density (BMD) and femoral neck (FN) T-scores are independent predictors of major osteoporotic fractures in the general population [227,228]. Fracture risk in people with SCI is closely associated with total hip, femoral neck, distal femur and proximal tibia BMD and duration of injury [128,229]. However, people with SCI generally present with a LS BMD that is equivalent to or higher than their age-matched peers when assessed with dual-energy x-ray absorptiometry (DXA) [166,167]. Several factors, such as posterior element changes due to degenerative joint disease, aortic calcification or calcifications of the longitudinal ligaments, may result in spurious overestimation of LS BMD, [170–172] and consequently, an underestimation of fracture risk. A cross-sectional study by Liu *et al*. [173] reported that the LS volumetric BMD (vBMD) measured with QCT in 29 individuals with chronic SCI was more than two standard deviations below the mean of aged-matched controls, while LS BMD assessed with DXA in the same subgroup was more than one standard deviation above the mean. This controversy regarding the differences in interpretation of lumbar spine areal and volumetric BMD is in part be explained by the differences in the technologies[163,230–235]. However, there is growing recognition in the field of densitometry that the assessment of Trabecular Bone Score (TBS), an indirect method to estimate bone microarchitecture independent of bone mineral density, may offer an alternate perspective on lumbar spine BMD interpretation among many impairment cohorts (i.e. diabetes, kidney transplant, parathyroid disease) including individuals with chronic SCI. [215] The International Society of Clinical Densitometry (ISCD) recommends that TBS can be used in association with FRAX® and BMD to adjust FRAX®-probability of fracture in post-menopausal women and older men, [215] and the adjustment of FRAX® for TBS results in a small yet statistically significant increase in fracture risk estimation [174].

TBS is a textural index that evaluates pixel grey level variation in DXA images, thereby providing an indirect estimation of trabecular bone microarchitecture without exposing the patient to additional sources of radiation [151]. Several cohort studies have reported that TBS, both alone or combined with LS BMD values, improves the prediction of major osteoporotic and hip fractures in the general population as compared to BMD alone [159–162]. Furthermore, a meta-analysis of 14 prospective cohort studies in able-bodied men and women without SCI showed that TBS is a predictor of fracture risk, independent of FRAX® [174]. However, there are no current fracture risk assessment tools validated in people with SCI, and the CAROC and FRAX® tools demonstrated

good agreement in postmenopausal women and men over 60 years of age and poor agreement in premenopausal women and young men in this population [126]. We do not know whether the analysis of LS TBS may add value to FRAX® in the prediction of major osteoporotic fractures in individuals living with chronic SCI. Therefore, the goal of this study was to describe LS TBS values after SCI, and to explore the agreement in risk of major osteoporotic fractures, and hip fractures between FRAX® and TBS-adjusted FRAX® in people with SCI.

2.2.2 Methods

Participants and study design

An exploratory secondary analysis was conducted using baseline data from an established cohort (n=70) [126,129]. Participants with chronic traumatic SCI were recruited from outpatient physiatry clinics at tertiary SCI rehabilitation hospitals in Ontario (Canada) according to the following inclusion criteria: a) age ≥ 18 years; b) ability to communicate in English and to give informed consent; c) a spinal cord impairment (C2-T12) of sudden onset (< 24 hours) associated with a stable motor neuron, neurologic deficit of trauma-like etiology occurred at least 24 months prior the beginning of the study. Exclusion criteria were: a) current or prior known conditions other than paralysis known to influence bone metabolism including: oral glucocorticoid use for ≥ 3 months, malignancy, known liver or malabsorption condition; b) weight > 150 kg (limit for dual-energy X-ray absorptiometry scanner); c) contraindications to pQCT testing (e.g. bilateral metal implants, severe spasticity and allergy to Ativan); d) women who either were pregnant, or were planning to become pregnant. Additional exclusion criteria specific to this analysis were applied. We excluded data from participants with orthopedic hardware within the lumbar spine region of interest as this precluded accurate BMD estimation and calculation of TBS values (i.e., three contiguous vertebrae in region of interest were required). Furthermore, we excluded LS scans performed prior to 2014, as they were not compatible with the version of TBS analysis software installed on the densitometer in our bone density lab. The study received ethics approval from the Clinical Research Ethics Board at the University of Toronto.

Demographics and medical history

Sociodemographic data, medical history, and injury characteristics were collected for every participant to describe the cohort members and calculate the 10-year fracture risk probability using Canadian FRAX® [120]. Information regarding medications, co-morbidities, and tobacco use were collected by using a subset of questions from the CaMOS medical history questionnaire [236], while alcohol consumption was investigated using the CAGE questionnaire [237]. Level and completeness of injury were assessed by a physiatrist according to the International Standards for Neurological Classification of SCI (ISNCSCI) [238].

Bone mineral density and TBS measurement

Lumbar spine, total hip and femoral neck, DXA scans were acquired by a ISCD certified technologist using a Hologic Discovery QDR 4500 (Hologic Inc., MA, USA) according to the standardized protocols provided by the manufacturer. TBS measurements were performed using the TBS iNsight™ software version 2.1.2.0 (Medimaps, Merignac, France). We used proposed thresholds for bone microarchitecture and estimated fracture risk based on TBS. TBS values ≥1.350 indicate a normal bone microarchitecture, values between 1.350 and 1.200 indicate partially degraded bone microarchitecture, while values below 1.200 indicate degraded bone microarchitecture [153]. TBS values > 1.310 correspond to a low risk of fracture, values between 1.310 and 1.230 correspond to moderate risk of fracture, and values below 1.230 correspond to high risk of fracture [174].

The Canadian version of FRAX® (https://www.sheffield.ac.uk/FRAX/tool.aspx?country=19) including femoral neck BMD (g/cm^2) was used to calculate the risk for major osteoporotic and hip fractures. The TBS-adjusted FRAX® (https://www.sheffield.ac.uk/TBS/) was used to determine the risk of fracture when TBS was considered. Fracture risk values ≥ 20% for major osteoporotic and ≥ 3 % for hip fractures are the commonly applied treatment thresholds [239].

DXA scans of the distal femur and proximal tibia were acquired using a polycarbonate-positioning device and analyzed using the Hologic LS software. Distal femur and proximal tibia BMD T and Z-scores were obtained from a local normative dataset for patients with SCI between the ages of 18-70 years of age (https://kite-uhn.com/clinical/tools/knee-dxa-protocol). Intra-class correlation

coefficients for repeated distal femur and proximal tibia BMD measures using the LS protocol in our lab are 0.99 and 0.97, respectively.

Statistical analysis

Descriptive statistics, mean (standard deviation) or median (minimum-maximum) for continuous variables and number (percent) for categorical variables, were used to present data regarding demographics, health status, BMD, TBS, and fracture risk. A Welch's T-test was performed to explore differences in TBS, FRAX® and TBS-adjusted FRAX® between men and women, between participants ≤49 years and ≥50 years, and between subgroups with and without history of fracture and with complete and incomplete injury. The agreement between FRAX® and TBS-adjusted FRAX® was assessed with a two-way mixed model interclass correlation coefficient ($ICC_{(3,1)}$) and Bland-Altman plots. ICC values above 0.75 indicate good agreement, while those below 0.75 indicate poor agreement.[240] Since TBS assessment is only validated in subjects with BMI values between 15 kg/m^2 and 35 kg/m^2 [151], a sensitivity analysis including only people with BMI within this range was performed to verify if including people beyond this range may affect TBS measurements. Subgroup analyses based on sex, history of fragility fracture, and severity of injury (ASIA A-B vs ASIA C-D), three risk factors for fragility fractures in people with SCI [98,107,127,176–179] are also presented. Statistical analysis was performed with SPSS Statistics version 24 (Armonk, NY, USA).

2.2.3 Results

DXA scans were performed on 70 participants; ten individuals were excluded due to the presence of hardware within the lumbar spine region of interest, one individual was excluded because BMD was not available for femoral neck due to the presence of hardware, and 22 scans were excluded as they were performed prior to 2014, and not compatible with the version of the TBS software installed in our lab. Therefore, baseline scans from 37 participants (age 54 ± 12 years; men n = 28, women n = 9; AIS: A-B n = 22, C-D n = 15; history of fragility fractures: n = 16; bisphosphonates therapy n =29) were included in the analysis (Table 1).

The mean BMD of the LS was 1.184 ± 0.225 g/cm^{2,} the femoral neck was 0.707 ± 0.195 g/cm^2, distal femur 0.651 ± 0.206 g/cm^2 and proximal tibia at 0.542 ± 0.145 g/cm^2 (Table 2). The

mean TBS was 1.324 ± 0.114 for men, and 1.380 ± 0.082 for women (Table 2). Twenty participants (54%, men: n = 16, women: n = 4) had degraded or partially degraded bone microarchitecture based on TBS. The mean 10-year fracture risk was 9.4% ± 12.9% for major osteoporotic fracture and 4.9% ± 12.5% for hip fracture for men, and 7.7% ± 5.4% and 1.6 ± 1.6% for women (Table 3). When adjusted for TBS values, the average 10-year fracture risk was 6.5% ± 6.7% for major osteoporotic fracture and 3.3% ± 7.6% for hip fractures for men, and 7.1% ± 4.9% and 1.3% ± 1.5% for women (Table 3). No statistically significant differences in TBS or fracture risk were observed between men and women, and participants ≤49 years and ≥50 years, nor between subgroups with complete and incomplete injury.

Table 4. Demographic and anthropometric characteristics of the participants.

	Total (n = 37)	Men (n = 28)	Women (n = 9)
Age (years) (mean ± SD, median)	54.0 ± 12.3, 52.2	54.6 ± 11.8, 53.5	52.4 ± 14.1, 49.9
Time from injury (years) (mean ± SD, median)	18.3 ± 8.5 14.8	18.2 ± 8.6, 13.5	18.5 ± 8.7, 14.8
Height (cm) (mean ± SD)	175.1 ± 8.9	178.2 ± 7.5	166.0 ± 6.8
Weight (kg) (mean ± SD)	79.2 ± 16.4	82.6 ± 16.6	68.7 ± 11.2
BMI (kg/m^2) (mean ± SD)	25.7 ± 4.4	25.9 ± 4.5	25.0 ± 4.4
History of fracture (n, %)	16 (42%)	10 (36%)	6 (60%)
AIS A-B (n, %)	22 (59%)	18 (64%)	4 (44%)
AIS C-D (n, %)	15 (41%)	10 (36%)	5 (56%)
Currently on bisphosphonate therapy (n, %)	29 (78%)	22 (79%)	7 (78%)
Currently on calcium supplementation (n, %)	36 (97%)	27 (96%)	9 (100%)
Currently on vitamin D supplementation (n, %)	37 (100%)	28 (100%)	9 (100%)

The 10-year fracture risk for major osteoporotic fractures was higher in individuals with a prior fragility fracture (i.e., the option "yes" was selected for the risk factor "previous fracture" when calculating the FRAX®) compared to those without, according to both FRAX® (14.4% ± 16.1% vs 4.9% ± 2.0%, p = 0.033) and TBS-adjusted FRAX® (10.9% ± 7.4% vs 3.4% ± 2.1%, p = 0.001). The differences in the 10-year fracture risk for hip fractures or in TBS between individuals with and without history of fragility fracture were not statistically significant. Sensitivity analysis including only individuals with BMI between 15 kg/m^2 and 35 kg/m^2 led to similar results. Based on FRAX®, 3 (8%) and 10 (27%) participants were above the treatment thresholds for risk scores associated with major osteoporotic (fracture risk value ≥20%) and hip fractures (fracture risk value ≥3%), respectively. After adjusting for TBS, 2 (5%) participants met the treatment threshold for risk scores for major osteoporotic fractures, and 7 (19%) of participants met the treatment threshold for risk score related to hip fracture. The $ICC_{(3,1)}$ between FRAX® and TBS-adjusted FRAX® was 0.77 for major osteoporotic and 0.93 for hip fractures. Some proportional bias for major osteoporotic fractures may be assumed from the Bland-Altman plot (Figures 1 and 2).

Table 5 .Bone mineral density (BMD) and trabecular bone score (TBS) values.

	Total (n = 38)	Men (n = 28)	Women (n = 9)	Motor complete injury (n = 22)	Incomplete injury (n = 15)	History of fracture (n = 16)	No history of fracture (n = 21)
Lumbar spine BMD (g/cm^2) (mean ± SD)	1.184 ± 0.225	1.204 ± 0.248	1.112 ± 0.135	1.211 ± 0.267	1.138 ± 0.151	1.208 ± 0.296	1.162 ± 0.163
Femoral neck BMD (g/cm^2) (mean ± SD)	0.707 ± 0.195	0.711 ± 0.211	0.698 ± 0.146	0.654 ± 0.188	0.785 ± 0.185	0.652 ± 0.212	0.750 ± 0.175
Distal femur BMD (g/cm^2) (mean ± SD)	0.651 ± 0.206	0.641 ± 0.202	0.691 ± 0.236	0.533 ± 0.120	0.820 ± 0.187	0.576 ± 0.172	0.704 ± 0.216
Proximal tibia BMD(g/cm^2) (mean ± SD)	0.542 ± 0.145	0.545 ± 0.154	0.542 ± 0.123	0.481 ± 0.104	0.644 ± 0.150	0.494 ± 0.185	0.585 ± 0.135
Trabecular bone score (TBS) L1-L4 (mean ± SD)	1.336 ± 0.107	1.324 ± 0.114	1.380 ± 0.082	1.343 ± 0.112	1.328 ± 0.106	1.315± 0.138	1.354 ± 0.079
TBS L1 (mean ± SD)	1.315 ± 0.149	1.303 ± 0.157	1.351 ± 0.132	1.313 ± 0.165	1.317 ± 0.134	1.278 ± 0.196	1.343 ± 0.103
TBS L2 (mean ± SD)	1.360 ± 0.130	1.348 ± 0.139	1.390 ± 0.104	1.358 ± 0.140	1.358 ± 0.122	1.332 ± 0.165	1.378 ± 0.099
TBS L3 (mean ± SD)	1.367 ± 0.118	1.356 ± 0.119	1.413 ± 0.110	1.386 ± 0.127	1.345 ± 0.103	1.368 ± 0.146	1.371 ± 0.095
TBS L4 (mean ± SD)	1.304± 0.128	1.291 ± 0.136	1.365 ± 0.070	1.315 ± 0.127	1.301 ± 0.130	1.293 ± 0.134	1.322 ± 0.122

Table 6. Ten-year fracture risk assessment according to FRAX® and TBS-adjusted FRAX® for both MOF and hip fractures.

	Total (n = 38)	Men (n = 28)	Women (n = 9)	Motor complete injury (n = 22)	Incomplete injury (n = 15)	History of fracture (n = 16)	No history of fracture (n = 21)
FRAX® - MOFs (%) (mean ± SD, median)	8.8% ± 11.4%	9.4% ± 12.9%	7.7% ± 5.4%	9.5% ± 14.6%	8.0% ± 5.9%	14.4% ± 161%	4.9% ± 2.0%
TBS-adjusted FRAX® - MOFs (%) (mean ± SD, median)	6.6% ± 2.8%	6.5% ± 6.7%	7.1% ± 4.9%	6.1% ± 6.5%	7.4% ± 6.0%	10.9% ± 7.4%	3.4 ± 2.1%
FRAX® - Hip (%) (mean ± SD, median)	4.0% ± 10.8%	4.9% ± 12.5%	1.6% ± 1.6%	5.6% ± 14.0%	1.8% ± 2.4%	8.0% ± 16.0%	1.1 ± 1.2%
TBS-adjusted FRAX® - Hip (%) (mean ± SD, median)	2.8% ± 6.7%	3.3% ± 7.6%	1.3% ± 1.5%	3.5% ± 8.4%	1.8% ± 2.4%	5.3% ± 9.7%	0.9 ± 1.0%

NOTE. MOFs = major osteoporotic fractures

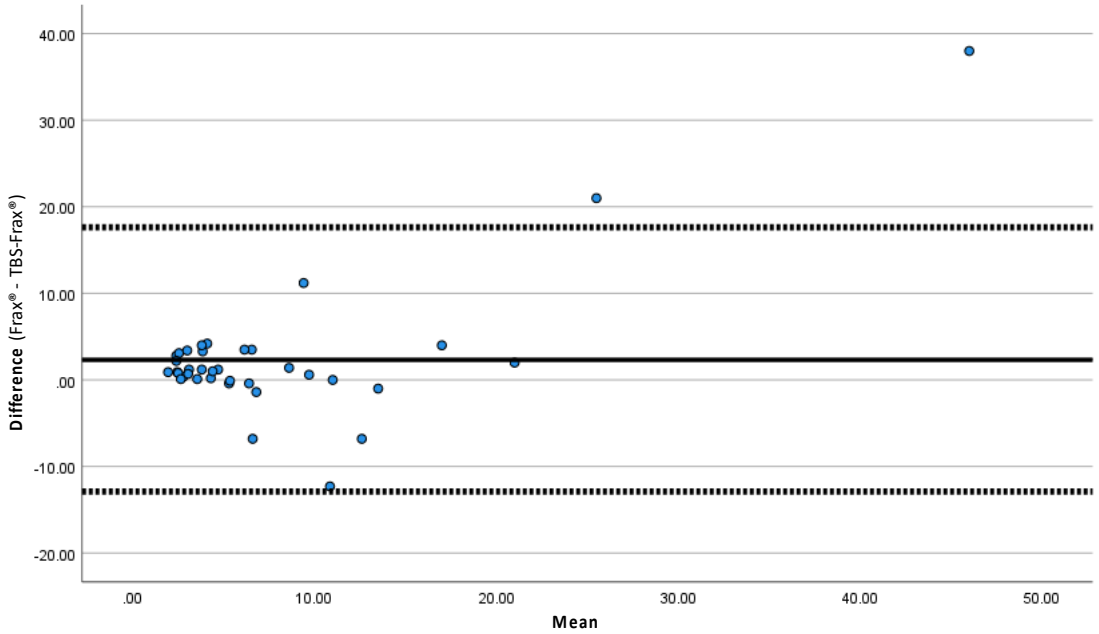

Figure 1. Bland Altman plot between FRAX® and TBS-adjusted FRAX® for major osteoporotic fractures.

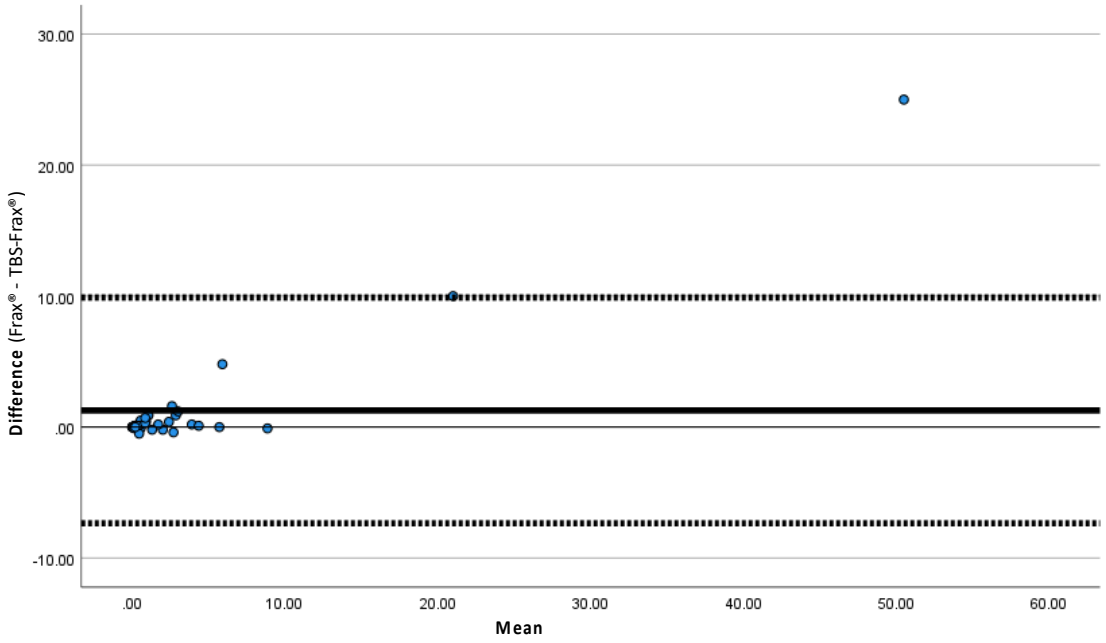

Figure 2. Bland Altman plot between FRAX® and TBS-adjusted FRAX® for hip fractures.

2.2.4 Discussion

TBS can be used in combination with FRAX® and BMD to adjust the FRAX®-probability of fractures in non-SCI post-menopausal women and older men [215], but no such recommendations can be made for individuals with SCI based on available evidence. This study attempted to provide evidence on the potential use of TBS in the estimation of fracture risk in adults with chronic SCI. More than 50% of our sample presented a partially degraded bone microarchitecture at the spine based on TBS values. No differences in TBS were detected between people with and without prior fracture or between subgroups of people with motor complete and incomplete lesions. Furthermore, the TBS-adjusted Canadian FRAX® resulted in slightly fewer people with SCI meeting treatment thresholds compared to the Canadian FRAX®. Thus, while spine TBS may identify individuals with degraded bone microarchitecture at the spine, it may not add value in the estimation of fracture risk in people with SCI.

In the non-SCI population, TBS predicts osteoporotic fractures and is lower in individuals with history of osteoporotic fractures compared to those without [159,241], but our subgroup analysis in a small cohort did not show differences in TBS between people with previous fragility fractures and those without. Moreover, women from the Manitoba Bone Density Program had lower TBS values compared to men, and a partially degraded bone microarchitecture, based on TBS [158]. In our study, women had a mean TBS well above the thresholds for normal bone microarchitecture, and higher than men, but the limited number of women included in the present analysis does not permit inferences on sex-related differences in TBS in people with SCI. We also did not find differences in TBS between people with motor complete and incomplete injuries. People with SCI present with BMD values at the lumbar spine below the mean of aged-matched controls when assessed with qCT, and above the mean when assessed with DXA; therefore, even though TBS does not appear to be affected by osteoarthritic changes [242], it is unclear whether other conditions, such as posterior element changes, subtle OVFs or vascular or ligamentous calcifications, contribute to increased TBS in people with SCI. Moreover, the majority of the people included in the present study (78%) were on bisphosphonate therapy, which is known to increase TBS [243–246]. Furthermore, the participants who were not on bisphosphonate therapy at baseline may have had

prior bisphosphonate exposure. It has been hypothesized that lumbar spine BMD continues to improve in the first few years after discontinuation of therapy [247], and we cannot exclude a similar effect on TBS values. Our findings suggest that measuring TBS at the lumbar spine in people with SCI might not be associated with the common fracture sites in people with SCI. Lobos et al. [175] demonstrated that nine people with SCI had TBS 6% and 19% lower than their able-bodied counterpart at distal femur and proximal tibia, respectively. However, the algorithm to calculate TBS includes adjustments for abdominal and truncal soft tissue thickness, and the authors applied an algorithm developed and validated for the lumbar spine to the distal femur and proximal tibia. The development of an algorithm to estimate TBS at the two sites where fractures most commonly occur in people with SCI (i.e., distal femur and proximal tibia) may allow clinicians the ability to assess bone microarchitecture and estimate fracture risk at fracture-prone sites in the future, following a large scale prospective validation study.

We detected good agreement between FRAX® and TBS-adjusted FRAX®. While, in the non-SCI population, the adjustment of FRAX® for TBS results in a slightly higher gradient of risk [174], in this cohort, a lower number of people met the treatment threshold for both major osteoporotic and hip fracture risk after we adjusted FRAX® for TBS. Therefore, TBS may not add value in the estimation of fracture risk in individuals with SCI, and basing treatment decisions on TBS would result in less people receiving treatment, which is counter to what we would hypothesize is needed given the relatively high fracture risk in the SCI population. The Clinical Practice Guidelines for Bone Health and Osteoporosis Management in Individuals with Spinal Cord Injury recommend treatment plan be determined based on the assessment of non-BMD risk factors [98,107,127,176–182], laboratory screening for secondary osteoporosis, BMD of hip, distal femur, and proximal tibia region BMD, and prior history of fracture, rather than on TBS or FRAX® thresholds .[182]

We acknowledge a number of limitations of the enclosed data. The scans analyzed were from a larger cohort, but we had to exclude a substantial proportion of the scans performed prior to 2014, as they were not compatible with the version of the TBS software installed in our lab. All the participants were on bisphosphonate therapy, or had interrupted it within a few years; therefore, the normal TBS values in our sample may due to current or prior bisphosphonate exposure, and individuals with chronic SCI with no history of anti-resorptive therapy may present with a greater degree of degraded bone microarchitecture. While we excluded participants with orthopaedic

hardware, we did not screen for other conditions, such as OVFs, calcification of the longitudinal ligaments or aorta, which may interfere with the accuracy of the TBS measurement or estimate of fracture risk. Further, lateral spine scans to assess changes in vertebral morphometry or to report the presence of OVFs using the Genant semiquantitative technique[47] were not conducted. Therefore, the impact of a variety of technical factors beyond osteoarthritis on TBS measurements requires further prospective investigation and validation before drawing firm conclusions regarding the utility or the clinical relevance of TBS in individuals with SCI. Moreover, only nine scans were from women; future studies aiming to prospectively describe LS TBS values in women or explore between-sex differences in TBS should be done with a higher proportion of women in the cohort.

2.2.5 Conclusion

Individuals with chronic SCI in this cohort presented with normal bone microarchitecture based on TBS. TBS was not different between people with motor complete and motor incomplete injury or with and without prior fragility fracture. Clinical decisions regarding fracture prevention should not be based on TBS or FRAX® in people with chronic SCI at this time. The estimates of fracture risk should be based on clinical risk factors for fracture, history of prior fracture and hip or knee region BMD.

Chapter 3
Exercise for improving outcomes in people with low bone mass and hyperkyphosis: two systematic reviews and meta-analyses

This chapter informed the upcoming Clinical Practice Guidelines for Management of Osteoporosis and Fracture Prevention in Canada, and was published as two manuscripts:

Ponzano, M., Rodrigues, I.B., Hosseini, Z., Ashe, M.C., Butt, D.A., Chilibeck, P.D., Stapleton, J., Thabane, L., Wark, J.D., Giangregorio, L. Progressive Resistance Training for Improving Health-Related Outcomes in People at Risk of Fracture: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. Phys Ther, 2021; 101(2): pzaa221. https://doi.org/10.1093/ptj/pzaa221

This paper was selected by the Editor-in-chief, Dr. Alan Jette, for an author interview. The podcast was recorded on February 6, 2021, and it is available at the following link: https://academic.oup.com/ptj/pages/podcasts.

Ponzano, M., Tibert, N., Bansal, S., Katzman, W., Giangregorio, L. Exercise for Improving Age-Related Hyperkyphosis: A Systematic Review and Meta-Analysis with GRADE Assessment. Arch Osteoporos, 2021; 16:140. https://doi.org/10.1007/s11657-021-00998-3

3.1 Study 3. Progressive Resistance Training for Improving Health-Related Outcomes in People at Risk of Fracture: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

3.1.1 Introduction

Osteoporosis is defined as a skeletal disorder characterized by compromised bone strength predisposing a person to an increased risk of fracture.[21] In adults with low bone mass, fractures often occur as a result of a fall.[248,249] Pain, reduced mobility, and difficulties in performing activities of daily living are common consequences of fractures.[2,23,250,251] Furthermore, the risk of subsequent fractures and the mortality rate are elevated after hip and OVFs.[3,29] Osteoporosis

clinical practice guidelines recommend exercise to prevent fractures;[252] however, the efficacy of exercise may vary by exercise type, population studied, or outcome of interest. For example, while bone mineral density (BMD) and fractures are important outcomes, it is also important to consider other outcomes relevant to people with osteoporosis, such as physical performance, falls, or health-related quality of life (HRQoL). Progressive resistance training (PRT) interventions can improve muscle strength in healthy older adults,[187] whereas multimodal programs including exercises that emphasize functional strength and balance are effective in reducing fall and fracture risk.[253,254] Some minor adverse events such as pain due to musculoskeletal issues can happen during PRT interventions,[190,254,255] and further evidence is needed to determine their frequency and severity. Many studies of exercise and BMD focus on postmenopausal women with normal BMD. PRT can maintain or improve bone mineral density (BMD) in postmenopausal women,[189,190,255] but there is little evidence regarding the effects of PRT on BMD in men.[191] Furthermore, there is a limited number studies of exercise that target individuals with low BMD or who are at risk of fracture. The benefits or harms of PRT may be different in individuals with low bone mass or a history of fractures. As part of the process to update the 2020¶ Clinical Practice Guidelines for Management of Osteoporosis and Fracture Prevention in Canada, we conducted a systematic review to explore the effects of PRT (alone or as part of multicomponent

exercise interventions versus no intervention, placebo, or attention control) on falls, fractures, and other health-related outcomes in men and postmenopausal women aged 50 years or older at increased risk of fracture. The present review is part of a series of reviews that will inform the Canadian Clinical Practice Guidelines for the Prevention and Management of Osteoporosis, including recommendations on risk assessment medications, nutrition, and several types of exercise. The efficacy of each type of exercise (e.g., walking, impact exercise, yoga, etc.) is being examined separately to inform recommendations specific to that type of exercise, and thus, a comparison between exercise types is not the purpose of this review.

¶ The release of the Clinical Practice Guidelines for Management of Osteoporosis and Fracture Prevention in Canada has been delayed.

3.1.2 Methods

This systematic review is reported according to the Preferred Reporting Items for Systematic Review and Meta-Analysis (Appendix C). The protocol was informed by the Cochrane Handbook for Systematic Review of Interventions[256] and registered via the International Prospective Register of Systematic Reviews at https://www.crd.york.ac.uk/prospero/ (registration no. CRD42019120158, registered and last updated on March 8, 2019). The protocol was co-developed by a working group consisting of researchers, physiotherapists, physicians, a patient advocate, and graduate students.

3.1.2.1 Data Sources and Searches

The literature search was conducted in the following databases with no date limits applied: MEDLINE (Ovid), EMBASE (Ovid), Cochrane CENTRAL (clinical trial), Cochrane Database of Systematic Reviews, CINAHL (allied health journal content), Epistemonikos, and Web of Science. The reference lists of included studies or previous systematic reviews on the topic were also searched for potential eligible studies. Search strategies were performed in August/September 2018 and updated in October 2019. The search strategy was developed using Medical Subject Headings and keywords related to prevention and treatment of osteoporosis in older adults, the effects of the interventions, and the outcomes of interest. Only randomized controlled trials (RCT) and quasi-RCTs were searched, as we anticipated that for some outcomes there would be few RCTs. No restrictions by language were applied for the literature search. The full search strategy is reported in the Appendix C.

3.1.2.2 Study Selection

Population

We included studies that met the following criteria: men and postmenopausal women aged 50 years or older with low femoral neck or lumbar spine BMD (T-score≤−1), diagnosis of osteoporosis or low bone mass, history of fragility fracture, or moderate or high risk of fragility fracture determined using any fracture risk calculators, such as CAROC,[257] FRAX,[120] or

GARVAN.[122] We excluded studies with individuals with (1) glucocorticoid-induced osteoporosis, (2) secondary osteoporosis, and (3) pathological fractures other than low-trauma fractures.

Intervention

We included studies that investigated the effects of PRT, defined as: "contracting the muscle against a resistance to 'overload' and bring about a training effect in the muscular system. The resistance is an external force, which can be one's own body placed in an unusual relationship to gravity (e.g., prone back extension) or an external resistance (eg, free weight). […]," according to the ProFane taxonomy.[258] We included trials that studied PRT alone or combined with other exercise or physical therapy interventions using any type of setting or level of supervision.

Comparator

Studies were included if they had at least 1 comparator group that received no intervention or a non-exercise or a nonphysical therapy intervention (e.g., educational intervention). The goal of this review was to determine the effectiveness of PRT in improving health-related outcomes in people at risk of fracture rather than comparing PRT with other interventions. Studies with an active or attention control group that participated in a different type of physical activity (e.g., stretching) were considered for inclusion if the attention control was not hypothesized to have an effect on the study's primary outcome or on 1 or more of the outcomes of interest.

Outcomes

The working group identified and ranked potential outcomes that would be critical or important for decision-making when creating exercise guidelines. The ranking was informed by surveys of 1108 members from the Canadian Osteoporosis Patient Network[259] and over 100 exercise professionals.[260] Outcomes were ranked using a 9-point Likert Scale, where a ranking of 7 and above was considered a critical outcome, 4 to 6 an important outcome, and 3 or less an outcome that was not important. Eight outcomes were ranked critical: (1) mortality, due to any cause such as aging, disease, or injury related circumstances that result in death; (2) fracture-related mortality, defined as deaths attributed to a fracture; (3) hip fractures, either self-reported or X-ray–verified fracture of the proximal femur that occurred at the femoral neck or trochanter in a low trauma

event, such as a fall from a standing height or less;[1] (4) fragility fractures, either self-reported or X-ray–verified fracture of spine, wrist, humerus, and pelvis that occurred following a low trauma event;[1] (5) number of people who experienced 1 or more falls, total falls, and fall-related injuries; (6) physical functioning and disability, assessed with any validated tool that measure activities of daily living using performance-based measures of physical functioning (e.g., gait speed, 5 times sit-to-stand, Timed "Up and Go" [TUG]); (7) health-related quality of life [HRQoL] determined using any validated measure such as a generic quality of life questionnaire or an osteoporosis-specific quality of life questionnaire; and (8) serious adverse events, defined as any untoward medical occurrence that, at any dose, results in death, a threat to life, inpatient hospitalization or prolongation of existing hospitalization, or in persistent or significant disability/incapacity,[261] or non-serious adverse events, defined as any reaction related to the intervention such as musculoskeletal injuries (e.g., sprains, strains, joint pain, overuse injuries) that do not require immediate medical attention. General pain and BMD were not voted as critical outcomes for the guidelines but were included in our review as they were rated as important. We included general pain outcomes determined using a pain intensity scale (e.g., Visual Analog Scale) or a pain subscale from a generic functional status questionnaire (e.g., SF-36, Nottingham Health Profile). We collected BMD measured at any site using dual-energy X-ray absorptiometry or peripheral quantitative computed tomography. Falls were identified as "unintentionally coming to the ground or some lower level and other than as a consequence of sustaining a violent blow, loss of consciousness, sudden onset of paralysis as in stroke or an epileptic seizure" from the Kellogg International Working Group on the Prevention of Falls by the Elderly.[5]

Timeframe

Studies were included if the intervention lasted at least 4 weeks, except studies with BMD as an outcome: these studies were only included in meta-analyses if the exercise intervention lasted 8 months or longer, to allow at least 1–2 remodelling cycles.[262,263]

3.1.2.3 Data Extraction and Quality Assessment

Pairs of reviewers (M.P., I.B.R., J.F., N.T., V.K.) independently assessed the titles and abstracts to confirm their eligibility. Full texts published in English, Italian, Portuguese, and Spanish were

retrieved and screened by pairs of reviewers (M.P., I.B.R., Z.H.). In case some information was missing, the authors of the original studies were contacted a maximum of 2 times. Conflicts between reviewers were resolved by discussion or, when an agreement was not reached, by a third author (L.G.). Pairs of reviewers (M.P., I.B.R., Z.H.) independently performed data extraction and assessment of the risk of bias using the Cochrane Risk of Bias Assessment Tool,[264] and disagreements were resolved by consensus or consultation with a third reviewer (L.G.). In case the reviewers were authors on an eligible study, they were not involved in data extraction or risk of bias assessment for that study. The Grading of Recommendations Assessment, Development and Evaluation approach was used to assess the certainty of the evidence.[265]

3.1.2.4 Data Synthesis and Analysis

Data were extracted using Covidence (https://www.covidence.org/home; Covidence, Melbourne, Australia) and then imported to RevMan 5.3 (Cochrane Community, London, UK; https://community.cochrane.org/help/tools-andsoftware/revman-5) for statistical analysis. Risk ratios (RR) or incidence rate ratio (IRR) with a 95% CI were calculated for dichotomous and count outcomes, respectively, whereas mean differences (MD) with a 95% CI for continuous outcomes were reported. For general pain and HRQoL, we used standardized mean difference (SMD) to pool data. Heterogeneity between trials was calculated by using the I^2 statistics, while visual inspection of funnel plots was used to assess publication bias. We performed sensitivity analyses removing studies that combined more than 1 intervention to explore whether the effects were similar when PRT-only interventions were included. We also performed sensitivity analyses that examined whether the effects were different when studies deemed to have high risk of bias were excluded.

3.1.3 Results

Trial Inclusion and Characteristics

We identified 6768 records through database searching, and 3973 remained after deduplication (Fig. X). After title and abstract screening, we assessed 465 full-text reports, and 53 studies, with

4618 participants (4% men) were included. Twenty-three studies included low bone mass as an inclusion criterion,[188,266,267,268(p),269–273,273–284] while 12 studies recruited only people with osteoporosis.[201,285–294] Nine studies recruited people with at least 1 vertebral fracture,[200,201,203,278,281,289,293,295,296] 6 studies recruited participants with at least 1 hip fracture,[297–301] and 4 studies recruited people with a previous fracture other than spine and hip.[276,284,302,303] Thirteen studies included PRT interventions only[274,279,281,283,289,291,292,296,298,299,303–305] and 40 reported on combined interventions, of which 12 were PRT and balance exercises;[200,201,203,284,286–288,290,293,294,306] 8 PRT and impact exercises;[188,188,267,272,282,300,301,307]; 8 PRT, balance, and impact exercises;[268–271,275,308–310] 3 PRT, walking, and impact exercises;[277,278,311] 2 PRT and walking;[276,312] PRT, balance exercises, and walking;[295,302] PRT and physiotherapy;[285,297] PRT and Nordic walking[273,313]; and 1 PRT, balance exercises, and Tai Chi.[280] The mean duration of interventions was 7.5 months (range 1–30 months), of which 29 were group-based programs,[188,201,266–273,275,280,283,286–290,293,296,298,299,301,302,304–307,313] 7 were individual interventions,[200,203,279,291,292,297,303] 10 alternated both group-based and individual programs,[274,281,282,284,295,308,308–310] and 6 studies did not provide this information.[276,277,294,300,311,312] Thirty three studies were funded by non-profit organizations,[188,200,201,203,266–271,278,282–284,286–288,291,293,295,296,298–300,304–306,308–311] 3 studies received support from both non-profit and private organizations,[290,303,307] 2 studies were funded by private

companies,[292,308] and 15 studies did not provide funding information.[272–277,279–281,289,294,301,302,312,313]

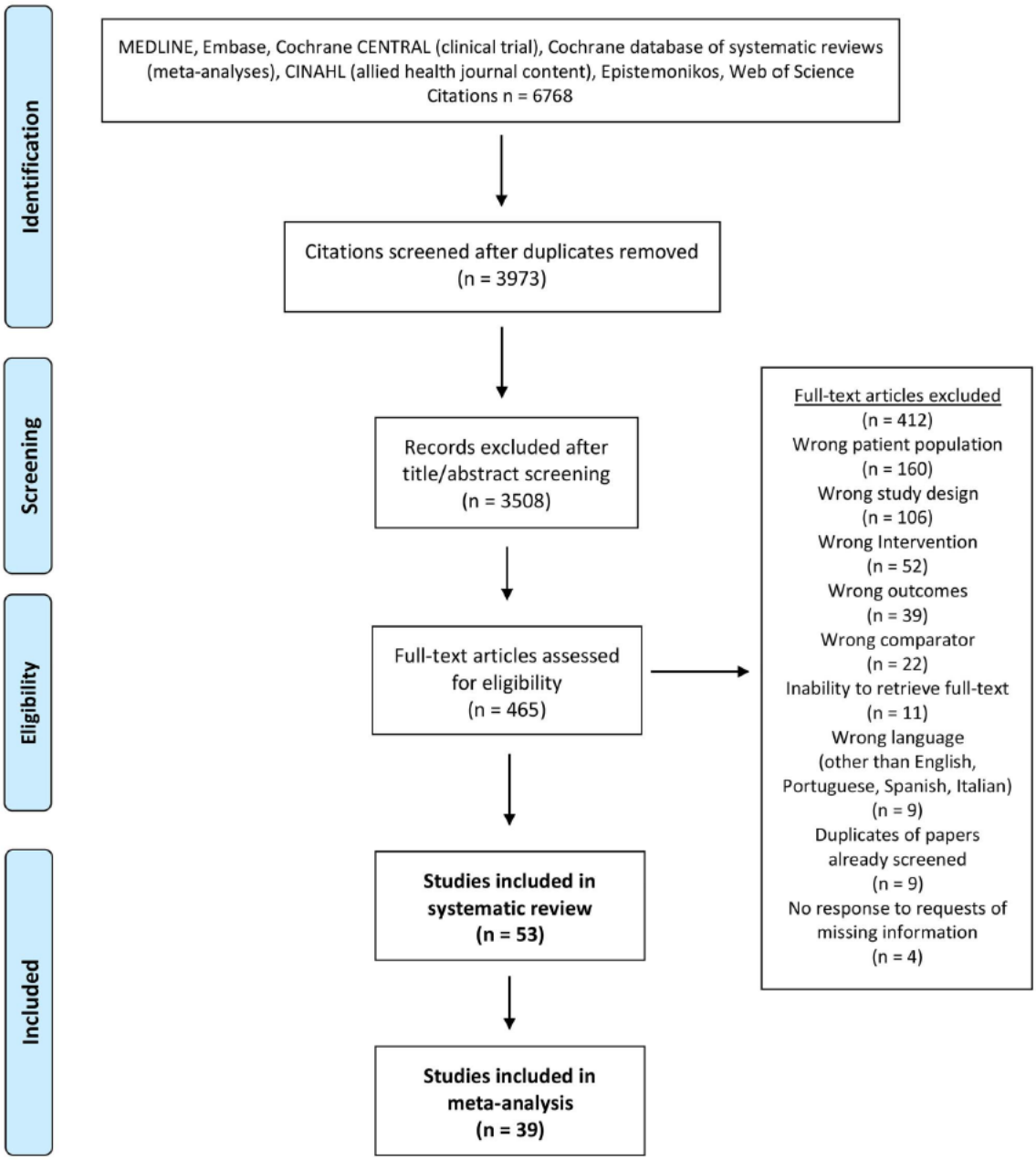

Figure 3. Flow chart of the study selection process.

Effects of PRT on Health-related Outcomes

Mortality

Effects on mortality were uncertain due to the low number of studies and events. Singh et al[8–13,15–17,25,30,40,41,51] reported 4 deaths in the intervention group and 8 in the control group. Barker et al[295]

reported 2 deaths in the intervention group, while Crotty et al[297] reported that 10 and 22 people died in the intervention and control group, respectively. None of the events appears to be related to the intervention.

Hip and Fragility Fractures

There were not enough studies with a sufficient number of fracture events to pool data. Furthermore, the heterogeneity in terms of populations, interventions, and fracture events and reporting did not allow conclusions to be drawn about the effects of PRT on the incidence of hip or fragility fractures.

Fractures Attributable to Intervention

Gold et al[296] reported 1 rib fracture that occurred during prone exercise, and 1 costal cartilage fracture that occurred when rolling from supine to prone during a 6-month PRT intervention in individuals with vertebral fractures.

Fracture Not Deemed Attributable to Intervention

Giangregorio et al[203] reported 16 fragility fractures in each group that were not related to the intervention. In addition, 3 non-vertebral non-fragility fractures were reported (2 intervention, 1 control). Gold et al[296] reported 2 fractures (1 hip, 1 metatarsal) that occurred during data collection.

Fractures Where Attribution Is Unclear

Crotty et al[297] reported that 3 hip fractures happened among 119 participants during a 1-month PRT and physiotherapy intervention compared with 1 hip fracture in the control group (121 participants). Five other studies[266,281,295,310] reported 17 fractures in 401 participants after PRT alone or combined with other interventions and 32 in the control groups (308 participants), but the authors did not state whether these fractures were attributable to the interventions.

Bone Mineral Density

BMD is considered a surrogate outcome for hip and fragility fractures. When trials were pooled, PRT alone or combined with other interventions of 8 months or longer duration may increase

femoral neck (MD = 0.02 g/cm^2, 95% CI = 0.01–0.03, 521 participants, 5 studies, I2 = 0%, very low certainty evidence; Fig. 4) but not lumbar spine BMD (MD = 0.02 g/cm2, 95% CI = −0.01 to 0.05, 209 participants, 4 studies, I2 = 34%, very low certainty evidence) assessed with dual-energy X-ray absorptiometry. Despite a statistically significant difference (P = .004), the effects of PRT on total hip BMD appear to be small and are of uncertain clinical significance (MD = 0.00 g/cm2, 95% CI = 0.00–0.01, 435 participants, 4 studies, I2 = 0%, very low certainty evidence; Fig. 5). Sensitivity analysis including PRT only studies resulted in similar findings for femoral neck BMD (MD = 0.03 g/cm2, 95% CI = 0.00–0.05, 183 participants, 2 studies, I2 = 0%, very low certainty evidence), whereas there were no positive effects on total hip BMD (MD = 0.01 g/cm2, 95% CI = −0.02 to 0.05, 183 participants, 2 studies, I2 = 5%, very low certainty evidence;). Furthermore, another study[311] reported statistically significant changes (P = .0305) in lumbar spine BMD in the intervention (+4.48% ± 2.63%) compared with the control group (+1.00% ± 5.00%).

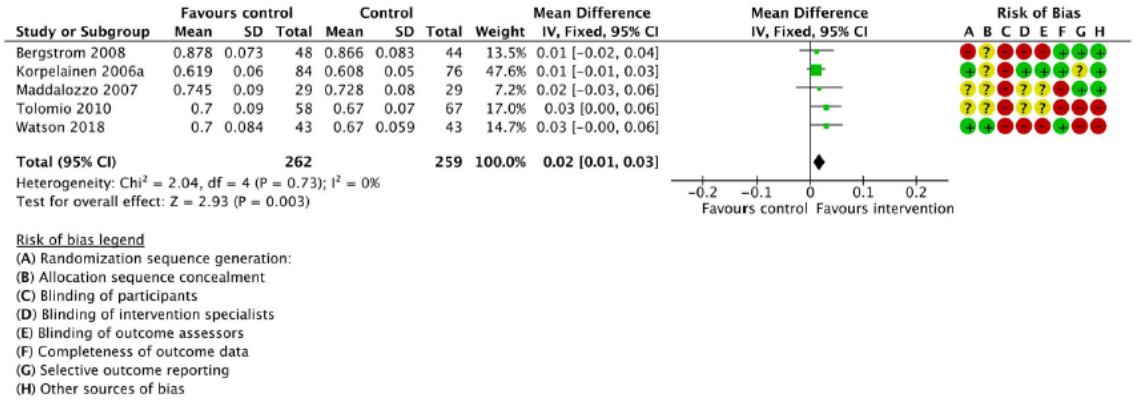

Figure 4. Forest plot of the effects of PRT alone or combined with other interventions on femoral neck BMD.

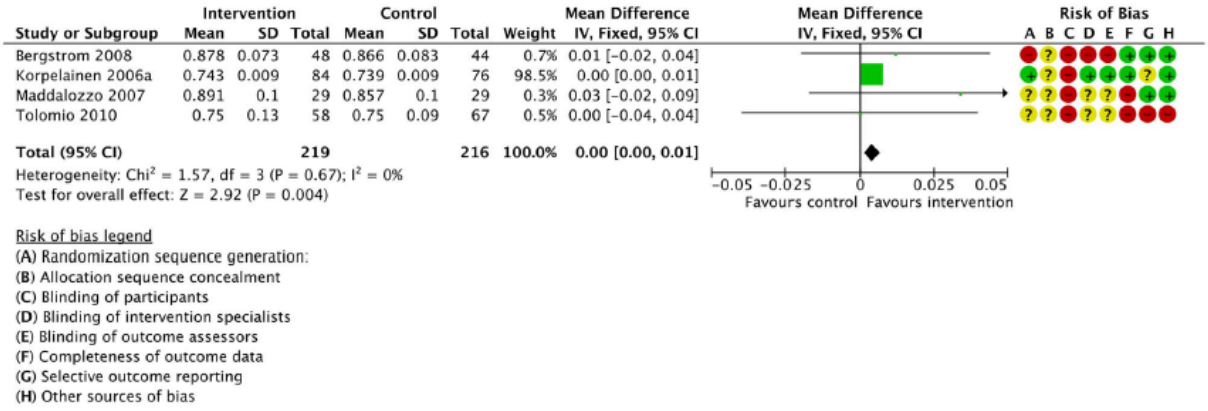

Figure 5. Forest plot of the effects of PRT alone or combined with other interventions on total hip BMD.

Number of People Who Experienced One or More Falls

The effects of PRT alone or combined with other interventions on the number of people experiencing 1 of more falls are uncertain (RR = 1.23, 95% CI = 1.00–1.51, 631 participants, 5 studies, I2 = 64%, very low certainty evidence). There were not enough PRT-only studies to perform a sensitivity analysis. Only 1 study[269] reported that 3 of 32 participants from the intervention group experienced at least 1 fall versus 2 of 32 participants allocated to the control group.

Total Number of Falls

The effects of PRT alone or combined with other interventions on the total number of falls are uncertain. (IRR = 1.05, 95% CI = 0.91–1.21, 1143 participants, 7 studies, I2 = 0%, very low certainty evidence). There were not enough PRT-only studies to perform a sensitivity analysis. Only 1 study[269] reported 18 falls among 32 participants from the intervention group and 10 falls among 32 participants allocated to the control group.

Fall-Related Injuries

There was uncertainty whether PRT alone or combined with other interventions reduced fall-related injuries in people at risk of fracture (IRR = 0.65, 95% CI = 0.31–1.37, 845 participants, 4 studies, I2 = 0%, low certainty evidence). One additional study[288] (not pooled because of low event rate) reported 1 fall-related injury in the control group (48 participants) and no events in the intervention group (45 participants) after a 5-month PRT and balance intervention. There were not enough PRT-only studies to perform a sensitivity analysis. Only 1 study[291] reported that 1 participant in the exercise group fractured her arm after a fall, without specifying whether it was caused by the intervention, while another study[269] reported no injuries due to falls.

Physical Functioning and Disability

PRT alone or combined with other interventions improved performance on the TUG test (MD −0.90 seconds, 95% CI = −1.01, −0.78, 911 participants, 13 studies, I2 = 93%, very low certainty evidence; Fig. 4). Sensitivity analysis including PRT-only studies resulted in similar findings (MD

−1.24 seconds, 95% CI = −1.67, −0.82; 241 participants, 5 studies, I2 = 95%, very low certainty evidence). We chose not to pool data for other physical functioning outcomes because many different physical assessments were performed across studies, and the number of studies for each outcome was small.

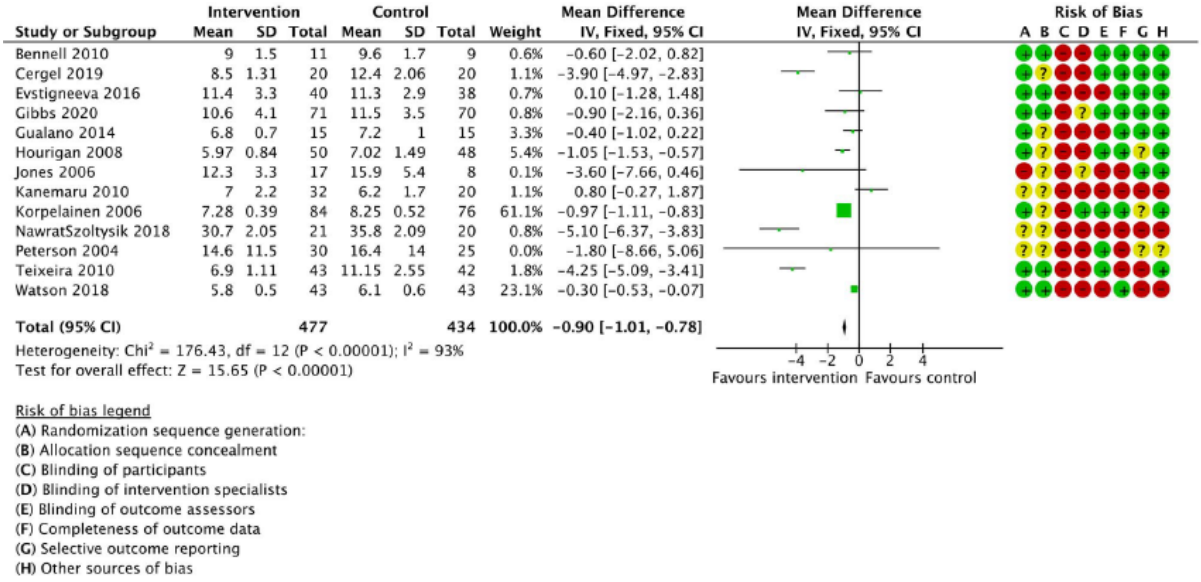

Figure 6. Forest plot of the effects of PRT alone or combined with other interventions on physical functioning and disability assessed with Timed "Up and Go" (TUG) test.

Health-Related Quality of Life

There was evidence of benefits of PRT alone or combined with other interventions on HRQoL (SMD = 0.32, 95% CI = 0.22–0.42, 1711 participants, 20 studies, I2 = 81%, low certainty evidence; Fig. 7). Sensitivity analysis restricted to PRT-only interventions resulted in positive effects of PRT on HRQoL (SMD = 0.75, 95% CI = 0.54–0.95, 412 participants, 8 studies, I2 = 80%, moderate certainty evidence).

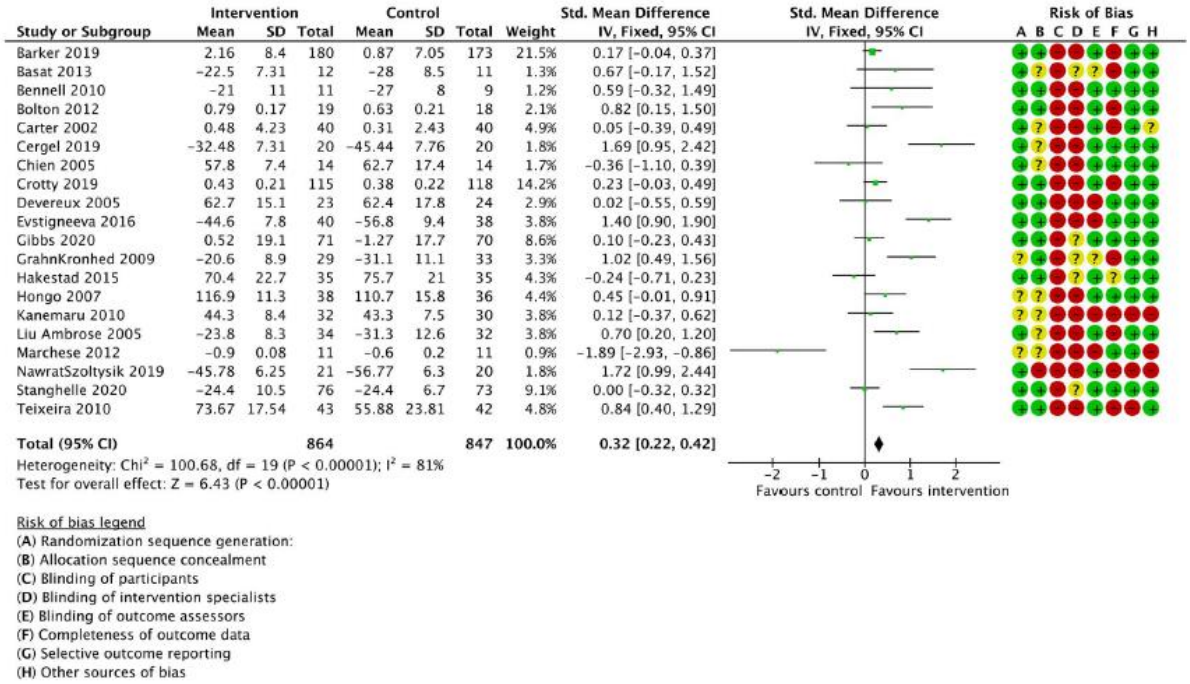

Figure 7. Forest plot of the effects of PRT alone or combined with other interventions on health-related quality of life.

Serious Adverse Events

Six studies provided data on serious adverse events. One study[203] reported serious adverse events during a trial of a 12-month PRT and balance intervention. Eighteen events among 71 participants were recorded among the intervention group vs 12 events among 70 participants allocated to the control group. However, none was reported to be related to the intervention. Five more studies[201,283,295,298,307] stated that no serious events related to the intervention occurred.

Minor Adverse Events

The effects of PRT alone or combined with other interventions on minor adverse event occurrence were uncertain (IRR= 0.94, 95% CI = 0.59–1.50, 300 participants, 4 studies, I2 = 0%, very low certainty evidence). There were not enough PRT-only studies that could be pooled to perform a sensitivity analysis.).

General Pain

PRT alone or combined with other interventions reduced general pain (SMD −0.26, 95% CI = −0.37 to −0.16, 1457 participants, 17 studies, I2 = 70%, very low certainty evidence; Fig. 8). A sensitivity analysis including PRT-only interventions revealed similar findings (SMD −0.47, 95% CI = −0.69 to−0.24, 320 participants, 5 studies, I2 = 84%, low certainty evidence).

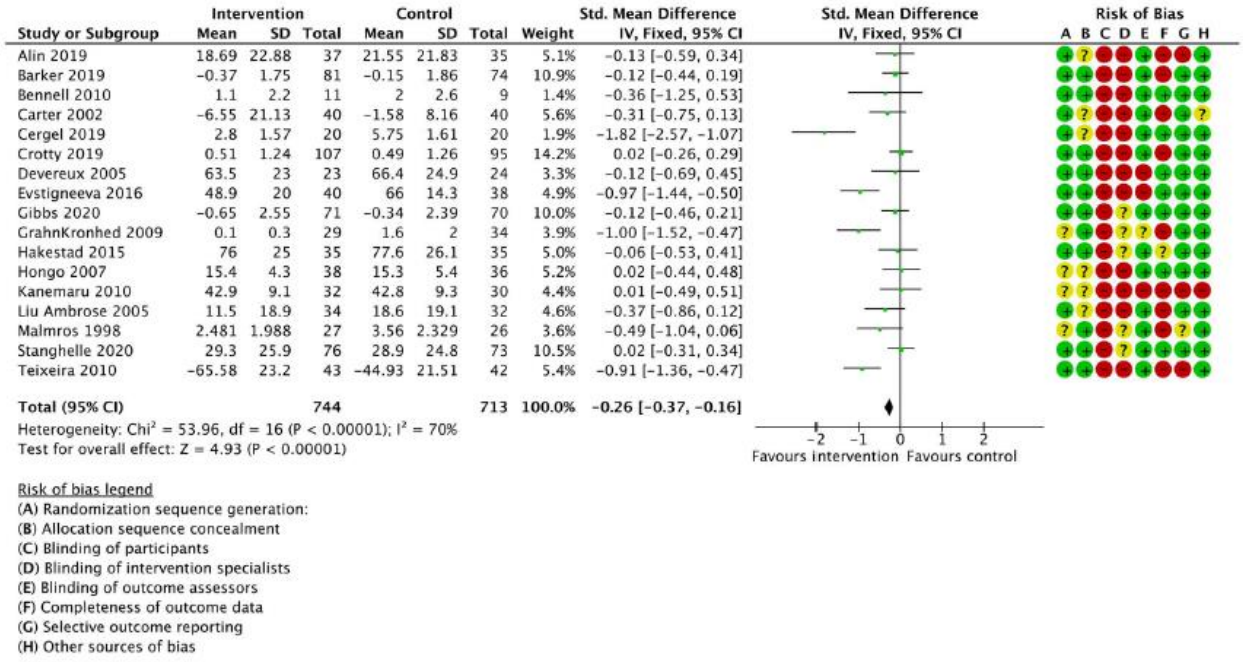

Figure 8. Forest plot of the effects of PRT alone or combined with other interventions on general pain.

Risk of Bias

Among the 53 included studies, 38 specified how the randomization sequence was generated and 19 studies described allocation concealment. Only 4 studies attempted to blind intervention deliverers. Outcome assessors were blinded to group allocation in 30 studies. Thirty-one studies were considered high risk of bias for completeness of outcome data, often due to the use of per-protocol instead of intention-to- treat analyses. Seventeen studies were unclear or at high risk of selective outcome reporting. Nine studies presented other potential sources of bias. Sensitivity analyses including only studies deemed low risk of bias did not alter the findings.

3.1.4 Discussion

PRT alone or in combination with other interventions may improve BMD at the femoral neck, physical functioning, and HRQoL in people at risk of fracture. Moreover, PRT reduced pain and did not appear to cause serious adverse events. Whether PRT has no effect on, or increases or decreases the risk of falls, the number of people experiencing a fall or risk of fall-related injuries is uncertain. However, the certainty of evidence is low for many of the outcomes. The sensitivity analysis including PRT-only interventions showed similar effects for all the outcomes except for BMD at the lumbar spine; therefore, we should encourage individuals at risk of fracture to participate in PRT to improve health-related outcomes. PRT may improve both physical functioning and HRQoL; however, the effects of exercise on HRQoL reported in other studies of older adults are heterogeneous or suggest no effect. Indeed, a systematic review of multicomponent exercise interventions for preventing falls in older adults did not report positive effects on HRQoL.13 However, it is possible that PRT interventions may be more effective or that training adaptations are more substantial for adults at later ages or with poorer physical condition[36]; therefore, the modest improvements in HRQoL observed in the present review may be explained by the inclusion of people with low bone mass or previous fracture. Nonetheless, the substantial-to-serious heterogeneity and the infrequent use of intention-to-treat analysis, even in the presence of high dropout rates, suggest

caution in the interpretation of the results. Our findings showed a mean improvement of 0.9 seconds in the TUG test performance. However, a minimal clinically important difference (MCID) for the TUG test has not been established in individuals with osteoporosis. Frank-Wilson et al[317] noticed a difference of 1.2 seconds in the TUG test between people who experienced at least 1 fall and those who did not, while the TUG test MCID ranges from 1.4 to 3.4 seconds in other populations with chronic musculoskeletal conditions.[318,319] However, community-dwelling older adults often have fast times at the baseline for the TUG test, so there may be ceiling effects or a small window for improvement with exercise. Therefore, determining the MCID for the TUG test in adults at risk of fracture would help in understanding the real clinical relevance of the improvements after exercise interventions. The present systematic review does not show any benefits of PRT for total number of falls or fall-related injuries, but it may increase the risk of

experiencing a fall. However, functional strength training combined with balance exercises is effective in reducing falls among older adults living in the community. A 2019 Cochrane review[164] demonstrated that multicomponent exercise programs reduced the rate of falls by 23% compared with control (IRR = 0.77, 95% CI = 0.71–0.83). No effects were observed when studies with PRT-alone interventions were pooled, but interventions that included functional strength training or PRT combined with functional strength and balance training were effective.[164] Therefore, balance and functional strength exercises, such as squats or sit-to-stands, should be recommended to prevent falls in people at risk of fracture. There are not enough studies with a sufficient number of fracture events to draw conclusions about the effect of PRT on hip or fragility fracture incidence. A systematic review investigating the effects of combined exercise interventions in adults 45 years and older reported a significant reduction in fractures (RR = 0.49, 95% CI = 0.31– 0.76) but no significant effects on vertebral fractures (RR = 0.56, 95% CI = 0.30–1.04).[191] Furthermore, Sherrington et al[254] reported a decrease in fall-related fractures after combined
exercise interventions (RR = 0.73, 95% CI = 0.56– 0.95), but the evidence is of low certainty. In this paper, we reported beneficial effects of PRT on femoral neck BMD, while the effects on hip and spine BMD are small and of uncertain clinical significance. We established a priori that a difference of 0.02 g/cm2 (corresponding approximately to a 2% increase) in BMD at the femoral neck, total hip, or lumbar spine might be clinically important. Our decision was substantiated by a recent meta-regression showing that a 2% increase in BMD at those 3 sites was associated with a reduction in the risk of vertebral (−28%), hip (−22% to −15%), and non-vertebral osteoporotic fractures (−10% to −11%).[320] Furthermore, a trial using high-intensity resistance training combined with impact training showed benefits on BMD, at least for relatively healthy women with low bone mass (average age 65 years).[188] A trial using the same high intensity impact and resistance training intervention in men was published after our search was complete and reported similar findings.[321] In keeping with our findings, a Cochrane review about exercise for prevention of osteoporosis among postmenopausal women 45 to 70 years revealed uncertainty about the effects of moderate-high–intensity PRT on total hip BMD but positive effects on femoral neck BMD (MD = 1.03%, 95% CI = 0.24–1.82).[190] However, the number of studies among people at risk of fracture who used BMD as an outcome is limited, and sample sizes were frequently small.

Therefore, adequately powered clinical trials are required to determine the effects of PRT interventions on BMD in people at risk of fracture.

While our review suggests that the effects of PRT on mortality and serious adverse events in individuals at risk of fracture are unknown, there is a growing body of evidence that PRT can reduce the risk of premature death independent of other types of exercise, and there is little evidence of harm.[322,323] Within the literature we reviewed, there were not enough studies or events to pool mortality data. However, a meta-analysis of observational studies revealed that participation in PRT was associated with a lower risk of death when performed alone (HR = 0.79, 95% CI = 0.69–0.91) or combined with aerobic exercise (HR = 0.60, 95% CI = 0.49–0.72).[322] Accordingly, a systematic review of population cohort studies showed that engaging in resistance training led to a 23% and 31% reduction in all-cause and cancer-related mortality, respectively.[323] PRT does not appear to cause serious harms, but the number of studies that documented adverse events was too low to draw definitive conclusions. Howe et al[190] and Sherrington et al[254] reported some minor adverse events associated with PRT, such as pain and joint or musculoskeletal issues. Accordingly, Latham and colleagues[255] reported only minor adverse events in most of the cases musculoskeletal pain. However, adverse events were either not monitored/reported or monitored only in the intervention groups. Adverse event reporting in PRT trials of older adults could be improved so that we can better understand the risk of adverse events during PRT, an outcome that is particularly salient in individuals at risk of fracture. While our findings suggest that PRT should be recommended for individuals at risk of fracture, identifying the ideal frequency or intensity of PRT is a challenge based on the heterogeneity and limitations of existing evidence. The average frequency of training across the studies was 3 times per week (median, n = 2), and the duration ranged from 1 to 30 months (median, n = 6). Several sources of resistance were used across studies, with body weight and free weights, mainly dumbbells and ankle weights, being the most common. Systematic reviews in older adults demonstrated that a moderately high intensity is required to elicit improvements in muscle strength and functional and disability outcomes.[187,324,325] Therefore, future RCTs should investigate the ideal training intensity for improving physical functioning and HRQoL and reducing fall and fracture risk in people at risk of fracture. Moreover, several factors affect the engagement in PRT programs, such as discussing the exercise program and its benefits with a

health care professional.[326,327] Conversely, barriers like pain, injury, illness, or fear of having a heart attack or stroke or of death need to be addressed to engage people in resistance training.[326] Many of the studies we reviewed involved supervised PRT, so individuals may need supervision, at least initially, to achieve the observed improvements in physical functioning and HRQoL or pain reduction. Indeed, despite a moderate to high adherence (85%) to a 6-week PRT home exercise program, Cergel et al[289] showed greater improvements in physical functioning and HRQoL and pain reduction in a supervised program compared with a home exercise program. Therefore, 2 to 3 sessions of PRT per week performed at a moderate to high intensity and including functional strengthening exercises seem to improve health-related outcomes with a minimal risk of adverse events. We acknowledge some limitations of our work. Selection bias might threaten the external validity of our work. Only 4% of the participants were men, and only a small number of studies included participants considered to be at high risk of fracture (eg, 6 studies of individuals with at least 1 hip fracture and 4 studies with at least 1 non-hip or non-spine fracture). Our findings may not be generalizable to individuals who are frail or at high risk of fracture. The majority of the interventions were multicomponent (eg, PRT plus balance, PRT plus impact, etc.), and we planned sensitivity analyses for studies using PRT alone, but the effects were not statistically significant or the number of studies often limited our ability to do so. Moreover, the number of the studies is limited for some of the outcomes, thus reducing the confidence in their interpretation. Studies examining the effects of PRT alone on health-related outcomes in adults at risk of fracture would be of value. The lack of consistency in blinding of intervention specialists and outcome assessors, the incomplete and selective outcome reporting present in many studies, and the substantial heterogeneity across studies suggest caution before making inferences for a few outcomes. Finally, we identified studies that were eligible but were missing information, and we contacted the authors; however, some did not respond. Accordingly, some data are missing, and we therefore had to exclude 4 studies.[328–331] PRT has beneficial effects on HRQoL and physical performance and may reduce pain in individuals at risk of fracture. There was no statistically significant effect of PRT on falls or risk of experiencing a fall or fall-related injury, while adverse events were infrequently reported and effects on fractures are unknown. Based on our findings, PRT may be used as a beneficial and safe strategy to improve health-related outcomes in people

at risk of fractures. However, more well designed and carefully conducted clinical trials are needed to resolve important issues concerning the role of PRT in this population.

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3.2 Study 4. Exercise for Improving Age-Related Hyperkyphosis: A Systematic Review and Meta-Analysis with GRADE Assessment

3.2.1 Introduction

The term hyperkyphosis defines a thoracic spine sagittal curvature of at least 40º,[51,197] and it is usually associated with forward head posture, shoulder protraction, and flattening of lumbar lordosis.[53] Hyperkyphosis increases the risk of reduced physical functioning, OVFs, and impaired pulmonary function.[33,53,54,60,197,332–334] Twenty to forty percent of older adults have hyperkyphosis,[52] which is associated with mortality independent of bone mineral density (BMD) and OVFs.[62,197] The etiology of hyperkyphosis is multifaceted and several risk factors are associated with its onset. Height loss greater than 4 cm and multiple thoracic wedge fractures are predictive of hyperkyphosis,[33] while women with hyperkyphosis have higher rate of incident OVFs.[54] Degenerative disc disease and poor spine mobility, resulting from calcifications and ossification of the anterior longitudinal ligament, may increase the Cobb angle.[32,335–338] Weakness of the spinal extensor muscles and shortening of pectoral and hip flexors muscles are associated with the presence of hyperkyphosis, even though it is not clear whether muscle shortening is cause or consequence of hyperkyphosis.[52,339–341] Individually tailored exercise programs may improve

kyphosis and back extensor muscle strength in individuals with hyperkyphosis. However, there is still uncertainty about the true effects of exercise on posture or degree of kyphosis. Two narrative reviews made a call for new studies, as the available evidence was conflicting and heterogeneous.[192,193] A recent meta-analysis showed modest improvements in kyphosis after exercise programs among participants 18 years old and older; however, the review combined studies of age-related hyperkyphosis with hyperkyphosis in younger adults.[196] A previous systematic review conducted in studies of adults aged 45 years or over could not perform a meta-analysis due to the limited number of studies available, and the findings from the included studies were contradictory.[195] Moreover, previous systematic reviews focused exclusively on kyphosis outcomes, while several studies have shown that quality of life and physical functioning are reduced in presence of hyperkyphosis.[33,53,60,334] In light of new studies published in the past decade, we performed a systematic review to determine the effects of targeted exercise on kyphosis angle, back extensor muscle strength or endurance, physical functioning, quality of life, pain, falls, and adverse events in adults 45 years or older. The present review is part of a series of reviews that will inform the upcoming Clinical Practice Guidelines for Management of Osteoporosis and Fracture Prevention in Canada, including recommendations on risk assessment, medications, nutrition, and several types of exercise. The efficacy of each type of exercise (e.g., progressive resistance training, walking, balance, impact exercise, yoga, etc.) is being examined separately to inform recommendations specific to the type of exercise.

3.2.2 Methods

3.2.2.1 Protocol

The present systematic review was reported according to the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA).[342] The protocol was informed by the Cochrane Handbook for Systematic Review of Interventions and registered via the International Prospective Register of Systematic Reviews (PROSPERO) at https:// www. crd. york.ac. uk/ prosp ero/ (number CRD42020180848, registered and last updated on August 28, 2020).

3.2.2.2 Search strategy and selection criteria

The literature search was conducted in the following databases: MEDLINE (Ovid), EMBASE (Ovid), Cochrane CENTRAL (clinical trial), Cochrane database of systematic reviews (meta-analyses), CINAHL (allied health journal content), Web of Science, and no restrictions by language were applied at this stage. Medical Subject Headings (MeSH terms) and keywords associated with kyphosis, posture, and exercise interventions were used to design the search strategy. The literature search was performed in May 2020. The full search strategy is reported in Appendix D. Selection criteria related to study design, population, intervention, comparator, outcome, and time are listed below.[343]

Study design

Based on our experience conducting a similar review in 2014,[195] we were not expecting to retrieve a large number of randomized controlled trials (RCTs) and quasi-RCTs. Therefore, in addition to RCTs and quasi-RCTs, we included pre-post design studies, cohort studies, and case–control studies to provide a comprehensive understanding of the research in this area. Only RCTs and quasi-RCTs were included in meta-analyses. Full texts published in English or Italian were screened, because members of the research team could speak those languages fluently.

Participants

We included studies on men and women aged 45 years or older with hyperkyphosis, defined as a thoracic spine curvature of 40Åã or more measured with any validated tools.[50,51] To be consistent with our prior review, we decided to make our criteria less restrictive so that we might capture more studies and make inferences with higher certainty. Therefore, we expanded the inclusion criteria to studies that did not specify how hyperkyphosis was measured but described their participants as having a flexed posture at baseline, or that had at least one group with a mean kyphosis angle of at least 40º at the baseline. We considered sensitivity analyses in studies of individuals with low bone mass or OVFs to determine if the effects varied by population.

Intervention

We included any exercise interventions or physical therapy that involved at least one active component performed independently by the participants, to distinguish active exercise from passive mobilization aided by a physical therapist. We hypothesized that exercise programs targeting back extensor muscles would be the most common and wanted to explore the efficacy of these programs separately. Accordingly, a sensitivity analysis was performed including studies with at least one exercise component targeting muscular strength or endurance of thoracic or lumbar spine extensor muscles, cervical retractors, muscles involved in shoulder external rotation or scapular retraction, or other muscles involved in stability or movement of the thoracic or lumbar spine (e.g., prone trunk lift to neutral, thoracic rotations/extension from lateral decubitus position, shoulder flexion and thoracic spine extension with back at the wall, etc.).

Comparator

We included in the meta-analysis studies that had at least one comparator group that received no intervention or a non-exercise or a non-physical therapy intervention (e.g., educational intervention). Studies with an active or attention control group that participated in a different type of physical activity were considered for inclusion in the meta-analysis if the attention control was not hypothesized to have an effect on kyphosis outcomes. Studies comparing two interventions or within-group comparisons from non-RCTs were included in narrative syntheses only.

Outcomes

Primary outcomes

We included studies that had the Cobb angle of kyphosis[67] as an outcome, or any other indirect measures of kyphosis (e.g., flexicurve index[31] or angle,[344] manual inclinometers,[75] goniometers,[85] kyphometer,[345] Spinal Mouse.,[82] etc.). When more than one measure of kyphosis was reported, we based the decision for inclusion in the main analysis on the level of evidence reported by Barrett et al.[346] Therefore, we prioritized the outcomes as follows: Cobb angle (with patient in standing position), kyphometer, spinal mouse, flexicurve, manual inclinometer, digital inclinometer. The direct measures of kyphosis not included in the main analysis have been reported in sensitivity analyses. Measurements of forward head posture (e.g., occiput-wall distance,[79] blocks method,[50

etc.) were included as surrogate outcomes of kyphosis. However, since all the studies included in the meta-analysis reported at least one direct measure of kyphosis, we did not pool surrogate outcomes. Studies that used apps for smartphones and tablets to assess spine curvature were also included, as well as studies that measured back extensor strength or endurance.

Secondary outcomes

We included the following secondary outcomes: (1) number of people who experienced one or more falls, total number falls and fall-related injuries; (2) hip fractures, either self-reported or X-ray-verified fracture of the proximal femur that occurred at the femoral neck or trochanter in a low trauma event, such as a fall from a standing height or less; and (3) fragility fractures, either self-reported or X-ray-verified fracture of the spine, wrist, humerus, and pelvis that occurred following a low trauma event; (4) physical functioning and disability, measured using a validated tool to assess ability to perform activities of daily living, or performance-based measures of physical functioning (e.g., gait speed, 5 times sit-to-stand, timed up and go [TUG]); (5) health-related quality of life (HRQoL), determined using any validated measure such as a generic quality of life questionnaire or osteoporosis-specific quality of life questionnaire; (6) pain outcomes determined using a pain intensity scale (e.g., visual analog scale) or a pain subscale from a generic functional status questionnaire (e.g., SF-36, Nottingham Health Profile); (7) serious adverse events, defined as any untoward medical occurrence that, at any dose, results in death, a threat to life, inpatient hospitalization, or prolongation of existing hospitalization, or in persistent or significant disability/incapacity;[261] (8) non-serious adverse events, which include any reaction related to the intervention such as musculoskeletal injuries (e.g., sprain, strains, joint pain, overuse injury); (9) mortality, due to any cause such as aging, disease, or injury-related circumstances that result in death. Selection of secondary outcomes was based on a survey circulated among over 1000 members of the Canadian Osteoporosis Patient Network[259] and over 100 exercise professionals.[260]

Timeframe

Studies were included if the intervention lasted at least 4 weeks, deemed the minimum time to observe an effect on the outcomes of interest, in keeping with previous systematic reviews in people with low bone mass or OVFs.[347,348]

Study selection process

The screening process was performed using Covidence (https:// www.covidence.org/home; Covidence, Melbourne, Australia). Two authors (MP and NT) independently reviewed titles and abstracts and the full texts of the records deemed eligible after the first level of screening. Conflicts between reviewers were resolved by discussion or, when an agreement could not be reached, by a third author (LG). We extracted the following information from each study: descriptive information about the study (title, authors, publication date and status, country, study design); population and participants characteristics (Cochrane PROGRESS Plus);[349] number of recruited participants, dropout rates and reasons, adherence rates and adverse events; intervention (frequency, intensity, type, duration and setting of the delivered intervention, qualification of the person delivering the intervention, if the programs were supervised/unsupervised or in group/alone and information about progression); type of comparator (if any); outcomes described above. In case of missing information, the corresponding authors of the individual studies were contacted.

3.2.2.3 Data synthesis and statistical analysis

Data were extracted using Covidence (https://www.covidence.org/home; Covidence, Melbourne, Australia) and then imported to RevMan 5.3 (Cochrane Community, London, UK; https://community.cochrane.org/help/tools-and-software/revman-5) for statistical analysis. We used descriptive statistics to describe studies, such as mean and standard deviation (SD), count and percent or median and inter-quartile range (Q1–Q3). Mean between-group post-intervention differences and confidence intervals or standard deviations were reported for every study, where applicable. We performed a fixed-effect meta-analysis and calculated a mean difference (MD) with a 95% confidence interval (CI) for continuous outcomes. When a variety of methods to measure kyphosis or other outcomes were used across the studies, we calculated a standardized mean difference (SMD) with a 95% CI. Incidence rate ratio (IRR) with a 95% confidence interval (CI) was calculated for dichotomous and count outcomes. Heterogeneity between trials was

assessed by using the I^2 statistic. We performed sensitivity analyses to determine if effects were similar if limited to studies of people with low bone mass or OVFs at baseline. Sensitivity analyses were also performed to determine whether including only exercise programs with at least one active component targeting back extensor strength or endurance led to similar findings. We did not assess publication bias, as the power of the test is too low to detect a real asymmetry via visual inspection of funnel plots when less than ten RCTs are pooled.[350]

3.2.2.4 Risk of bias and assessment of the certainty of evidence

Two reviewers (MP and NT) independently assessed risk of bias of RCTs and quasi-RCTs using the Cochrane Risk of Bias Assessment Tool.[351] Discordance was resolved by consensus or by a third author (LG). Reviewers were not involved in data extraction or risk of bias assessment of studies on which they were an author. The Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach was used to assess the certainty of the evidence.[265]

3.2.3 Results

We identified 3723 unique records (Fig. 9). After title and abstract screening, we assessed 56 full-text reports, and 23 studies, with 1399 participants (6% men) were included (the reasons for exclusion are reported in the Appendix A). Eleven studies included only participants with hyperkyphosis at the baseline[205,344,352–357] but only two[355,358] were RCTs with a non-active control group and could be pooled in the meta-analyses. Five studies included participants with both hyperkyphosis and low bone mass or vertebral fractures at baseline.[276,285,289,295,359] The median duration of the interventions was 2.5 months (Q1–Q3 = 2, 5.55), and the median frequency was 3 days per week (Q1–Q3 = 2, 5). One study evaluated the effects of yoga,[344] and one other study combined physical therapy and taping.[360] Three studies included only a back extensor muscle strengthening intervention,[289,352,361] while other studies combined back extensor muscle strengthening with postural exercises,[205,276,353–355,358,359] balance training,[295,353,362–365] mobility exercises,[364,366] physical therapy,[285] impact exercises,[188] taping,[364] walking,[295] or Nordic Walking.[365] Nine studies had group interventions,[266,276,344,352,352,355,358,365,366] and seven others had individual interventions,[205,295,353,356,359,360,364] while four studies included both group and individual components[285,289,358,363] and three studies did not report this information.[357,361,362] Four

RCTs[285,295,359,360] reported adherence as percentage of participants who completed all or most sessions, and it ranged from 38 to 100% (median 75.5%), while six RCTs[289,344,355,358,363,364] reported the percentage of sessions completed and it ranged from 70.3 to 100% (median 84.5%). Thirteen studies received funding from non-profit organizations[205,285,295,344,353–355,358] and two studies received private funding,[276,360] while eight studies did not report funding information.[289,352,352,356,359,361,364,365] The characteristics of included studies are reported in the Appendix B (Table B.1). The GRADE summary of findings is reported in Fig. 10.

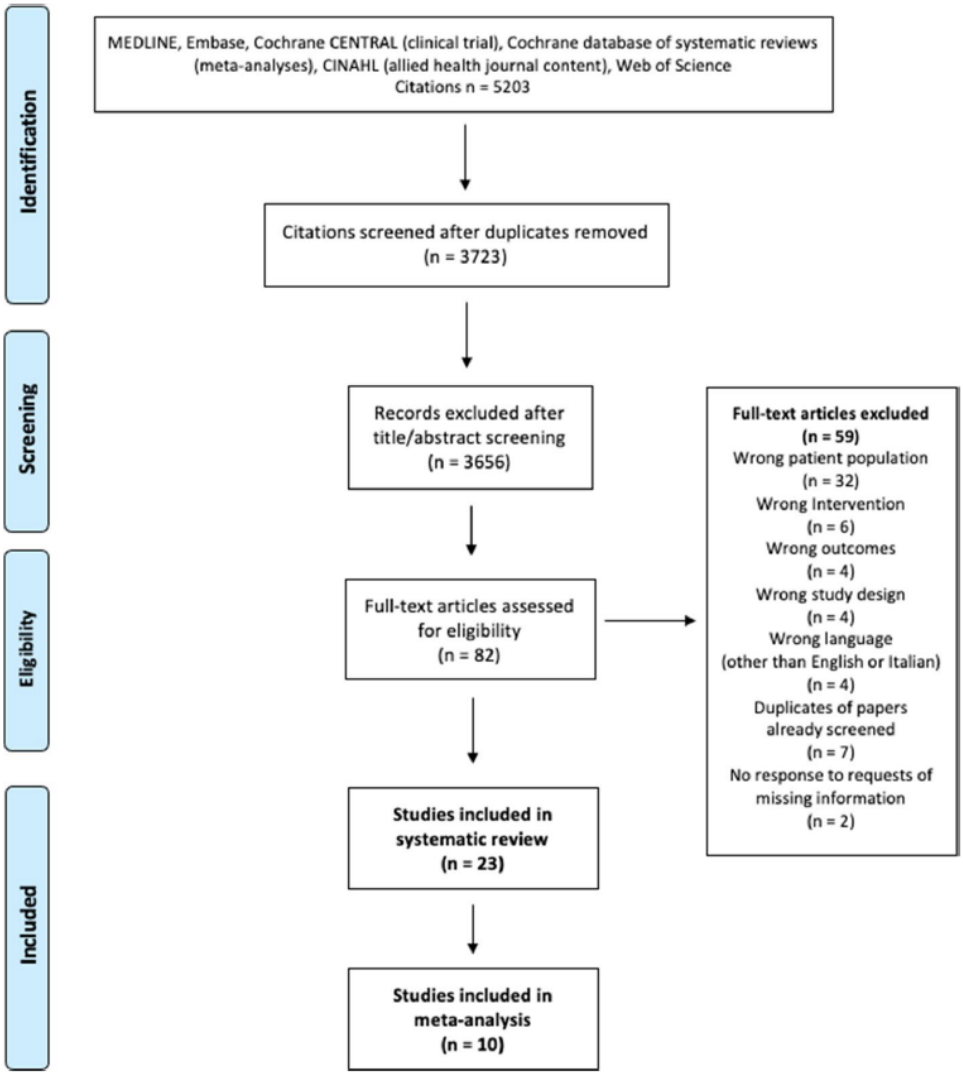

Figure 9. PRISMA flow chart

Effects of interventions on primary outcomes

Kyphosis outcomes

Kyphosis index or angle was reduced after exercise or physical therapy interventions (SMD −0.31; 95% CI − 0.46, − 0.16; 727 participants; 9 studies; I2 = 77%; moderate certainty evidence; Fig 11. Only two studies[355,358] recruited exclusively participants with hyperkyphosis at the baseline (Table B.1 Appendix B). A sensitivity analysis limited to studies targeting back extensor muscle strength showed similar findings with less heterogeneity (SMD − 0.23; 95% CI − 0.38, − 0.08; 679 participants;8 studies; I2 = 39%; high certainty evidence; Figure C.1, Appendix C). A sensitivity analysis limited to only studies with people with both hyperkyphosis and low bone mass or vertebral fractures did not show a statistically significant effect (SMD − 0.07; 95% CI − 0.26, 0.11; 459 participants; 5 studies; I2 = 0%; moderate certainty evidence; Figure C.2, Appendix C)). Two RCTs reported on kyphosis outcomes but could not be included in the meta-analysis. Bergstrom et al.[276] did not observe statistically significant between group differences after a 6-month progressive resistance training and walking program, but the authors did not report the data regarding kyphosis outcomes. Greendale et al.[344] included only participants with hyperkyphosis at the baseline, and reported a statistically significant between-group difference in kyphosis index measured with flexicurve (median − 3.64%; Q1– Q3 = − 8.98%, 1.34%; p = 0.004) but not in the degree of kyphosis assessed with kyphometer (median − 5.17%; Q1–Q3 = − 8.38%, 0.93%; p=0.44) after 6 months of yoga classes. Seven RCTs measured kyphosis but were not included in pooled analyses because they compared the effects of two different interventions (Appendix B). Other sensitivity analyses (e.g., including alternative kyphosis outcome measures or home exercise programs instead of supervised ones) related to kyphosis outcomes did not show different findings (Figures C.3, C.4, C.5, Appendix C). Seven studies measured kyphosis with an inclinometer,[266,285,289,352,352,359,364] six studies utilized a kyphometer,[205,276,344,354,355,358] five studies utilized a flexible ruler (flexicurve),[266,295,344,361,367] three studies measured the Cobb angle with the subject in the standing position,[355,357,358] three studies used photometric or stereophotogrammetric techniques,[362,365,366] three studies measured the tragus-to-wall distance,[352,354,367] two studies measured the occiput-to-wall distance,[205,366] one study measured the Cobb angle with DXA with

the subject in the lateral decubitus,[266] one study utilized the Spinal Mouse,[360] one study used the Rancho Bernardo Blocks method,[344] and one other study used the Posture Pro 8 software.[356]

Certainty assessment							Summary of findings				
							Study event rates (%)			Anticipated absolute effects	
Participants (studies) Follow up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty of evidence	With no intervention	With exercises targeting back extensor muscles, core stability or posture	Relative effect (95% CI)	Risk with no intervention	Risk difference with exercises targeting back extensor muscles, core stability or posture
Kyphosis curve (follow up: range 6 weeks to 8 months; assessed with: Kyphosis angle or index, lower score is better)											
679 (8 RCTs)	not serious	not serious	not serious	serious [a]	none	⊕⊕⊕◯ MODERATE	335	344	-	-	SMD **0.23 SD lower** (0.38 lower to 0.08 lower)
Back extensor strength (follow up: range 4 months to 6 months; assessed with: dynamometer [Newton, higher score is better])											
150 (3 RCTs)	very serious [b]	not serious	not serious	serious [c]	none	⊕◯◯◯ VERY LOW	72	78	-	The mean back extensor strength ranged from **34.75-65.41** Newtons	MD **10.51 Newtons higher** (6.65 higher to 14.38 higher)
Back extensor endurance (follow up: range 6 weeks to 6 months; assessed with: Timed loaded standing test [seconds, higher score is better])											
597 (5 RCTs)	not serious	very serious [d]	not serious	not serious	none	⊕⊕◯◯ LOW	292	305	-	The mean back extensor endurance ranged from **47.1-123.0** seconds	MD **9.76 seconds higher** (6.4 higher to 13.13 higher)
Rate of falls (follow up: range 3 months to 6 months; assessed with: Total number of falls)											
537 (3 RCTs)	not serious	not serious	not serious	very serious [c,e]	none	⊕⊕◯◯ LOW	20/263	27/274	**Rate ratio 1.15** (0.64 to 2.05)	76 per 1,000	**11 more per 1000 patient(s) per years** (from 27 fewer to 80 more)
Fall-related injuries (follow up: mean 3 months)											
348 (1 RCT)	not serious	not serious	not serious	very serious [c]	none	⊕⊕◯◯ LOW	One study reported 2 fall-related injuries in the intervention group (175 participants) and 3 fall-related injuries in the control group (173 participants).				
Fragility fractures (follow up: mean 3 months)											
348 (1 RCT)	not serious	not serious	not serious	very serious [c]	none	⊕⊕◯◯ LOW	The number of events was too low to make inferences.				
Physical functioning (follow up: range 6 weeks to 3 months; assessed with: Time Up and Go test [seconds, lower score is better])											
260 (4 RCTs)	not serious	very serious [d]	not serious	serious [c]	none	⊕◯◯◯ VERY LOW	125	135	-	The mean physical functioning ranged from **7.0-16.4** seconds	MD **0.28 seconds lower** (0.48 lower to 0.08 lower)
Quality of Life (follow up: range 6 weeks to 8 months; assessed with: PROMIS, QUALEFFO-41 [score presented as higher score is better])											
613 (5 RCTs)	not serious	serious [d]	not serious	not serious	none	⊕⊕⊕◯ MODERATE	298	315	-	-	SMD **0.26 SD higher** (0.1 higher to 0.42 higher)
Pain (follow up: range 1.5 months to 6 months; assessed with: VAS scale, lower score is better)											
306 (5 RCTs)	not serious	very serious [d]	not serious	not serious	none	⊕⊕◯◯ LOW	148	158	-	The mean pain was **13.0** points	mean **1.49 points lower** (1.92 lower to 1.07 lower)
Serious adverse events (follow up: range 3 months to 12 months)											
744 (5 RCTs)	not serious	not serious	not serious	very serious [c]	none	⊕⊕◯◯ LOW	No serious adverse events occurred during the interventions (n=379).				
Minor adverse events (follow up: range 2.5 months to 12 months)											
744 (5 RCTs)	serious [f]	not serious	not serious	serious [c]	none	⊕⊕◯◯ LOW	73/365	215/379	**Rate ratio 1.29** (0.95 to 1.74)	216 per 1,000	**63 more per 1000 patient(s) per years** (from 11 fewer to 160 more)

Figure 10. GRADE summary of findings table. CI: Confidence interval; SMD: Standardized mean difference; MD: Mean difference. Explanations. A. Confidence intervals close to the no difference line. B. Outcome assessors were not blinded in one study, and two studies had incomplete and selective outcome reporting. C. Low number of studies and/or participants. D. Serious unexplained heterogeneity. E. Confidence intervals overlap with the no

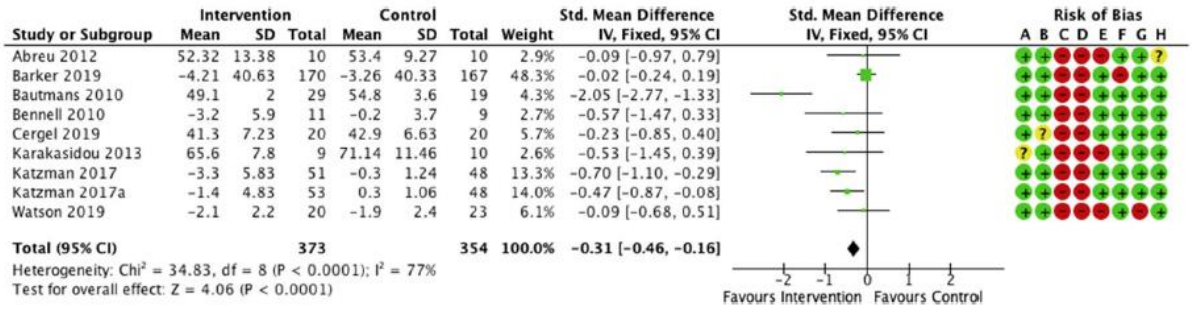

Figure 11. Forest plot of the effects of exercise or physical therapy interventions on kyphosis angle or index. Risk of bias. A Random sequence generation; B allocation concealment; C blinding of participants; D blinding of intervention specialists; E blinding of outcome assessors; F incomplete outcome

Back extensor muscle strength

Exercise had a positive effect on back extensor muscle strength (MD 10.51 N; 95% CI 6.65, 14.38; 3 RCTs; 150 participants; I2 = 0%; very low certainty evidence; Fig.12). The three RCTs reporting back extensor muscle strength as an outcome were performed in people with hyperkyphosis and low bone mass or vertebral fractures, and included interventions targeting back extensor muscle strength. Two pre-post trials showed improvements in back extensor strength after a 1-month and a 3-month back extensor strengthening program, respectively.[353,354]

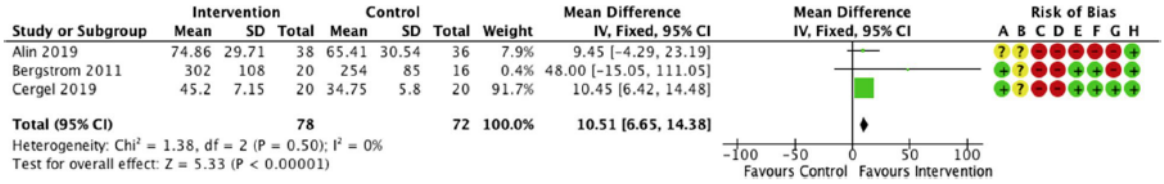

Figure 12. Forest plot of the effects of back extensor strengthening programs on back extensor strength. Risk of bias. A random sequence generation; B allocation concealment; C blinding of participants; D blinding of intervention specialists; E blinding of outcome assessors; F incomplete outcome

Back extensor muscle endurance

Exercise improved back extensor muscle endurance assessed with the timed loaded standing test (MD 9.76 s; 95% CI 6.40, 13.13; 5 studies; 597 participants; I2 = 95%; low certainty evidence; Fig. 13). Sensitivity analysis including only studies performed among people with both hyperkyphosis and low bone mass or vertebral fractures showed a significant mean difference in

back extensor endurance in favor of exercise (MD 29.81 s; 95% CI 22.61, 37.01; 397 participants; 3 studies; I2 = 96%; low certainty evidence; C.7, Appendix C).

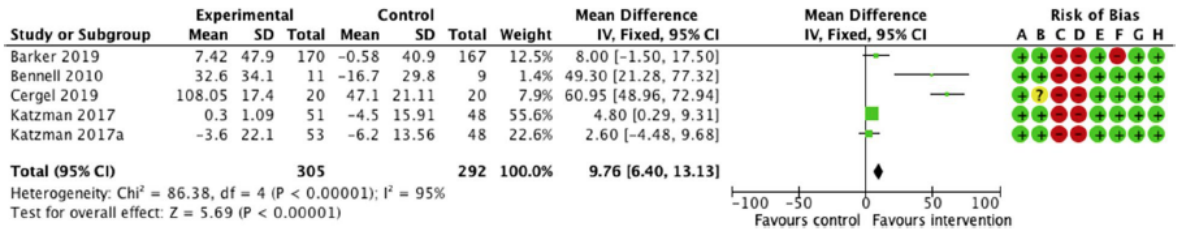

Figure 13. Forest plot of the effects of back extensor strengthening programs on back extensor endurance assessed with timed loaded standing test. Risk of bias. A Random sequence generation; B allocation concealment; C blinding of participants; D blinding of intervention specialists; E blinding of outcome assessors; F incomplete outcome data; G selective outcome reporting; H other sources of bias

Effects of interventions on secondary outcomes

Falls and fractures

No studies reported on hip fractures as an outcome. Barker et al.[295] reported 6 fragility fractures in the exercise group (216 participants) and 8 fragility fractures in the control group, but they do not state that any were attributable to the intervention. Three studies reported falls as an outcome, and they all were performed among people with both hyperkyphosis and low bone mass or vertebral fractures, and targeted back extensor muscle strength. Effects of exercise on the rate of falls were not statistically significant (IRR 1.15; 95% CI 0.64, 2.05; 537 participants; 3 studies; I2 = 0%; low certainty evidence; C.8, Appendix C). Physical functioning, quality of life, and pain Four studies reported TUG test as an outcome, and they all targeted back extensor muscle strength. Exercise interventions resulted in a small, statistically significant improvement in the TUG test (MD − 0.28 s; 95% CI − 0.48, − 0.08; 260 participants; 4 studies; I2 = 94%; very low certainty evidence; C.9, Appendix C). We chose to pool data for the TUG test as it was the test most frequently performed. Other physical functioning assessments were performed across studies, but the number of studies for each outcome was very small and the results varied across studies (Table D1, Appendix D). There was an improvement in HRQoL with exercise alone or combined with physical therapy (SMD 0.21; 95% CI 0.06, 0.37; 661 participants; 6 studies; I2 = 78%; moderate certainty evidence; C.10, Appendix C). A sensitivity analysis of studies that targeted back extensor muscle strength showed similar findings (SMD 0.26; 95% CI 0.10, 0.42; 613 participants; 5 studies; I2 = 78%;

moderate certainty evidence; C.11, Appendix C). Findings from a sensitivity analysis including only studies in people with both hyperkyphosis and low bone mass or vertebral fractures were consistent (SMD 0.28; 95% CI 0.08, 0.48; 413 participants; 3 studies; I^2 = 87%; moderate certainty evidence; C.12, Appendix C). There was a statistically significant reduction in general pain with exercise alone or combined with physical therapy (MD − 1.44 points; 95% CI − 0.39, − 0.13; 352 participants; 6 studies; I2 = 91%; low certainty evidence; C.13, Appendix C). A sensitivity analysis including studies in people with both hyperkyphosis and low bone mass or vertebral fractures showed similar effects on pain (MD − 1.49 points; 95% CI − 1.92, − 1.07; 306 participants; 5 studies; I2 = 95%; low certainty evidence; C.14, Appendix C). The interventions of the studies included in this sensitivity analysis targeted back extensor muscle strength.

Adverse events

Only six studies reported on adverse events. Five studies[285,295,355,358,363] stated that there were no serious adverse events associated with the intervention. The effect on the rate of minor adverse events was not statistically significant (IRR 1.29; 95% CI 0.95, 1.74; 707 participants; 5 studies; I^2 = 41%; low certainty evidence; C.16, Appendix C), and adverse events were attributable to interventions only in two studies. Bennell et al.[285] reported six minor adverse events that were related to intervention among 11 participants (shoulder pain: n = 2; flare-up of a wrist injury: n = 1; sore knee: n = 1; sore waist with particular exercises: n = 1; irritation with the tape: n = 1) and all were resolved with intervention modifications. Bautmans et al.[360] stated that some patients reported discomfort during the execution of overhead exercises, while others experienced mild skin irritations due to the tape and pain during the mobilizations (not pooled). Kaijser Alin et al.[363] reported twelve minor adverse events in intervention group (38 participants) and 25 in the control group (37 participants), without specifying whether they were due to the intervention, and muscle or joint complaints occurred at a similar rate in both the groups (4 intervention, 3 control). Katzman et al.[358] reported 30 minor adverse events in the intervention group (51 participants) and twelve in the control group (48 participants), but none was directly attributed to intervention. Katzman et al.[355] reported 56 minor adverse events (including 4 falls) in 53 participants in the intervention group, and 31 minor adverse events (of which 7 were falls and 22 musculoskeletal pain) during the 3-month waitlist period (48 participants). Katzman et al.[355] stated that the majority of the

musculoskeletal complaints were pre-existing and none of the events was directly attributable to the intervention. Barker et al.[295] reported two deaths and 26 adverse events (including 5 falls and 6 fragility fractures) in the exercise group (216 participants) compared to 22 adverse events (including 4 falls and 8 fragility fractures) in 196 participants of the control group, but they did not state that any were attributable to the intervention. Watson et al.[266] did not report any fractures after the intervention.

Risk of bias in individual studies

Among the 23 included studies, 19 were RCTs or quasi-RCTs. The risk of bias graph is reported in Fig. 6. The risk of bias summary for individual studies is reported in the Appendix E (Figure E.1). Sensitivity analyses including only RCTs considered at low risk of bias did not alter the findings.

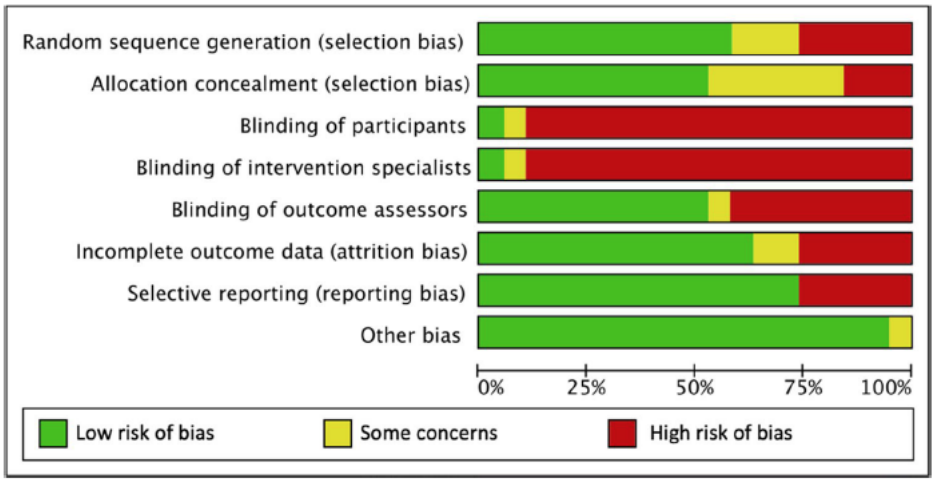

Figure 14. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.

3.2.4 Discussion

There is moderate-to-high certainty evidence that multicomponent interventions, often targeting back extensor muscle strength, cause a small improvement in hyperkyphosis. Furthermore, small improvements in physical functioning and HRQoL, along with a reduction in general pain, have been observed. However, the effects of back extensor exercise programs on kyphosis outcomes

among people with low bone mass or vertebral fractures were less certain. The findings support the inclusion of recommendations in favor of exercise programs that target hyperkyphosis and back extensor muscles in adults with hyperkyphosis. Our review included a larger number of studies and for some outcomes, moderate-to-high certainty evidence, when compared to the previous systematic review from Bansal et al.,[195] where the limited number of studies did not permit a meta-analysis, the evidence was conflicting and the included studies of low quality. One other systematic review[196] reported larger standardized mean differences for effects on measures of thoracic kyphosis (SMD 1.4; 95% CI − 2.15, − 0.66); however, they also included studies performed in younger adults whose hyperkyphosis may have a different etiology and, compared to older adults, they are less likely affected by factors that may interfere with the training process and reduce the margins for improvements in kyphosis, such as vertebral fractures, ossification of ligaments, or degenerative disc disease. Furthermore, Gonzalez-Galvez and colleagues[196] utilized a random-effect model in their meta-analyses, while we adopted a fixed model, as it is recommended to estimate the same underlying intervention effect in a specific population and, consequently, trials with larger sample sizes were given more weight.[350] Moreover, in keeping with the findings of our meta-analyses, a few prospective and pre-post studies[205,354,362] (of which two included only people with hyperkyphosis[205,354]) showed beneficial effects of multicomponent interventions that included back extensor exercises in reducing the kyphosis. Even though a minimal clinically incidence rate ratio in the degree of kyphosis has not been determined yet, our findings support recommending exercise, and perhaps a focus on back extensor muscle exercises, for improving age-related hyperkyphosis. Among the included studies, the ones that demonstrated improvements in back extensor strength or endurance included specific exercises to target back extensor muscles, such as shoulder flexion and thoracic spine extension with back at the wall. However, the evidence is of low or very low certainty because of the risk of bias or high heterogeneity. Given that persons with hyperkyphosis have specific spinal strength and endurance impairments that are associated with adverse health outcomes, this study highlights the importance of targeted exercise in this population to reduce risk. Two pre-post trials in people with hyperkyphosis showed similar improvements after a 1-month and a 3-month back extensor strengthening program, respectively.[353,354] Trunk extensor strength is associated with better performance on the Six-Minute Walk Test, the Sitting and Rising Test, and the Berg Balance

Scale,[368] and the ability to limit trunk motion after trips and slips appears to discriminate between older adults who fall and those who do not.[369] We report very low certainty evidence that multicomponent or back extensor strengthening interventions can improve performance on the TUG test in people with age-related hyperkyphosis. Our results are in line with previous systematic reviews which showed improvements in the performance on the TUG test after progressive resistance training, with or without back extensor exercises, in people with low bone mass or osteoporotic vertebral fractures.[164,347] A MCID for the TUG test has not been established in individuals with osteoporosis. Frank-Wilson et al.[317] noticed a difference of 1.2 s in the TUG test between people who experienced at least one fall and those who did not. However, community-dwelling older adults often have fast times for the TUG test at the baseline, so there might be ceiling effects or limited margin for improvement. A lower gait speed is associated with an increased risk of experiencing multiple falls in older adults;[370] therefore, improvements in functional performance may help prevent falls. We did not detect any effects of back extensor strengthening programs on the rate of falls, but the studies were not designed or powered to examine falls as an outcome. Other interventions incorporating balance and functional training successfully reduced the rate of falls and risk of being a person who falls among older adults.[371] Exercise may improve HRQoL and general pain, and the reduction in general pain exceeded the MCID for chronic musculoskeletal pain.[372] We have observed similar small improvements in HRQoL and general pain in people with low bone mass after progressive resistance training interventions.[347] People with hyperkyphosis commonly present upper- and mid-back pain,[33] and usually report a poor quality of life. Indeed, the physical limitations resulting from hyperkyphosis affect the performance of several daily activities and increase the fear of falling, resulting in social limitations and low satisfaction with life.[51,60,373] However, none of the included studies was designed to measure quality of life or pain as a primary outcome. Considering the impact of poor quality of life and pain, adequately powered trials should investigate alternative interventions and strategies to improve quality of life among people with hyperkyphosis. Back extensor strengthening or physical therapy interventions in older adults with hyperkyphosis appear to be safe, as no serious adverse events occurred. Some minor adverse events happened, but only Bennell et al.[285] reported that the events were attributable to the intervention. Similarly, systematic reviews of exercise interventions in older adults reported that some minor adverse events may

occur, mostly joint or musculoskeletal pain.[190,254,255] Bautmans et al.[360] reported some mild skin irritations due to the tape and pain during the mobilizations or overhead exercises, but some patients stated that, at the end of the program, they experienced less pain, were able to walk longer, and were more flexible. Implementation of the findings of our review may be informed by our pre-planned sensitivity analyses. The substantial heterogeneity resulting from the main analysis (I^2 = 77%) can be explained in part by variability in interventions. Heterogeneity was lower (I^2 = 39%) when we limited the analyses to studies that included back extensor muscle exercises (alone or combined with other exercises/interventions), as part of an a priori sensitivity analyses driven by our hypothesis that improving back extensor muscle strength or endurance is important for reducing hyperkyphosis. Back extensor strengthening combined with other exercises targeting posture (e.g., spine extension, core stability, etc.) was the most common exercises used in the studies we analyzed, frequently executed with elastic bands or body weight, both in standing and supine/lateral decubitus positions. Based on the existing evidence, it is not possible to recommend an ideal intensity or volume. The frequency of the training ranged from 2 to 7 days a week (median 3) and the duration ranged from 1.5 to 8 months (median 2.8). Exercise programs targeting specific impairments often require some instruction or supervision, and disability and lack of transportation are barriers to participation in in-person community exercise classes or services.[374,375] Katzman et al. [56] pilot tested a remotely delivered exercise intervention in people with hyperkyphosis, showing good acceptability and improvements in kyphosis and physical activity outcomes, suggesting that using technology to deliver exercise interventions in older adults with hyperkyphosis may be an area for further investigation. We acknowledge some limitations of our work. Due the limited number of studies, we could not perform sensitivity analyses of studies that recruited only participants with hyperkyphosis. Many studies included individuals with no hyperkyphosis at baseline, and this may result in a ceiling effect, in that it would be difficult to improve kyphosis in people with no hyperkyphosis at baseline. Exercise tolerance may also be different in people with hyperkyphosis compared to those without. Therefore, future studies of interventions to address hyperkyphosis should target only individuals with hyperkyphosis at baseline. Only 6% of the participants were men; therefore, caution is recommended before generalizing the results. More than a half of the studies did not blind outcome assessors, and most of the studies present concerns about generation and allocation of the random sequence. Moreover,

most of the studies did not report on adverse events, raising some concerns for selective reporting bias. Therefore, even though only a few minor adverse events were noted, future investigations should comprehensively assess the safety of exercise and other interventions in this population. We identified studies that were eligible but were missing information; we contacted the authors, but some did not respond. Consequently, some data are missing and we had to exclude two studies.[32,376] We screened only full texts in English or Italian; therefore, some eligible references might have been excluded. Finally, the submission of the manuscript was delayed and thus it is possible that new papers have emerged since our search.

3.2.5 Conclusion

Interventions targeting hyperkyphosis, often including back extensor muscle strengthening, may improve kyphosis and back extensor strength in older adults with hyperkyphosis. Furthermore, they may result in small improvements in physical functioning and HRQoL, along with a reduction in general pain. However, many studies included also individuals without hyperkyphosis at the baseline. Therefore, to have a more accurate estimation of the magnitude of the effects, future trials to improve hyperkyphosis should recruit only individuals with hyperkyphosis at baseline. Given that only a few minor adverse events were reported, exercise interventions to correct age-related hyperkyphosis can be implemented in clinical practice.

Chapter 4
Recommendations for the non-pharmacological management of osteoporotic vertebral fractures.

This chapter informed the Guidelines for the management of the Symptomatic Vertebral Fragility Fractures of the Royal Osteoporosis Society (UK).

The findings from this chapter will be presented as one manuscript, which has been submitted to *Osteoporosis International*.

4.1 Study 5. International Consensus on the Non-pharmacological Management of Osteoporotic Vertebral Fractures

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Availability of data and material: The data being reported are accurate and are coming from the official source.

Code availability: Not applicable

Contribution: The corresponding author declares that all authors have met all three of the following criteria for authorship, thereby accepting public responsibility for appropriate portions of the content: substantial contributions to conception and design, or acquisition of data, or analysis and interpretation of data; drafting the article or revising it critically for important intellectual content; approval of the version to be published and all subsequent versions.

4.1.1 Introduction

OVFs are the most common type of fracture in people with osteoporosis,[24,25,377] and are associated with several morbidities and increased mortality.[27,378] One in five women with an incident osteoporotic OVF will experience another one within one year,[29] and the risk of death is nine times higher following an OVF.[379] OVFs may cause pain, loss of height and progressive thoracic kyphosis, which may lead to difficulties in performing daily activities.[24,30,380,381]

Non-pharmacological interventions such as exercise, taping, bracing and spine-sparing strategies are sometimes used to improve posture and reduce pain, disability and fracture risk,[382–384] but the evidence is limited and no best practice guidance exists. A 2019 Cochrane review[164] on the effects of exercise in people with OVFs showed that the number of studies was inadequate to determine the effects on falls, fractures, adverse events, pain and health-related quality of life, while there were small improvements in physical function (e.g., performance on the Timed Up and Go test). Randomized controlled trials (RCTs) and systematic reviews of interventions in people with osteoporosis or hyperkyphosis showed that exercise, alone or combined with other interventions, may improve posture, physical functioning, fear of falling and quality of life in people with OVF, but the evidence is often heterogeneous or conflicting.[278,347,358,385–387] Furthermore, guidelines for the management of non-specific back pain recommend staying active and practicing general physical activity,[388–391] but the evidence does not allow us to draw recommendations on specific types of exercise or other non-pharmacological techniques to reduce pain after OVFs.

Resistance, balance and aerobic exercise training are recommended for people with osteoporosis, with or without OVFs, and it is ideal that individuals with OVF are educated on these forms of training as part of a consultation with a physiotherapist to ensure the adoption of spine sparing strategies.[383,392] However, the absence of specific guidelines for the management of people with OVFs[383] represents a barrier for healthcare providers. A survey among over 100 physiotherapists, kinesiologists and exercise instructors that was circulated to inform the upcoming Canadian Clinical Practice Guidelines for the Prevention and Management of Osteoporosis revealed that 46% of the participants were not comfortable guiding exercise in people at high risk of fractures, and 92% wanted more guidance to support safe exercise in this group.[260] Therefore, we performed a Modified Delphi consensus process to generate multidisciplinary biopsychosocial recommendations for the non-pharmacological management of OVFs.

4.1.2 Methods

We established a steering committee that included: physicians and other healthcare practitioners (HCPs) in geriatrics, internal medicine, physiotherapy, and dietetics; researchers with expertise in

rehabilitation, pain, nutrition, malnutrition, osteoporosis, post-fracture care and knowledge translation (KT); patients and stakeholders. The steering committee decided to focus on the following strategies for the non-pharmacological management of OVFs: pain management, bracing, exercise, safe movement education and training, and nutrition. We adopted a five-step modified RAND/UCLA Delphi consensus process[393] consisting of: literature search and content analysis (phase I), creation of the survey by our team (phase II), expert panel selection and recruitment (phase III), first round of the rating process (phase IV), and second round of the rating process (phase V) (Figure 1).

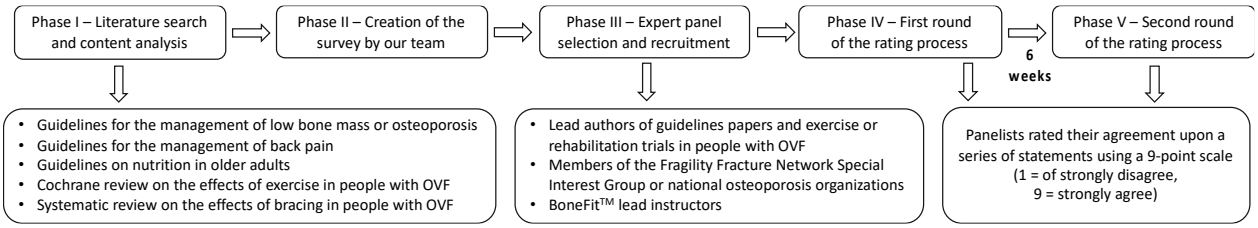

Figure 15. The modified RAND/UCLA Delphi consensus process.

Phase I – Literature search and content analysis

We performed literature searches to collect direct or indirect evidence or recommendations that could be applied in the management of people with OVFs to inform the statements of the survey. We performed three literature searches in PubMed to retrieve: a) existing guidelines for the management of low bone mass or osteoporosis; b) existing guidelines for the management of back pain; c) existing guidelines on nutrition management in older adults, and only guidelines pertaining to the non-pharmacological management of low bone mass, back pain and nutrition in older adults were included. We also included two systematic reviews led by our team on the effects of exercise interventions[164] and bracing[394] in people with OVF, and five clinical trials of exercise interventions in people with OVF,[285,289,395–397] to extract the exercises prescribed, organize them by therapeutic goal, and present them to the panelists of our Modified Delphi for input on their appropriateness. The eligible papers were then uploaded in the NVivo 12 software (version 12.6.0; QRS International, Burlington, MA, USA), and we performed a conceptual content analysis[398] of each included paper to identify any information on pain management, bracing, exercise, safe movement

education and training, and nutrition that may be relevant in the non-pharmacological management of OVFs.

Phase II – Creation of the survey by our team

Two authors (MP and LMG) generated draft statements based upon the content analysis and information gathered during phase I. These statements were finalized after interviews with 10 people with OVF and 10 healthcare practitioners working with people with OVF.[399,400] The statements were then converted into a survey (Appendix E), which was finalized after two videoconferences and two rounds of revisions by the team members.

Phase III – Expert panel selection

We invited potential panelists who met the following inclusion criteria: degree in physiotherapy, medicine (with specialization in physiatry, geriatrics, rehabilitation medicine or similar fields), and other physiotherapy- or kinesiology-related degrees; self-reported clinical or research experience in management of osteoporotic OVFs; and ability to understand, read and write in English. We used purposeful and convenience sampling techniques to recruit eligible participants among: first and last authors of guidelines papers and exercise or rehabilitation trials in people with OVFs; members of the Fragility Fracture Network Special Interest Group; representatives from the National Osteoporosis Foundation, the Royal Osteoporosis Society and other national osteoporosis organizations; BoneFit™ lead instructors. No exclusion criteria based on country, ethnicity, or gender were applied. Potential contributors were contacted via email. We aimed to recruit 20 participants to complete each round; therefore, considering the absence of a formal method to determine sample size in Delphi studies and the potential challenges in recruitment, we contacted 76 potential participants. The steering committee performed recruitment and selection of the panelists but was impartial to the rating process. The study received ethics approval from the University of Waterloo Research Ethics Board (ORE #43154).

Phase IV and V – First and second round of the rating process

The experts who agreed to participate were emailed a link to the online survey, generated using Qualtrics (Qualtrics^{XM}, Seattle, US, https://www.qualtrics.com/); both rounds of rating were

anonymous. Participants were asked to agree or disagree upon 49 statements by using a 9-point Likert scale (Appendix E); a space for optional open-ended comments was provided for every statement. The survey ended with a few open-ended questions, that arose in prior surveys, interviews, or input from of health care providers who manage people with OVFs[400] and that are not addressed by the extant literature (Appendix E). Consensus for each statement was determined by counting the number of panelists whose rating was outside the 3-point region containing the median. The minimum consensus threshold for each statement was established *a priori,* based upon the resultant number of respondents, in accordance with the RAND/UCLA approach (Appendix E).[393] Participants were asked to complete the first round within four weeks; two weeks after the end of the first round, we invited to participate to a second round all the potential contributors that were contacted to participate in the first round. Participation to the first round was not a requirement to participate to the second round. Two authors (MP and LG) reviewed the answers from the first round. For statements where consensus was not reached, and for the answers to the open-ended questions, the two authors generated a new set of statements based on feedback received (Appendix E). Statements where a consensus was reached during the first round were enriched with the feedback provided by the panelists. The experts who agreed to participate to the second round were emailed a summary of the distribution of the ratings for every statement from the first round, a list of the final statements where consensus was reached in the first round, and a link to the survey for the second round, where they were asked to rate the revised statements where consensus was not reached. Participants were asked to complete the survey within four weeks. Reminders were sent via email after two weeks during both rounds. We decided a priori to not invite dietitians to the modified Delphi consensus process, due to the limited exposure to OVF patients in community practice.[401] A registered dietitian is part of our team (HK), and we invited four external dietitians with expertise on vitamin D, calcium, and bone health to review the statements on nutrition after the survey was closed to finalize recommendations. We calculated the percentage of consensus for each statement, as well as the mean percentage of consensus across statements for each round. A third round was not performed because the predefined level of consensus for each statement was reached after the second round. Demographic information (i.e., age, gender, race, main occupation, years of experience at current occupation) were collected at

the beginning of the survey and presented as descriptive statistics (mean ± standard deviation [SD]), or counts (n) and percentages [%]).

4.1.3 Results

Thirty-one (response rate: 41%) and 27 (response rate: 36%) experts from Asia, Europe, North America, and Oceania participated in the first and the second round, respectively. The mean age was 55 ± 11 years for the first round and 54 ± 12 years for the second round. The panelists included physiotherapists, rheumatologists, and geriatricians who have been practicing their occupation for over 20 years on average (Appendix E). In the first round, the mean percentage agreement was 76.6% ± 16.0%, and there was lack of consensus on 20 out of 49 statements (n = 15 on exercise, n = 3 on nutrition, n = 1 on bracing, n = 1 on pain management; Appendix E). The second round included 30 statements; the mean percentage agreement was 90.7% ± 6.5%, and consensus was reached for all the statements (Appendix E). Three of the four dietitians we contacted agreed to provide feedback on the recommendations on nutrition.

4.1.3.1 General recommendations

1. Individuals with vertebral fracture should:

a. Avoid prolonged or continuous bed rest.

   A few days of bed rest might be indicated in presence of severe pain immediately after the fracture, but prolonged or continuous bed rest should be limited as much as possible.

b. Avoid heavy physical exertion, lifting, or activities that exacerbate pain during the 12-week period following fracture (e.g., carrying groceries, lifting pets or children, yard work).

   When to resume these activities will depend on the severity of fracture(s) and symptoms. Resume activities involving heavy physical exertion gradually.

c. Receive education on pain expectation.

   For example: that, for most people, pain and activity tolerance will get better over time, but it may take 3 months or longer; and that they can gradually start or resume exercise and physical activities of daily life, leisure, or work as pain diminishes.

d. Receive education that having a spine fracture increases the risk of having another fracture. Individuals with vertebral fractures must be referred to their physician to learn about treatment strategies (including medications, fall prevention, etc.) to prevent further fractures.

2. In general, bracing (i.e., taping, rigid, dynamic, or soft orthoses) is not recommended for individuals with vertebral fractures.

   Some people believe that selected patients, immediately after fracture, can benefit from using braces intermittently in the acute stage, if it means reducing fear or giving the patient confidence to mobilize or resume activities. Evidence from clinical trials is heterogeneous and of very low certainty, and there is high risk of bias. Bracing should not be used routinely and should not be used at all in subacute or chronic stages post-fracture.

3. When the therapeutic goal is to improve respiratory function, individuals with acute or chronic vertebral fractures can be taught diaphragmatic breathing exercises.

   For example: in the supine position supine with knees bent and feet flat on lying surface, cueing focus on lower rib expansion and diaphragm contraction on inhale through nose, and exhaling through pursed lips with focus on lower ribs moving in, pelvic-floor and deep abdominal muscle contraction). Progression involves practicing breathing exercises during sitting or standing.

4. In the acute and chronic stages after a vertebral fracture, healthcare professionals are encouraged to use "how to" language rather than only suggesting activity restrictions, and to be mindful of choosing words carefully, to promote optimism rather than create fear and activity avoidance.

   Health care professionals can provide examples of activities that should be modified or avoided (e.g., bend at your hips instead of rounding your back; get someone to lift heavy objects for you instead of doing it yourself).

5. For individuals with fear-related beliefs (e.g., fear of pain, fractures, falling, movement, etc.), consider education on coping techniques, body awareness, spine safe movement strategies, and movements to modify or avoid, being mindful of choosing words carefully to avoid creating fear and activity avoidance.

6. Refer to a physiotherapist or occupational therapist to perform an assessment of fall risk and physical functioning, or a home hazard assessment, where appropriate.

7. When body image is a concern at any stage post-vertebral fracture, health professionals could consider using education or approaches informed by cognitive behavioural therapy to enhance self-esteem and improve the perception of body image.

4.1.3.2 Recommendations on pain management

Strategies to manage back pain and discomfort (in acute or chronic stages) associated with vertebral fracture include:

1. Assessment by a healthcare professional for pain-related psychological risk factors (e.g., pain catastrophizing, pain-related fear, anxiety, social isolation, low mood) that could increase the risk of persistent pain and disability.

   If present, consider referral to a health professional (e.g., physiotherapist, occupational therapist, psychologist) who has expertise in pain and psychological factors.
2. Avoiding prolonged sitting and, and when sitting, do so with attention to posture, as well as when getting in and out of the seated position.

   If prolonged sitting is necessary, for example at work, get up and move around every 30 minutes and consider consulting an ergonomist about alternative strategies, such as perched sitting or standing desks.
3. Lying supine on the floor, bed, or firm surface, with feet flat on surface and knees bent, to unload the spine, encourage spinal extension and stretch pectoral and front shoulder muscles.

   Individuals with hyperkyphosis can use one or more pillows under the head. While there is no RCT evidence to support this statement, there is a prior consensus process encouraging this approach.[383] *A frequency of 2-4 times per day for 15-20 minutes each bout has been suggested.*[383]
4. Education on movements to avoid or modify (e.g., rapid, repetitive, weighted, sustained or end-range flexion or twisting of the spine) and on strategies to reduce loads on the spine (e.g., hip hinge, step-to-turn, getting up and moving around every 30 minutes) during physical activities of daily life, leisure, and work.

Where possible, refer to a physiotherapist for assessment and education, or suggest free resources for education, to get detail on the types of movements to modify or avoid.

5. Pacing or "graded activity" to help facilitate increased activity tolerance, or to avoid doing too much too soon.
6. Self-application of cold or heat for sore or painful areas can be performed if it helps to manage pain, with education on when and how to safely apply it.
7. In presence of chronic pain after the fracture has healed (>12 weeks post fracture), consider whether the patient would benefit from a referral to an interdisciplinary pain management clinic or psychologist that specializes in the biopsychosocial management of pain, or, to a physician for the medical management of pain.

4.1.3.3 Recommendations on performing daily activities safely

Individuals with vertebral fractures are often given advice not to lift things, or bend or twist the spine. However, lifting things, forward bending, and twisting the spine are often impossible to completely avoid in the daily life.

Recommendations on safe movement education for individuals with vertebral fractures include:

1. Consult a physiotherapist or occupational therapist on safe movement during activities of leisure or daily life.
2. Bend at the hips, knees, and ankles rather than rounding the back.
3. Rather than twisting the torso, use a step-to turn, so that the trunk, knees, and toes face the same direction.
4. When holding objects out front, hold them close to the body, and when holding something in hands at sides of body, split and distribute the weight evenly across both hands (e.g., carrying shopping bags).
5. Use slow and controlled movements rather than sudden movements.
6. Look for print or online resources from a national osteoporosis society.

4.1.3.4 Recommendation on exercise and physical activity

1. Ideally in consultation with a physiotherapist or exercise physiologist, individuals with a vertebral fracture should initiate an individualized exercise program focusing on goals such as improving back extensor endurance, spinal mobility, physical functioning, and balance.

   The exercise program can be introduced within 4-12 weeks after vertebral fracture, as tolerated, or when acute fracture-related pain has diminished, or after 12 weeks, based on patient preference and clinician judgement. Exercises to consider are provided in the Appendix E.

   Individuals with a vertebral fracture should be referred to a physiotherapist or exercise physiologist, so that exercises can be phased in and tailored according to the patient's needs, health conditions, abilities, fracture type and symptoms, and time post-fracture (e.g., start with focus on teaching body mechanics, individualized selection and phasing in of exercises).

   When access to physiotherapy or exercise physiologist is not possible, refer patients to print or online resources from a national osteoporosis society.
2. When pain has diminished and the fracture has healed (usually around 12 weeks post fracture), individuals with vertebral fracture should initiate an exercise program, ideally in consultation with a physiotherapist or exercise physiologist, and informed by a baseline assessment, so that it can be tailored to the patient.

   The exercise program should include balance and functional training and progressive resistance training, focusing on form first and then progressing to moderate intensity (i.e., 70-80% of estimated 1 repetition maximum (RM), or 8-12 RM, determined during baseline assessment - an estimated 1 RM is suggested as the safety of 1 RM testing has not been established).
3. There is evidence that progressive resistance training may address activity limitations and improve physical functioning in individuals with vertebral fracture. There are very little data on the effects of exercise on BMD in this population. Functional or muscle strength training should target muscles of upper and lower extremities, back extensor muscles and stabilizers of pectoral girdle.

When selecting exercises, consider fall risk and the loads on the spine (e.g., modify or avoid rapid, repetitive, weighted, sustained or end-range flexion or twisting of the spine). Clinical judgement is required regarding the selection of exercises, especially ones that involve overhead movements, or hip and lower back extension (e.g., bridging) in the presence of lumbar spine fractures. Exercises to consider are provided in the Appendix E.

4. Certain exercises or physical activities are sometimes considered risky for people with one or more vertebral fractures, including: deadlift, overhead press, sit-ups, clean and jerk, deep squats, spinal flexion movements in yoga, golf, ball sports, or anything involving sudden, end-range, or resisted spinal flexion, sudden or end-range spinal twisting. Some exercises, like yoga, squats, overhead presses, and modified deadlifts may be acceptable if the patient can perform them with good alignment, or if they could be modified to be safer, ideally supervised by an exercise professional.
5. Individuals with vertebral fractures often have questions about whether they can participate in certain physical activities of leisure or daily life (e.g., lifting, yoga, golf, running, Pilates). If the person has a history or a strong preference to perform an activity, the activity should be encouraged if it can be performed safely, or modified; however, the patient is encouraged to discuss their options with a health care provider.

   Factors that may affect decision-making include the patient's physical health, functional status, and history of the activity, as well as time since fracture and time on therapy.

4.1.3.5 Recommendations on nutrition

All individuals with osteoporosis should follow national guidelines or their healthcare provider's recommendations related to protein, calcium, and vitamin D intake. Inadequate intake of nutrients and calories can result in weight loss, and specifically loss of bone and muscle. When weight management or early satiety are a concern for individuals at any stage postvertebral fracture, consider the strategies below to ensure adequate intake:

1. Referral to a dietitian.
2. Weight monitoring at the discretion of the dietitian and client.

3. Dietitian to assess and educate on the recommended daily intake of protein, calcium, and vitamin D.

   Where diet is inadequate, recommend nutrient enhancement through nutrient dense foods and where required, supplementation based on guidelines and best practice.
4. Consider how functional impairments may impact food-related activities (e.g., bending over in the kitchen, standing in the kitchen, grocery shopping etc.), and develop a plan to address this, or refer to an occupational therapist.
5. In presence of poor appetite and weight loss, suggest energy and protein dense foods to support weight maintenance or gain.

   Recommend meal programs and food access related supports (e.g., grocery shopping delivery, meals delivered to home) where required.
6. If dysphagia is suspected, refer to a dietitian, speech language pathologist or occupational therapist for assessment, education on the safest foods and use of texture-modified foods.
7. Create an eating environment that supports food intake (e.g., preparation of appealing food).
8. Where required, increase variety in diet, considering individual food preferences and food matrices of different foods (e.g., yogurt vs milk vs cheese) to support both health.

4.1.3.6 Recommendations on physical assessment

1. Sudden onset or acute exacerbation of pre-existing back or radicular pain, decreased mobility due to pain, increase or sudden worsening of thoracic kyphosis, loss of height or shortness of breath might indicate a new fracture or progression of an existing fracture, and the need for cessation of exercise/therapy and referral back to physician.
2. The assessment of spinal range of motion should be avoided in people with an acute vertebral fracture or multiple fractures.

   If the fracture has healed, consider weighing the need for assessment with the potential risk, and whether their functional mobility can be assessed via observation during functional tasks (e.g., getting out of bed or chair). If it is necessary to assess spinal range of motion, consider

a modified version, or cue the movement so it is slow and controlled. Do not continue if the movement is painful.

3. Some experts feel that assessment of self-limited forward reach (i.e., to assess balance) should be avoided in all people with vertebral fractures, or only in people with acute or painful fractures. Others think that it may be safe in some scenarios. Factors that might influence whether it is safe or necessary include: whether shoulder flexion to 90 degrees is pain free, if you can ensure they are not reaching forward and rotating trunk at same time, if you have a spotter, if standing balance is not impaired, if there is no fracture-related pain, or if it is relevant for ADLs, or if the patient identified it as a task they are having difficulty with.

4.1.4 Discussion

Our international consensus process provides multidisciplinary biopsychosocial recommendations that target different HCPs (e.g., physiotherapists, physicians, exercise professionals, dietitians) to guide clinical practice and future research among people with OVF. Pharmacotherapy is recommended to prevent fractures in people with osteoporosis[257] and, given the high risk of having a subsequent fracture after the first OVF, we provide guidance on how to safely perform those activities of daily living that might increase the risk of fracture, such as bending forward, turning, and holding or carrying objects. While we advocate for the referral to physiotherapists and exercise professionals, we convey the message that they should also provide advice on safe movement techniques and pain management strategies that people can perform independently in their daily lives. We emphasize the "how to" rather than providing restrictions and limitations, as it is paramount that individuals with OVF receive guidance on how to modify activities that might be risky, rather than avoiding them, thus preventing or limiting negative effects on their mental health (e.g., anxiety, social isolation, and depression). Furthermore, we encourage the referral to a physiotherapist or occupational therapist to perform an assessment of fall risk and physical functioning, or a home hazard assessment. Our recommendations are in line with a 2017 network meta-analysis of interventions for preventing falls in older adults, that demonstrated that exercise, alone or combined vision assessment and treatment, or with environmental assessment and modification, is associated with a reduced risk of injurious fall compared to usual care.[402]

Furthermore, we reached consensus on controversial topics, such as bracing and prolonged bed rest. Bracing remains an area where further research is needed. In general, it is not recommended, although there were a few respondents that thought that selected patients may find a brace helpful. The limited evidence suggests that we should not support the routine use of bracing. Bed rest can be used in the acute phase, in presence of severe pain, but should not be used routinely and should not be used in the sub-acute and chronic phases. We reached consensus upon the need of early mobilization, as early as tolerated by the patient, and provide guidance on therapeutic goals, as well as examples of exercises based on the stage after the fracture, with tailored exercise programs to improve back extensor endurance and spinal mobility in the acute and subacute phase, to gradually introduce exercises to improve balance, physical functioning, and muscle strength in the chronic phase after an OVF. Our recommendations in favour of back extensor and balance training are supported by existing literature. Sensitivity analyses from a systematic review in people with age-related hyperkyphosis recently published by members of our team showed that exercise may improve back extensor strength and endurance, pain, and physical functioning in people with low bone mass or OVF.[387] Back extensor endurance was moderately associated with better balance performance in 31 women with OVF,[403] and poor balance is a risk factor for falls in older women with and without osteoporosis.[404,405] A 2019 Cochrane review on the effects of exercise for preventing falls in the community showed that balance and functional training, alone or combined with progressive resistance training, reduce the number of falls.[254] Therefore, we recommend starting a tailored exercise program to improve balance and back extensor strength and endurance as early as tolerated, and we established consensus on the most appropriate exercises for different therapeutic goals in people with OVF.

Finally, we provide some nutritional recommendations to address common consequences of OVFs. The importance of protein, calcium and vitamin D for maintaining bone health is well known,[406–408] and HCPs should provide guidance on how to meet the recommended protein, calcium, and vitamin D intakes, and refer their patients to the numerous resources accessible to the public on the websites of national and international osteoporosis organizations. However, maintaining the recommended nutritional intake can be challenging after an OVF. Some people with OVF reported a reduction in their caloric intake during the first few weeks after fracture, as pain and immobility made preparing and consuming food challenging.[399] Unintentional loss of

body weight is a concern, as it can cause further disability and increase the risk of death.[409–411] We provide guidance on how to ensure an adequate nutritional intake, and we recommend the referral to a dietitian, in case of suspected malnutrition, or to an occupational therapist, in presence of functional impairments or environmental factors that impact food-related activities (e.g., preparing food, grocery shopping etc.).

We acknowledge some limitations to our work. While we invited people from 16 countries in Asia, Europe, North America, and Oceania, none of the experts identified themselves as BIPOC. Further, we did not specifically formulate recommendations on behavioural change techniques to change practice or habits, as it was beyond the scope of the project. Researchers leading studies in people with OVF are encouraged to partner with experts in behaviour change, to test the efficacy of behaviour change techniques in people with OVF and inform their incorporation in future interventions. Our consensus process bridges some gaps in the non-pharmacological management of OVFs. We recommend a multidisciplinary biopsychosocial management of OVFs to improve pain and promote safe movement strategies, exercise, and adequate nutrition. Future studies should test the efficacy of these recommendations for improving outcomes relevant to people with OVF, and the effectiveness of their implementation in routine clinical practice.

Chapter 5
Co-development, acceptability, and usability of a virtual intervention for the management of osteoporotic vertebral fractures (VIVA)

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5.1 Introduction

OVFs are the most common type of fractures in people with osteoporosis.[24–26] However, only about one third of OVFs come to clinical attention,[34] and approximately 50% occur in people with T-score greater than -2.5.[37] One in five women with an incident OVF will experience another one within one year,[412] and the risk of death is nine times higher after OVF.[3] OVFs may cause pain, loss of height and progressive thoracic kyphosis, which can impair physical function, pulmonary function, and appetite.[24,30,413] OVFs are associated with thoracic hyperkyphosis, which is correlated to higher risk of non-spine fractures and earlier mortality among older women, independent of spine BMD and risk factors.[197,414] External loads, like groceries, laundry or carrying weights, increase the forces on vertebrae, and increase fracture risk,[415] but OVFs often occur during twisting movements or forward bending with no external loads. Exercise may

represent a strategy to improve physical functioning and manage pain after OVFS, but further evidence is needed before making final conclusions on its real-world effectiveness.[347,387,416]

The Medical Research Council has recommended that the development and evaluation of complex interventions be based on theory, tailored to the local context (according to the integrated knowledge translation [IKT] approach),[417] informed by systematic evidence, and built on previous smaller-scale studies.[418] Interventions that are developed using behaviour change theories lead to that larger effects compared to those that are not theory-based.[419,420] The Patient-Centred Outcomes Research Institute identifies "community stakeholders" as patients, caregivers, patient advocates and members of the general public,[421] and the benefits from the involvement of community stakeholders at every stage of the research process are widely recognized.[417] We led an international consensus process on the non-pharmacological management of OVFs[422] which provided recommendations on pain management, nutrition, safe movement strategies, and exercise, that should be started as soon as tolerated to improve back extensor endurance, spinal mobility, physical functioning, and balance. However, the efficacy of these recommendations for improving outcomes relevant to people with OVFs, and the effectiveness of their implementation in the daily life have not been investigated yet. Therefore, we co-developed VIVA (Virtual Intervention for Vertebral frActures), a virtually delivered education and training program that represents the first step in the implementation of the recommendations for the management of OVFs, and we delivered it to a small sample of people with OVFs to test its acceptability and usability.

5.2 Methods

5.2.1 Co-development of VIVA

In accordance with the IKT principles,[417], we established a steering committee that included: physicians and other healthcare professionals (HCPs) in geriatrics, internal medicine, physiotherapy, and dietetics; researchers with expertise in rehabilitation, pain, nutrition, malnutrition, osteoporosis, post-fracture care and knowledge translation (KT); patients and stakeholders. We used the Behavior Change Wheel (BCW) and the Theoretical Domains Framework (TDF)[423] to guide the development of the intervention (Figure 1). We adopted a three-

stage process to design our intervention: understand the behaviour; identify intervention options; identify content and implementation options. The APEASE criteria (i.e., Affordability; Practicability; Effectiveness and cost-effectiveness; Acceptability; Side-effects/safety; Equity)[424] were used to inform the design and the acceptability and usability evaluation of the intervention.

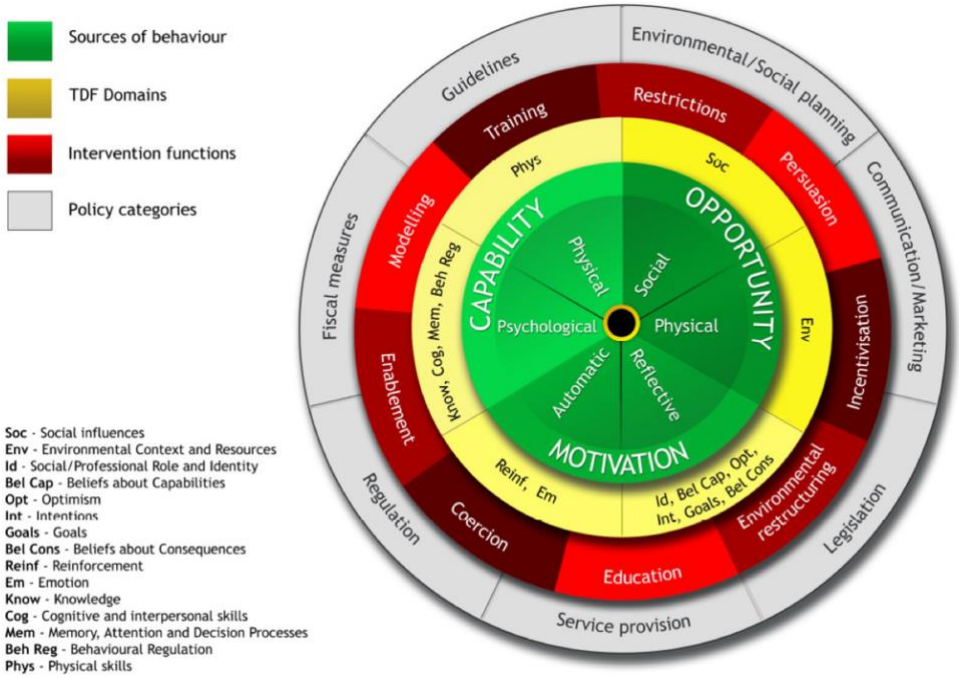

Figure 16. Behaviour Change Wheel and Theoretical Domains Framework.[424]

Stage 1: Understand the behaviour

We conducted focus groups and individual interviews with people with osteoporosis[374] and OVFs,[399] which revealed the absence of patient-centred strategies for managing pain and improving physical functioning after OVF. Acute or chronic pain, and living with fear of falling, re-fracturing, or doing movements that can exacerbate pain, transportation (public transit not available, or available at times that do not match exercise schedule) and bad weather are reported barriers that interfere with activities of daily living and exercise, and a healthy nutrition in people with osteoporosis.[202,374,399,425,426] Therefore, the steering committee identified pain management,

safe movement, nutrition, and exercise as priorities to be addressed in people with OVFs. Accordingly, VIVA was designed to target four behaviours to be performed by individuals with OVFs: 1) adopting safe movement techniques during activities of daily living; 2) performing pain management strategies daily; 3) exercising at least 3 times per week; and 4) following tips for optimal nutrition daily.

Stage 2: Identify intervention options

To increase capability, we selected education, enablement, and training as intervention functions to improve physical skills, knowledge, and behavioural regulation (Table 1). To maximize opportunity, we identified enablement, environmental restructuring, and modeling as intervention functions to target environmental context and resources, and social influences. To enhance reflective motivation, we chose enablement and persuasion as intervention functions to improve beliefs about capabilities and consequences and goal setting abilities (Table 1). We identified communication and service provision as the most appropriate policy categories for the delivery of VIVA. We designed VIVA to be delivered by a trained physiotherapist over Zoom (https://www.zoom.us, San Jose, CA, USA), to minimize transportation barriers and maximize retention and adherence. We created one-page information sheets on pain management, safe movement strategies, exercise, and tips for an optimal nutrition, and delivered the prototypes to two individuals with OVF and three physiotherapists with expertise in OVFs to gather their feedback and perspectives as to what we could improve. One-page information sheets, photos and videos of exercises, safe movement and pain management techniques, weekly exercise prescriptions, and the diary to track the weekly adherence to the program are delivered to the participants throughout the intervention in a personal online portal (Physiotec; https://physiotec.ca/ca/en/; Saint-Hubert, QC, Canada).

Table 7. Needs for change, theoretical domains, and intervention functions used in VIVA.

COM-B component		**What needs to happen for the behavior to occur?**	**Theoretical Domains Framework**	**Intervention functions**
Capability	Physical	Have skills to perform safe movement and pain management strategies and exercises.	Physical skills	Training
	Psychological	Know the correct techniques of exercises, safe movement, and pain management strategies. Know strategies for proper nutrition.	Knowledge Behavioral regulation (breaking habits and action planning)	Education Enablement
Opportunity	Physical	Having tools and a dedicated space at home to exercise, as well as resources with instructions on how to perform the behaviors and create an action plan.	Environmental context and resources	Enablement Environmental restructuring
	Social	Receiving videos of exercises, safe movement and pain management techniques performed by older adults. Receiving demonstration of correct execution of exercises and techniques.	Social influences	Modeling
Motivation	Reflective	Create an action plan and establish a weekly routine to practice exercises and pain management techniques, as well as incorporating safe movement and nutritional strategies in the daily life.	Goals (goal setting and action planning) Intentions Beliefs about capabilities Beliefs about consequences	Enablement Persuasion

Stage 3: Identify content and implementation options

The goal of VIVA is to implement the recommendations for the non-pharmacological management of OVFs.[422] Two authors (MP, LMG) selected the behaviour change techniques and drafted an outline of the intervention, which was finalized after one videoconference and two rounds of revisions via email by the team members. The final VIVA prototype was then reviewed for feedback on its contents, acceptability, equity, practicability, and safety by two individuals with OVF, who provided feedback in a 120-min meeting, and three physiotherapists, who provided feedback during three individual 45-to-60 minutes meetings.

5.2.2 Acceptability and Usability evaluation

We delivered VIVA to eight participants, as five participants are often sufficient to capture up to 85% of usability issues,[427] and we wanted to account for potential attrition. Inclusion criteria were: age 50 years or older; pain due to one or more OVFs; access to internet and computer or tablet with camera and microphone. Potential participants were excluded if they presented contraindications to exercise according to the Get Active Questionnaire[428] from the Canadian Society for Exercise Physiology (https://csep.ca/2021/01/20/pre-screening-for-physical-activity/), or if they assumed oral glucocorticoids in the last 12 months for ≥3 months at a prednisone equivalent dose of ≥7.5mg/day.

Acceptability

We operationalized acceptability as participants' satisfaction with treatment, which involves a comprehensive appraisal of intervention components, mode of delivery and experienced benefits.[429,430] We performed semi-structured interviews with each participant at the end of the intervention and performed thematic[431,432] and content[433] analyses conducted at the semantic level. The qualitative analysis was performed using NVivo version 12 (QSR International Pty Ltd, Doncaster, Australia) and involved the following steps: 1) audio-recording and transcription of the interviews verbatim; 2) two authors (MP, NT) familiarized with the interviews; 3) MP and NT coded the first two transcripts and developed an initial analytical framework; 4) MP and NT coded a subsequent two transcripts to form the final analytical framework; 5) MP and NT coded each of the remaining transcripts using the final analytical framework; new codes were discussed and

incorporated; and 6) interpretation of the data collected. We conceptualized our categories in a thematic map, and compared our themes to the data within the codes to explore if a pattern existed. We performed a content analysis (Hsieh & Shannon, 2005) to identify the VIVA components that were better accepted by the participants and those that may need some revisions before implementing VIVA on a larger scale.

Usability

We operationalized usability as perceived usefulness, easiness of practice, satisfaction with 1-on1 sessions, satisfaction with supporting resources. We evaluated the usability of VIVA by mean of an online survey (Qualtrics; Qualtrics^{XM}, Seattle, US, https://www.qualtrics.com/) consisting of four statements, and the participants had to select the category that best represented their perception of VIVA using a 5-point Likert scale:

1. The Virtual Intervention for Vertebral Fracture (VIVA) was useful.
(1=not at all useful, 2= somewhat useful, 3=undecided, 4= useful, and 5=very useful).
2. The information received were easy to practice during the week
(1=difficult, 2= somewhat difficult, 3=undecided, 4= easy, and 5=very easy).
3. I was satisfied with the 1-on-1 sessions
(1=not at all satisfied, 2=somewhat satisfied, 3=undecided, 4= satisfied, and 5=very satisfied).
4. I was satisfied with the supporting resources (e.g., one-page information sheets, videos)
(1=not at all satisfied, 2= somewhat satisfied, 3=undecided, 4= satisfied, and 5=very satisfied).

This study received ethics approval from the University of Waterloo Research Ethics Board (ORE #43705).

5.2.3 Secondary outcomes

The 5-level version of the EuroQol-5D (EQ-5D-5L)[434] was administered to calculate a health state utility value based on mobility, ability to self-care, ability to perform usual activities,

pain/discomfort, anxiety/depression. The EQ-5D-5L Health utilities for the Canadian population range from -0.148 for the worst to 0.949 for the best EQ-5D-5L states.[435] We administered the Exercise Self-Efficacy Questionnaire, a questionnaire informed by the Health Action Process Approach[436–439] that includes two questions with six and five statements each, respectively. For each statement, the participants selected the category that best aligned with how they felt, using a 5-point categorical scale as follows: 1 = not at all true; 2 = barely true; 3 = unsure; 4 = mostly true; 5 = exactly true. The Exercise Self-Efficacy Questionnaire has been reported to have very good internal consistency (Cronbach's α = .82)[436,440,441]. The self-reported questionnaires were administered online using Qualtrics (Qualtrics^{XM}, Seattle, US, https://www.qualtrics.com/). Participants were asked to track their adherence using a calendar in the Physiotec online portal. Adherence was defined as the number of days when participants performed the unsupervised home program (100% adherence = unsupervised home program performed 28 times). We set the criterion for success at 60% of adherence to the daily home program.[203]

Intervention delivery fidelity

To enhance the fidelity of the delivery of the intervention,[442] we created a study manual outlining the principles, the intervention components, the therapeutic goals based on the time after the fracture, and the modes of delivery of VIVA that the physiotherapist was asked to follow, and two virtual "training meetings" between the physiotherapist and the researcher (MP) were scheduled before the beginning of the intervention. We operationalized fidelity as adherence, differentiation, and competence of the physiotherapist.[442] Adherence refers to whether the intervention was delivered as intended.[443] Differentiation concerns the extent to which the physiotherapist delivered the intervention according to the therapeutic goals of VIVA, avoiding contamination with treatments that are not part of VIVA.[442,444,445] Competence relates to the manner in which the physiotherapist delivered the intervention;[442] examples of competence skills include but are not limited to tailoring the intervention on participants' characteristics,[446,447] being flexible and adapting the intervention as needed,[448] communicating information clearly and with an engaging and interactive way,[449] and clarifying information and providing constructive feedback.[450] We aimed to record three sessions per participant and assessed adherence, differentiation and competence. We reviewed the SOAP (Subjective, Objective, Assessment, and Plan) notes from

the physiotherapist to assess adherence and differentiation for the sessions that were not recorded. Checklists of 13 and 9 items were used to assess fidelity from recordings and SOAP notes, respectively. Items that were checked received a score of 1(i.e., *done*), items not checked were assigned a 0 (i.e., *not done*). Each session received a score based on the percentage of the checked items. We reported percentage fidelity based on recordings, percentage fidelity based on SOAP notes, and overall percentage fidelity.

Data analysis

We presented sociodemographic data as mean and standard deviation (SD), or count (n) and percentages (%). We reported usability data as count (n) and percentages (%) of participants who selected each of the answer options. We reported secondary outcomes as mean with a 95% confidence interval (CI). Descriptive statistics have been conducted on SPSS Statistics (version 28.0.1; IBM Corp., Armonk, NY, USA).

5.3 Results

5.3.1 Co-development of VIVA

After consultation with patient advocates and physiotherapists, the steering committee decided that VIVA should include seven 1-on-1 virtual sessions delivered by a physiotherapist over five weeks as follows: two sessions per week for the first two weeks, and one session per week in the next three weeks (Figure 2). After a tech consultation session, participants are asked to complete an online survey, which includes: demographic questions, medical history (including but not limited to information about the OVF/s, potential other fractures or previous injuries, risk factors for fragility fracture, exercise/physical activity habits), a questionnaire to assess the risk for malnutrition (SCREEN II questionnaire[451]), one questionnaire to assess the health status,[434] and the Exercise Self-Efficacy Questionnaire.[436–439] After the completion of the survey, participants have a 60-minute virtual intake session with the physiotherapist; the physiotherapist has the opportunity to ask further questions about participants' medical history, administers the Physical Activity Screen (PAS),[452] performs physical functioning assessments (i.e., 30-second chair-stand test[453] and balance tests from the SPPB[454]), reviews the answers to SCREEN II with the participant,

discusses nutritional goals and strategies, and delivers a one-page information sheet with nutrition tips. After the intake, each virtual session lasts 45 minutes and is divided in three parts: education, training, behavioural support/goal setting. In the first part of the session, after a meet and greet where the physiotherapist asks whether the participant has any questions or concerns, the physiotherapist chooses the topic for the session and the following week, provides education, and delivers the associated resource (e.g., one-page information sheet, video, etc.) in Physiotec online portal. The physiotherapist then demonstrates selected exercises/safe movement/pain management strategies according to the topic chosen, and asks the participant to demonstrate it, to ensure they can execute it with the proper form. Finally, the physiotherapist and the participant set the goals for the week and create a weekly action plan. The physiotherapist asks the participants about preferred days and times to practice exercises and pain management strategies and then provides the prescription. The physiotherapist will remind the participant to incorporate safe movement techniques and nutrition tips into their daily life. Intervention functions, behaviour change techniques and the intervention components are reported in Table 2.

Table 8. Intervention functions with corresponding behaviour change techniques and description of the intervention components.

COM-B component		**Intervention functions**	**Behaviour Change Techniques**	**Intervention description**
Capability	Physical	Training	Demonstration of the behaviour Instructions on how to perform the behaviour Feedback on the behaviour Behavioural Practice Self-monitoring	Instructions and demonstrations of exercises and movement strategies to improve muscle strength, increase mobility and reduce pain. Feedback on form and technique. Home unsupervised exercise prescription. Self-monitoring of the adherence to the program.
	Psychological	Education Enablement	Information about health consequences Information about social and environmental consequences Feedback on behaviour Self-monitoring	Education on strategies for pain management and safe movement, and to ensure an adequate nutritional intake. Creation of a plan to incorporate pain management and safe movement strategies in the daily life.
Opportunity	Physical	Enablement Environmental	Goal setting Action planning	Setting goals and creation of a weekly plan.

		restructuring	Restructuring the physical environment	Delivery of resources. Home unsupervised exercise prescription. Creation/re-organization of a safe space in the house for performing exercise and pain management techniques.
	Social	Modeling	Demonstration of the behaviour	Delivery of videos of exercises, safe movement and pain management techniques performed by older adults.
Motivation	Reflective	Enablement Persuasion	Information about health consequences Information about social and environmental consequences Goal setting Action planning Feedback on outcome Credible source	Education on benefits of pain management and safe movement strategies, exercise and having an adequate nutritional intake. Set weekly goals and create a weekly plan. Use positive language and communication during 1-on-1 sessions to increase confidence in participants' abilities and the benefits of the intervention. Delivery of videos of exercises, safe movement and pain management techniques performed by people with OVF.

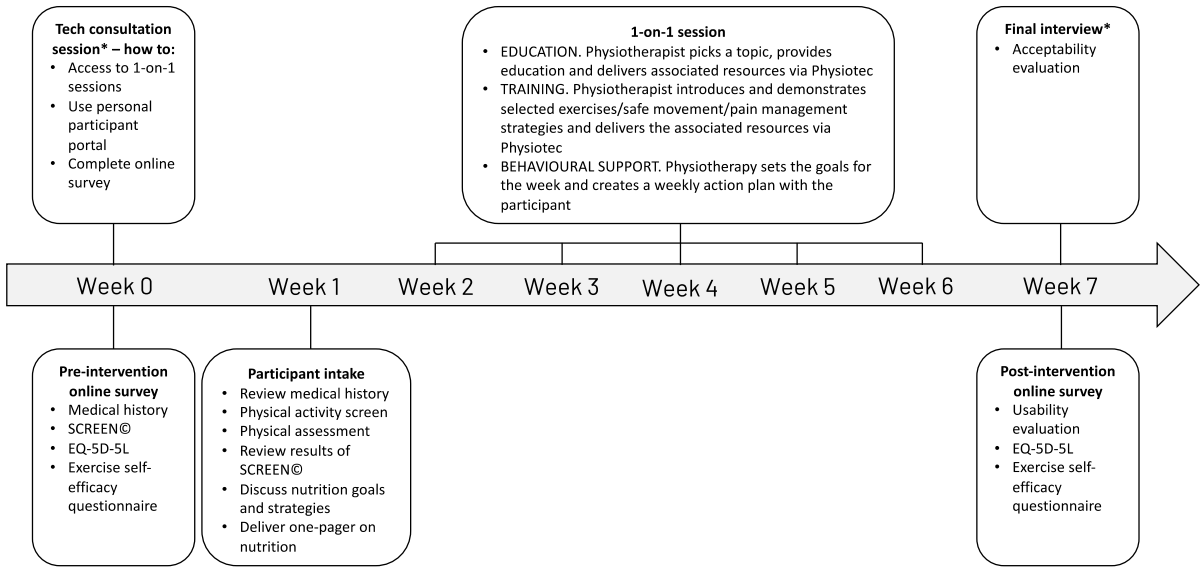

Figure 17.VIVA timeline. NOTE. * = delivered by the researcher (MP).

5.3.2 Acceptability and Usability evaluation

Thirteen individuals were screened for eligibility. Three persons declined to participate, and two did not meet our inclusion criteria (Table 3). Eight Caucasian women aged 68.71 ± 5.65 years with chronic pain after OVF participated into this study. All the participants had their last OVF more than three months prior to the beginning of the study. At baseline, five participants selected the option "*I have moderate pain or discomfort*" and three participants selected the option "*I have severe pain or discomfort*" from the EQ-5D-5L questionnaires. Four participants were at risk for malnutrition (SCREEN II score <50).

Table 9. Socio-demographic characteristics of the participants.

Marital status (n, %)	
Married	n = 5, 87.5%
Divorced	n = 3, 12.5%
Highest level of education (n, %)	
Graduate school	n = 1, 12.5%
University	n = 1, 12.5%
College	n = 4, 50.0%
High school	n = 2, 25.0%
Place of residence (n, %)	
Urban	n = 4, 50.0%
Suburban	n = 2, 25.0%
Rural	n = 1, 12.5%
Unknown	n = 1, 12.5%
Employment status (n, %)	
Retired	n = 7, 87.5%
Full-time	n = 1, 12.5%
Personal income (n, %)	
<20,000$/year	n = 2, 25.0%
21,000$-40,000$/year	n = 3, 37.5%
41,000$-60,000$/year	n = 1, 12.5%
Unknown	n = 2, 25.0%
Number of vertebral fractures (n, %)	
One fracture	n = 2, 25.0%
Two fractures	n = 3, 37.5%
Four fractures	n = 1, 12.5%
Nine fractures	n = 1, 12.5%
Ten fractures	n = 1 , 12.5%

Acceptability

Four main themes emerged from the final interviews with participants: perceived improvements in pain; increased self-confidence; satisfaction with 1-on-1 session and resources; and ease of use.

Perceived improvements in pain

Participants perceive that their pain improved. While they are aware that pain could not completely go away in five weeks, they feel that it might in the long term, if they keep practicing what they have learnt in the program ("*I could be on the road to feeling 100% better at some point if I keep doing this, hopefully*"). A few people mentioned that they were able to reduce pain or sleep medications during VIVA ("*I've only taken pain medications once since I've been in your program*").

Increased self-confidence

After participating in the program, participants feel more confident in their ability to control their pain and their life in general ("*I was really glad that I was able to have this opportunity, because now, I can move forward, I have a better understanding of what's going on and how to*"). Participants recognize that, during VIVA, they learned things that are easy to incorporate in their daily life ("*a lot of what you had provided, I was able to transfer into other tasks that I was doing"),* and that the safe movement techniques that they learned during VIVA made their activities of daily living easier and more enjoyable ("*I was pulling weeds doing the proper stance that she had showed me").*

Perception of 1-on-1 sessions and other resources

Participants were very satisfied with the 1-on-1 sessions and the possibility to attend them from their home, and with the fact that the physiotherapist demonstrated the exercises/safe movement techniques, that they would perform and receive feedback. A few participants had previous experience with non-pharmacological management of their OVFs, and were not satisfied; conversely, they were very happy with the contents of the virtual sessions and of the home exercise

prescriptions ("*I think all the exercises were very geared to; easy going; help you to build up stamina*"). Participants were happy to have a chance to receive clear and progressive instructions on how to resume normal activities of the daily living ("*[physiotherapist] went over like teaching me how to rake and how to get onto the floor and get up off the floor and in steps*"). Participants were satisfied with the one-page information sheets, with their layout and the details of the information reported ("*the pictures and the instructions were very helpful as to how to do the exercises and how many*"). Participants were extremely satisfied with the videos, that *"were very self-explanatory for anyone that isn't familiar"*.

Easiness of use

Overall, participants found VIVA easy to use. Furthermore, the fact that the physiotherapist delivered the videos in the Physiotec online portal right after the 1-on-1 session was very appreciated by participants, as they would go over them right away while they could still remember the explanation of the physiotherapist from the session. The impressions about the personal online portal are controversial. Some found *"that whole participation web page type thing was very, very handy"*, while some other people did not like having to log in and out to access their prescription and the related resources. However, there was a general tendency towards printing out the material, even among the participants who liked the online portal, as it was more convenient to have printed copies or taking screenshots with their tablets. Some difficulties when downloading the resources was reported by a few participants, and a couple participants asked to have the resources mailed to them as they did not have a printer available.

Table 10. Content analysis and considerations for implementation.

Intervention component	Positive (n)	Negative (n)	Lessons learned
Overall perception of the program	8	Useful but working with physiotherapist in-person is better. (n=1)	Virtual delivery is accepted by most people; referral to in-person treatments may be necessary for some patients.
Perceptions of the 1-on-1 sessions	8	Physiotherapist should communicate in advance the equipment needed for the session (e.g., yoga mat, ball, etc.). (n=1)	The topic is decided at the beginning of 1-on-1 sessions, based on participant's feedback, but the physiotherapist might

			send in advance a list of equipment that could be needed in the upcoming session.
Perceptions of the videos	7	Did not watch them; reading one-pagers was faster because physiotherapist demonstrated exercises during 1-on-1 sessions. (n=1)	Most people liked videos and found them easy to follow. It is important that the other supporting resources are detailed so that people that do not watch the videos can rely on them.
Perceptions of the one-page information sheet	8	NOTE. Two participants printed them out, one took a screenshot with the iPad, and two requested to receive them via mail at the end of the program.	Accessing the resources was easy, but many people preferred to download them. Resources and prescription might be sent via email to participants at the end of each session. A diary to track adherence might be mailed to participants before the beginning of the intervention. Recourses can be mailed to those people who do not have a chance to print them out at the end of the treatment.
Feedback on online portal	1	Logging in and out to access videos and resources or tracking adherence was cumbersome. (n=1)	
Easiness of use	6	Problem logging in the first time (n=1). Was not able to download resources (n=1).	
Easiness to understand	8	Some videos did not show the movements on different body planes and so were more difficult to understand. (n=1)	The information were easy to understand; however, videos should show exercises from different views.

Usability

All the participants believed that VIVA was *very useful* and were *very satisfied* with the 1-on-1 sessions. Three participants (37.5%) found the information received *very easy* to practice, four participants (50.0%) believed they were *easy* to practice, and one participant (12.5%) found them *somewhat difficult*. Four participants (50.0%) were *very satisfied* and four (50.0%) were *satisfied* with the supporting resources delivered throughout the program.

5.3.3 Secondary outcomes

The secondary outcomes are reported in Table 4. Mean changes and confidence intervals show potential for benefits in health status and participants' ability to make concrete plans about *how* to exercise. All the participants completed baseline and post-intervention assessments, and all the participants attended seven 1-on-1 sessions. Only two participants tracked adherence to the home program: one participant completed all the daily home sessions, one participant completed 27/28 sessions. Two participants reported the adherence for only two weeks and one week, respectively.

Four participants did not report adherence. No adverse events attributable to the intervention occurred.

Table 11. Secondary outcome values at baseline, end of intervention and mean change after the intervention.

	Baseline (mean [95%CI])	Post-intervention (mean [95%CI])	Change (mean [95%CI])
EQ-5D-5L			
Health Status (n = 7)	0.48 [0.44 to 0.53]	0.52 [0.45 to 0.59]	0.05 [0.02 to 0.09]
Mobility* (n = 7)	1.71 [1.06 to 2.37]	1.43 [0.88 to 1.97]	-0.20 [-1.56 to 1.16]
Self-care*	1.25 [0.93 to 1.57]	1.13 [0.88 to 1.37]	-0.20 [-0.76 to 0.36]
Usual Activities*	2.38 [1.86 to 2.89]	2.38 [2.02 to 2.73]	0.00 [-0.88 to 0.88]
Pain/Discomfort*	3.38 [3.02 to 3.73]	2.75 [2.26 to 3.24]	-0.80 [-1.84 to 0.24]
Anxiety/Depression*	2.13 [1.55 to 2.70]	2.13 [1.35 to 2.90]	0.00 [0.00 to 0.00]
Health today	66.25 [53.56 to 78.94]	67.63 [57.49 to 77.76]	-3.00 [-10.24 to 4.24]
Exercise self-efficacy questionnaire			
"Do you already have concrete plans regarding exercise?"			
Concrete plans about when to exercise	4.00 [3.48 to 4.52]	4.50 [4.13 to 4.87]	0.20 [-0.36 to 0.76]
Concrete plans about how to exercise	3.25 [2.93 to 3.57]	4.50 [4.13 to 4.87]	1.20 [0.16 to 2.24]
Concrete plans about where to exercise	3.88 [3.30 to 4.45]	4.50 [4.13 to 4.87]	0.60 [-0.51 to 1.71]
	3.63 [3.11 to 4.14]	4.50 [4.13 to 4.87]	0.60 [-0.50 to 1.71]
Concrete plans about how often to exercise	2.88 [2.19 to 3.56]	3.25 [2.22 to 4.28]	0.80 [-1.42 to 3.02]
Detailed plan for when something interferes with exercise plan	4.29 [3.52 to 5.06]	4.14 [3.40 to 4.88]	0.00 [0.00 to 0.00]
Intention to perform exercise for ≥30 minutes on most days of the week			
"*How sure are you that you can exercise regularly?*"	4.25 [3.76 to 4.74]	4.13 [3.68 to 4.57]	-0.20 [-1.24 to 0.84]
Can be physically active on a regular basis, even if it is difficult.	4.33 [3.88 to 4.97]	4.29 [3.76 to 4.81]	-0.40 [-1.51 to 0.71]
Can perform exercise on most days of the week.	4.57 [4.20 to 4.94]	4.14 [3.13 to 5.16]	0.00 [0.00 to 0.00]
Capable of exercising regularly, even if doesn't see success at once.	4.38 [3.86 to 4.89]	4.13 [3.35 to 4.90]	0.00 [0.00 to 0.00]
Can resume regular exercise even if stops doing it for a while.	4.50 [4.13 to 4.87]	4.38 [3.86 to 4.89]	0.00 [0.00 to 0.00]
Can keep exercising regularly, even if it takes a long time to make it a habit			

Note. * = Lower score is better.

Intervention delivery fidelity

Two participants did not provide consent to have their sessions recorded, while 6 sessions could not be recorded due to technical problems (e.g., connection issues). Therefore, we assessed intervention delivery fidelity from 12 recordings and 44 SOAP notes. The overall fidelity was 95.54%. The fidelity assessed from recordings and SOAP notes was 95.51% and 95.57%, respectively.

5.4 Discussion

VIVA was acceptable to the participants with OVF, who were very satisfied with the perceived benefits in terms of pain, increased self-confidence in their ability to manage pain and perform their activities of daily living, and the opportunity to receive the treatment directly from their homes. Overall, participants were satisfied with the online portal, although most of them preferred to download and print the home program and the resources. However, tracking adherence through the online portal was not convenient for most of the participants.

Participants were very satisfied with the program and the 1-on-1 sessions, and were satisfied with the supporting resources The engagement of potential end users since the research design phase may have contributed to the high levels of acceptability and usability. The resources, the contents and the timeline of the program reflect the needs of patients and physiotherapists, whose input ensured that VIVA was easy to use and as similar as possible to the real-world scenario. Our results are in line with those from Katzman et al.,[205] who delivered an exercise and posture training program via video clip viewing and text messaging reminders to adults with hyperkyphosis, and the program was feasible and acceptable to the participants. Acceptability and usability of telerehabilitation is usually high among patients with cancer, [455] cardiovascular disease,[456–458] or rheumatic diseases.[459] Considering that people with OVFs face unique issues, such as fear of moving, falling or (re)fracturing, poorer metal health, and pain catastrophizing,[399,460] determining the acceptability and usability of VIVA was a necessary step before implementing it on a larger scale.

A few participants reported increased confidence in their ability to manage pain and, while the nature of our study does not allow to make final inferences from quantitative data, the increase in the self-reported measure of planning *how* to exercise is in line with the perception of participants emerged from the qualitative interviews. Participant had high exercise self-efficacy at baseline, which is fundamental for the formation of specific action plans, and has also been shown to predict the successful adoption and maintenance of healthy behaviours, as well as enhance the sustainability of clinical improvements.[461,462] Participants had high levels of intention planning at baseline and, given the mediating role of action planning and self-efficacy between the intention and the adoption and maintenance of healthy behaviours,[463] exploring whether action planning and self-efficacy mediate the effects of VIVA on the adoption and maintenance of the target behaviours would guide researchers and clinicians in designing more effective interventions utilizing the most appropriate behaviour change techniques for people with OVFs.

This study provided valuable insights for the implementation of VIVA. While some participants found the online portal very handy and easy to use, others would have preferred to receive paper copies of the one-pagers, or to receive them via email and print them out. Two participants did not have access to a printer, therefore mailing resources to participants can be an option to consider. Participants would have liked to download videos, without having to open the online portal to view them. Adherence tracking was an issue, as participants did not like to have to log in to track their adherence. Daily diaries where one-page recording sheets are designed like a weekly calendar worked well in a home-exercise program for people with OVF,[203] while daily text messages to which participants had to reply by text with 1 (if they practiced the program) or 0 (if they did not) were feasible and acceptable to adults with hyperkyphosis.[205] Based on the feedback from participants, and hybrid option that combines an online portal and paper-based resources, with paper-based daily calendars or text messages prompts to track adherence, may warrant further exploration.

This study presents some limitations. Only women with OVFs expressed interest to participate in the study; therefore, we cannot generalize the acceptability and usability of VIVA to men with OVFs. Furthermore, even though VIVA is designed for people who are in pain due to an OVF, regardless of the time after the fracture, only people with chronic OVFs participated in this acceptability study. Therefore, exploring the acceptability of VIVA among people with acute

OVF would provide further insights for clinical practice. Qualitative studies and self-reported outcomes can present some social desirability bias and, while APEASE criteria informed the design and the acceptability and usability evaluation of the intervention, they were not evaluated as outcomes, as part of them were beyond the scope of the present project.

Conclusion

VIVA was acceptable to the participants, who perceived improvements in pain and self-confidence. Participants believe that VIVA was easy to use and the contents easy to practice, although a hybrid model with both online and printed resources might be preferred.

Chapter 6
Overall discussion and conclusion

Individuals with SCI and OVFs are subgroups of people with osteoporosis that are at high risk of fractures and present unique impairments, limitations, and restrictions that require population-specific and individually tailored assessments and interventions. People with SCI most commonly experience fractures at the distal femur and the proximal tibia, and there are no methods to identify those people at higher risk. Individuals with OVFs present with physical/functional, psychological, and social impairments and there is very limited evidence as to how address such impairments.

My doctoral research focused on providing clarity about the role of LS BMD in people with SCI and on the development, acceptability, and usability testing of a virtual intervention for the management of pain after OVF. Covid-19 pandemic did not allow us to design an intervention in people with SCI; therefore, considering the similarities of the gaps in fracture risk assessment and prediction, as well as the lack of intervention options, we identified a gap in the non-pharmacological management of OVFs, and conducted a multi-step process that led to the co-development of a virtual intervention.

6.1 Fracture risk assessment in individuals with spinal cord injury

The Clinical Practice Guidelines for Bone Health and Osteoporosis Management in Individuals with Spinal Cord Injury recommend the assessment of hip, distal femur, and proximal tibia region BMD, in accordance with the International Society for Clinical Densitometry (ISCD) Position Statements regarding routine BMD testing after SCI/D, as soon as medically stable.[182]
The findings of the present dissertation validate such recommendations, as the assessment of LS BMD in people with SCI may be misleading.

6.1.1 Pitfalls in lumbar spine densitometry in individuals with SCI

The findings from the present work confirm that LS BMD should not be considered to estimate bone health and fracture risk in individuals with SCI. Facet sclerosis and degenerative changes were the most prevalent sources of error in our cohort, and they have been proven to elevate BMD compared to patients without such issues.[464] Challenging detection of bone edges was the second most common issue reported by the raters; however, it is not possible to discern whether that was

due to errors in positioning the patient for the scan, in the analysis, or to the poor quality of the images. Errors in detecting bone edge can cause spuriously higher or lower BMD: designing the edge inside the spine cause a spuriously higher BMD, as the area is smaller and includes tissue with high mineral content, while mapping wider vertebral edges leads to a falsely lower BMD, as the area would be increased and tissue with lower density would be included in the ROI. We also reported several vertebrae with outliers BMD values, but it is not possible to determine the exact cause of those increases. When DXA image is not available or is of poor quality, outlier BMD values among vertebrae may be indicative of compression fractures or degenerative changes, and a radiography may be performed to rule out potential compression fracture.

This study added some rationale as to why LS BMD should not be considered in fracture risk assessment in individuals with SCI. However, despite a good interrater agreement, we could observe a larger percentage difference for some items. While the prevalence of potential sources of error deemed to have a larger effect on BMD (e.g., surgical hardware, heterotopic ossification) was very similar across raters, differences in interpretation may result in incorrect decisions in clinical practice (e.g., inappropriate scans included for analysis). It might be relevant to explore the impact of every single issue on LS BMD variations, but the limited sample size and the average presence of multiple scan per issue would not allow enough statistical accuracy and precision.

An investigation potential sources of error at the hip, that is reportedly affected by heterotopic ossification, narrowing of coxofemoral joint space, and ectopic calcifications,[465] would be more clinically relevant. Furthermore, most of the fractures in people with spinal cord injury occur at the knee region (i.e., distal femur and proximal tibia). Craven et al co-developed a protocol for the acquisition of distal femur and proximal tibia by using a custom-made polycarbonate positioning device (https://kite-uhn.com/clinical/tools/knee-dxa-protocol), and the current guidelines recommend that clinicians use hip, distal femur, and proximal tibia region BMD and prior history of fracture as the primary considerations for predicting lower extremity regional fracture risk.[182,215] Furthermore, when making diagnosis and defining treatment plan, it is recommended that physicians consider secondary causes of low BMD unrelated to SCI.[182,466]

6.1.2 TBS and fracture in the SCI population

TBS, both alone or combined with LS BMD values, improves the prediction of major osteoporotic and hip fractures in the general population compared to BMD alone [159–162], and is a predictor of fracture risk, independent of FRAX®[174], in able-body individuals. The findings of this dissertation do not allow to extend such inferences to individuals with SCI, as measuring TBS at the lumbar spine in people with SCI might not be associated with the common fracture sites in people with SCI. More than a half of the individuals in our cohort presented a partially degraded bone microarchitecture at the spine based on TBS values. We can speculate that, even though TBS does not appear to be affected by osteoarthritic changes [242], it is possible that other conditions, such as posterior element changes, OVFs or vascular or calcifications, spuriously increase TBS in people with SCI similarly to BMD. The fact that we did not find differences in TBS between people with motor complete and incomplete injuries is not surprising, as BMD appears to be not affected by the level and severity of SCI.[467] Moreover, most of the individuals in our cohort were on bisphosphonates therapy. There is evidence that lumbar spine BMD continues to improve in the first few years after discontinuation of therapy [247] and, while there is not such evidence regarding TBS, it is possible that current or past bisphosphonates exposure contributed to increase TBS values. The exploration of TBS in individuals with SCI who have not received bisphosphonates treatments might allow to provide a more comprehensive picture of TBS values in this population, as well as the effects of bisphosphonates therapy on TBS. Measuring TBS at distal femur and proximal tibia may allow to estimate bone microarchitecture in the region that is most prone to fractures. Lobos et al. [175] attempted to do so; however, they applied an algorithm to calculate TBS at the lumbar spine to the distal femur and proximal tibia. TBS algorithm includes specific adjustments for abdominal and truncal soft tissue thickness, and thus cannot be applied to region with different soft tissue thickness.

FRAX® can be adjusted for TBS and the adjustment of FRAX® for TBS results in a slightly higher gradient of risk [174]. We detected good agreement between FRAX® and TBS-adjusted FRAX®. However, our findings show that a lower number of participants in our cohort would meet the treatment threshold for both major osteoporotic and hip fracture risk after the adjustment of FRAX® for TBS. Therefore, TBS may not add value in the estimation of fracture risk in individuals with SCI, and including TBS as a factor to define treatment course would result in less people

receiving treatment, which would have negative consequences in a population at high fracture risk. The 10-year fracture risk for major osteoporotic fractures was higher in individuals with a prior fragility fracture compared to those without, when assessed with FRAX® and TBS-adjusted FRAX®. While FRAX® and TBS-adjusted FRAX® are not recommended to assess fracture risk people with SCI, our findings may provide further validation of the new guidelines that recommend prior history of fracture, as well as hip, distal femur, and proximal tibia region BMD, be used as the primary factors for predicting lower extremity regional fracture risk. Therefore, while spine TBS may identify individuals with degraded bone microarchitecture at the spine in the general population, it may not add value in the estimation of fracture risk in people with SCI at this time.

6.1.3 Limitations and future directions

The limitations of the single studies are presented in the corresponding chapter. Although statistical agreement was present, there was a >10% difference in opinions about whether DXA scans should be appropriate for analysis, and this may need further exploration under a clinical perspective. Furthermore, although observations were very similar for major issues deemed to have a larger effect on BMD, large percentages differences were observed for most of the potential sources of error. A quality audit may be performed to reduce the observed differences and provide insights on whether errors were due to acquisition, analysis, or interpretation of the scan. The goal of our dissertation was to determine whether the presence of potential sources of error could be determined by looking at the DXA images, as it would happen in clinical practice, where a technologist or a physician must determine whether a scan is appropriate for BMD analysis. However, lateral radiography of the spine would have allowed to ascertain the presence of issues with more certainty, as well as determine whether the prevalence of sources of error was different depending on level and severity of injury. The fact that we did not account for the presence of potential sources of error when presenting TBS data and its implication on fracture risk assessment is another limitation that, however, may represent a subsequent development of the enclosed projects. Our cohort included individuals with chronic spinal cord injury. Trabecular bone content is reduced by 4% per month in the acute phase;[93] therefore exploring TBS values in the acute and subacute phase may provide more valuable insights on bone microarchitecture. Finally, most of

the fractures occur at distal femur and proximal tibia, but TBS is not validated for the application to the knee region. The development of an algorithm to estimate TBS at the two sites where fractures most commonly occur in people with SCI (i.e., distal femur and proximal tibia) may allow clinicians the ability to assess bone microarchitecture and estimate fracture risk at fracture prone sites in the future. An overarching limitation is that there are not calculators to estimate fracture risk in the SCI population. Some cross-sectional and prospective data on the prevalence and incidence of fracture after a SCI is available, but the development a SCI-specific tool to estimate fracture risk, with appropriate treatment thresholds, would be clinically relevant in terms of fracture prevention.

6.2 Non-pharmacological interventions for people at risk of osteoporotic fractures

The research presented in the second part of this dissertation was informed by the Knowledge-To-Action approach.[468] Previous reviews and consensus processes highlighted the need for new evidence on the effects of exercise for improving outcomes in people with low bone mass, with and without OVFs, and hyperkyphosis. This thesis synthesized evidence on the effects of exercise in people with low bone mass and hyperkyphosis, generated consensus recommendations for the non-pharmacological management of osteoporotic OVFs, and co-developed a remotely delivered education and training intervention for individuals in pain due to OVFs (Fig. 6).

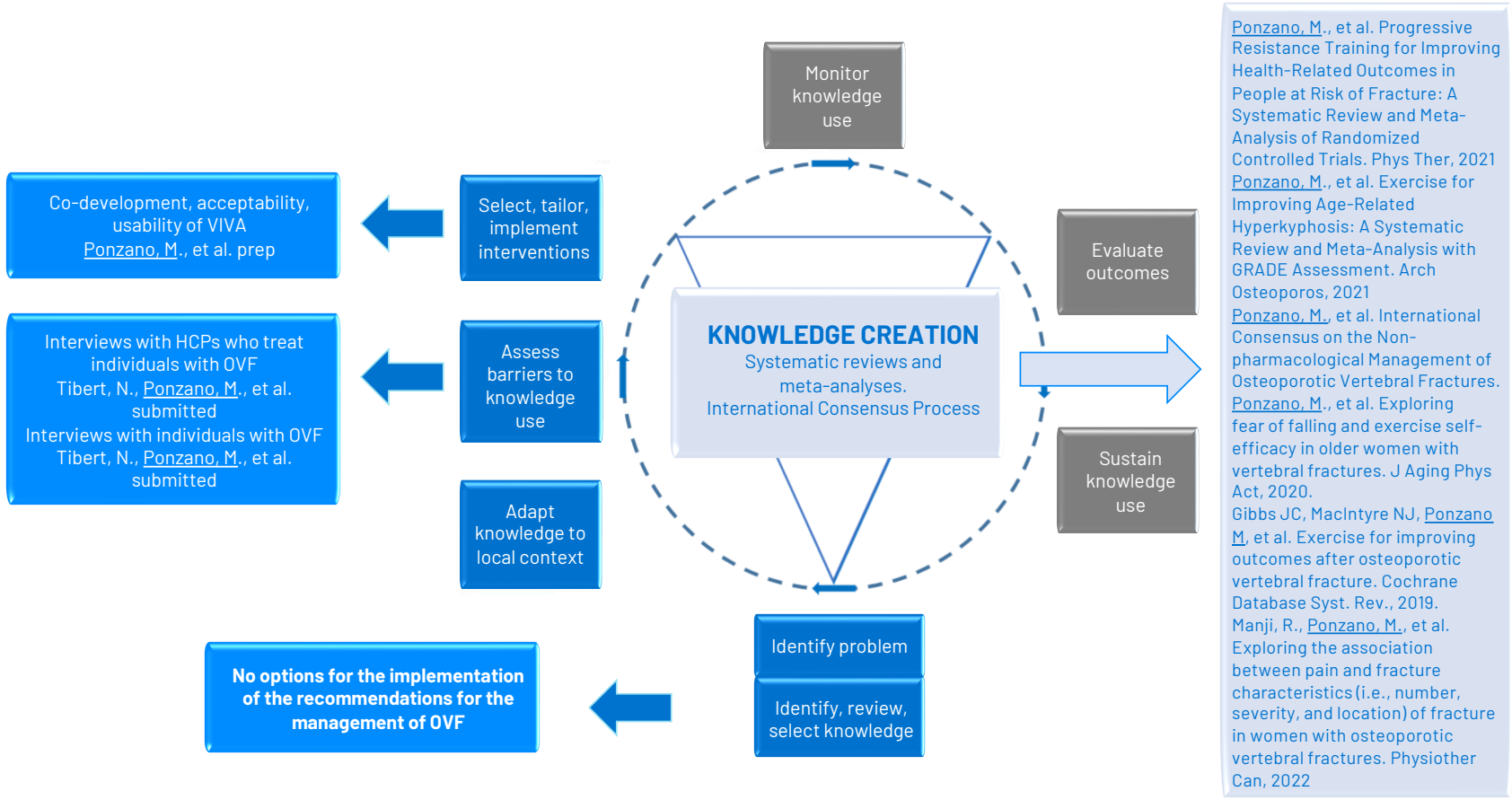

Figure 18. The process to co-develop the Virtual Intervention for Vertebral frActure (VIVA) mapped to the Knowledge-To-Action cycle. Reproduced with permission and adapted from Graham et al.[468]

6.2.1 Knowledge-to-action gap

Individuals with OVF face unique needs[460] and, while pharmacological treatment is recommended to prevent fractures in people with osteoporosis,[257] there are several knowledge gaps in the non-pharmacological management of OVFs. The first step is understanding whether the gap pertains to knowledge production or knowledge dissemination.[469] Systematic reviews on exercise and bracing interventions uncovered a gap in knowledge production. For instance, the number of trials investigating the effect of exercise[164] or spinal orthoses[394] in people with OVFs is limited. Pain is a debilitating consequence of OVFs, and there is a need for adequately powered RCTs that investigate the effects of non-pharmacological strategies to manage pain. Therefore, as an attempt to bridge a knowledge gap in the non-pharmacological management of OVFs, we decided to perform a Modified Delphi Consensus process.[422] Evidence that is solely based on expert opinion is classified as weak and ranks at the bottom of evidence-based medicine hierarchy of medical knowledge.[470] However, when meta-analyses are inconclusive, or findings from RCTs are conflicting, consensus must be obtained from experts in the field.[471] Moreover, the statements submitted to the panelist were informed by guidelines pertaining to the non-pharmacological management of low bone mass, back pain and nutrition in older adults, two systematic reviews led by our team on the effects of exercise[164] and bracing[394] in people with OVF, and five clinical trials of exercise interventions in people with OVF.[285,289,395–397] This creation and synthesis of knowledge, which include Chapters 3,4, and other publication I have authored and co-authored,[164,348,394,472–474] highlighted the need for future studies to test the effects of exercise and other non-pharmacological interventions in people with OVF. On the other hand, the fact that approximately most of physiotherapists, kinesiologists and exercise instructors are not comfortable guiding exercise in people at high risk of fractures or would like more guidance[260] also indicates a gap in knowledge dissemination. Two systematic reviews could not draw definitive conclusion on successful strategies to encourage clinicians and policy makers to use systematic reviews in decision-making due to the limited number of studies.[475,476] Future studies are needed to test strategies for the dissemination and uptake of systematic reviews and clinical practice guidelines for the management of individuals with low bone mass or OVFs.

6.2.2 Assessment of barriers to knowledge use

Over the past years, our lab has conducted research to assess barriers and explore how to adapt the knowledge to the local context. Exploratory secondary analyses and cross-sectional studies that I authored and co-authored revealed how pain and fear of falling and refracturing is a commonly reported barrier to exercise and physical activity by individuals with OVF.[202,399] A systematic review of qualitative and quantitative studies in middle-aged and older adults reported environmental factors and resources as the most commonly identified barriers.[477] This is in line with what emerged from our interviews with people with OVF, who reported a lack of knowledge on exercise, partly due to difficulties in obtaining resources on how to perform exercise and activities of daily living.[374] VIVA was the first step to implementing an intervention that aims to improve pain in in post-menopausal women and men ≥50 years with acute or chronic pain due to an OVF. Older adults report social influences, reinforcement, and assistance in managing change as motivators, while goal setting, belief that an activity will be beneficial, and social influences are important motivators in middle-aged adults.[477] Individual with low bone mass or with OVF desire to receive guidance not only on the best types of exercises, but also prescriptive details and instructions on how to perform them safely at home.[374] This step of the KTA cycle was very informative to the design of VIVA, as it uncovered the knowledge-to-action gaps from a participant perspective, thus informing the resources (one-page information sheets, pictures, and videos) and the modality of delivery (Physiotec online personal portal) to make them easily accessible to the participants.

Similarly, the assessment of the barriers to knowledge use is another step of the KTA that allows for an optimal delivery of interventions. A survey among over 100 physiotherapists, kinesiologists and exercise instructors that was circulated to inform the upcoming Canadian Clinical Practice Guidelines for the Prevention and Management of Osteoporosis reported that 46% of the participants were not comfortable guiding exercise in people at high risk of fractures, and 92% wanted more guidance on exercise and safe movement techniques in this population.[260] We therefore decided to perform a qualitative study to gather a deeper and more insightful perspective from HCPs, that would help us design a more effective and usable intervention. Most HCPs voiced a lack of knowledge among HCPs on how to manage osteoporosis and OVFs, and reported to be often afraid of referring patients.[400] Furthermore, physiotherapists use a small number of

behavioural change techniques in their clinical practice,[478] and that might interfere with the adoption and maintenance of healthy behaviours. The development of educational programs for HCPs working with patients at risk of fractures is imperative. The dissemination of the recommendation for the non-pharmacological management of OVFs (Chapter 4) will be a first step, while the high levels of acceptability and usability of VIVA prompt the implementation of its contents, that would provide more insights on the behaviour change techniques effective in individuals with OVF.

6.2.3 Development and implementation of the intervention

In a previous qualitative exploration, individuals with osteoporosis reported the availability of accessible community exercise programs as a facilitator of participation in exercise and physical activity.[374] We therefore opted for a virtual delivery of VIVA, to ensure the highest levels of accessibility and acceptability. However, we decided to deliver VIVA in the form of individual sessions, as that would have allowed to address all participants' needs or health conditions, and tailor the exercises and the progression. Our barriers assessment revealed that many people were not able to understand posture corrections, good alignment, and describe the execution of the exercises.[374] At the end of the intervention, participants were highly satisfied with the program and the resources provided throughout, which they believed very clear and easy to understand. Home exercise programs with intermittent supervision have been widely tested in older adults or individuals with osteoporosis.[278,479,480] The Otago exercise program showed a reduction in falls and improvements in physical functioning in women 80 years or older after resistance training and balance exercises.[479] Participants received four home visits by the physiotherapist in the first two months; afterwards, participants were encouraged to continue the exercise programme, and to contact the physiotherapist as needed.[479] Papaioannou et al showed improvements in HRQoL after a home exercise program with minimal supervision,[278] while the B3E trial, a 12-month home-based intervention informed by motivational interviewing[481,482] and the Health Action Process Approach,[483] showed improvements in functional leg muscle strength in women with OVFs.[200] The co-development of VIVA was informed by the Behaviour Change Wheel (BCW) and the Theoretical Domain Framework (TDF), as we anticipated that targeting capability, opportunity,

and motivation would be the most effective way to address most of the physical and mental barriers faced by individuals with OVF. Furthermore, in light of a future implementation on a larger scale, framing the behaviour change techniques used in VIVA according to BCW and TDF will help to ensure a high intervention delivery fidelity, as the physiotherapist will have a detailed and comprehensive framework to follow when tailoring the prescription of the intervention. The choice of secondary behavioural outcomes was informed by the Health Action Process Approach,[483] as action planning and goal setting are behaviour change techniques utilized in the delivery of VIVA, and we believed it will be of value to evaluate whether VIVA improves self-efficacy and planning abilities. Katzman et al[205] delivered an exercise and posture training to people with hyperkyphosis via videoclips and text messages to promote adherence, and the intervention was acceptable to the participants. However, considering the risk of subsequent fractures in people with OVF, pain and fear, we believed that telerehabilitation, with a physiotherapist working individually with the participants twice and then once a week, combined with and unsupervised daily program would be the most effective way to ensure a proper form of exercises, as well as providing feedback and making participants feel confident. However, even though telerehabilitation is acceptable to various conditions, including persons with rheumatic diseases,[459] considering the unique issues faced by people with OVFs and according to the recommendations of the Medical Research Council,[418] we decided to performed a smaller-scale study to determine the acceptability and usability of VIVA before implementing it on a larger scale. VIVA will be presented as a toolkit with photos, videos, and print/pdf resources for patients on pain management, nutrition, safe movement strategies and exercise, and behavioural support for goal setting and action planning, that can be used in a virtual or hybrid setting. The next steps in the implementation of VIVA should target two different categories of end-users: patients and physiotherapists. In term of study design, a pilot feasibility RCT with recruitment at ≥2 sites would be the logic next step, and delivering VIVA to the Quebec population in French language would provide valuable insights towards a future Canada-wide implementation. If VIVA will be feasible, a pragmatic RCT (according to the PRagmatic Explanatory Continuum Indicator Summary (PRECIS)-2) should test the effectiveness of the Canadian-wide implementation (according to the RE-AIM, Reach, Effectiveness, Adoption, Implementation and Maintenance, framework)[484] of VIVA at improving pain. VIVA high values of acceptability and usability, along with self-reported improvement in pain perception and self-

confidence, showed promising results in terms of adoption of the behaviour. In addition, a follow-up after a few weeks of self-practice of the newly adopted behaviour will allow to assess the maintenance of the behaviour. Finally, VIVA should be disseminated to physiotherapists working with individuals with OVFs through a multi-step process. First, the VIVA toolkit should be delivered to a local sample of physiotherapists to obtain their feedback in terms of acceptability and usability. Afterwards, an evaluation of the implementation of VIVA should be performed among physiotherapists working in ≥2 provinces, including Quebec, and then extended to physiotherapists working in multiple provinces Canada-wide. The content of VIVA should be also disseminated through continuing education workshops and webinars for physiotherapists and exercise professionals.

6.2.4 Limitations and future directions

Several limitations must be acknowledged when it comes to interventions to improve outcomes in people with low bone mass, hyperkyphosis, or OVF. First and foremost, men are very rarely recruited in intervention studies. It is true that osteoporosis and fragility fractures are most common in women, yet they still occur in men, and there is not conclusive evidence on the efficacy of exercise and other non-pharmacological interventions in men with osteoporosis. Future studies performed in men are required to extend the recommendations for the non-pharmacological management of osteoporosis and fragility fractures to male individuals. Researchers are encouraged to partner with fracture liaison services and patient research liaisons to the increase the number of men recruited in research studies.

Most of the studies in people with hyperkyphosis and OVF recruited at least 50% people with hyperkyphosis and OVF but did not have the presence of hyperkyphosis or OVF as inclusion criteria. The presence of individuals with low bone mass and without hyperkyphosis or OVF may reduce the confidence in the outcomes of such studies. However, the improvement in physical functioning, HRQoL, and pain provide evidence on the importance of back extensor strengthening for people at risk of fracture. Researchers should keep in mind that exercise tolerance may be different in people with hyperkyphosis or symptomatic OVFs compared to those without, and recruiting participants with no hyperkyphosis or no symptomatic OVFs may result in a ceiling effect, in that it would be difficult to improve postural or pain outcomes in people who do not

present such symptoms. Therefore, future studies aiming to address posture outcomes or consequences of OVFs should target only individuals with hyperkyphosis and OVF, respectively.

Interventions built on behaviour change theories are more effective than those who are not.[419,420] However, the majority of the studies included in the systematic reviews that I authored and co-authored were not based on theory. Without specific target behaviours and behaviour change techniques it is difficult to elicit the adoption and the maintenance of healthy behaviours, and the absence of a clear and defined behavioural framework challenges the implementation of the interventions. Future trials in older adults with low bone mass OVF should be based on theory, with a transparent and detailed description of all the stages of the development, to ensure that the intervention is implemented as intended, as well as the identification of the components that may be responsible for less positive outcomes than expected, or that were not acceptable to the participants.

Moreover, adverse events reporting is a concerning limitation common to exercise studies in several populations. Most of the studies in the systematic reviews that I authored and co-authored did not report on adverse events. Therefore, it is impossible to drive definitive conclusions on the safety of exercise in people with low bone mass. Only a few reported some minor adverse events, and future investigations are call assess and determine the safety of exercise and other interventions in this population. Finally, rigorous methods for a comprehensive assessment and reporting of adverse events in exercise trials should be developed.

6.3 Conclusion

The present dissertation focused on individuals with SCI and OVFs, two subgroups of people with osteoporosis that are at high risk of fractures, and present unique impairments, limitations, and restrictions that require population-specific and individually tailored assessments and interventions. The findings of the present work confirm current recommendations that suggest fracture risk in people with SCI be based on hip, distal femur, and femoral neck BMD and on an analysis of non-BMD risk factors. The high number of issues across LS DXA scans advocates for a review of the images, and not only of BMD values, when examining densitometry scans. TBS can predict fractures in several population, but it cannot be recommended as a tool to predict

fractures in people with SCI. The research reported in the present dissertation did not allow to understand whether TBS values are spuriously elevated by potential sources of errors, and fracture risk assessment cannot be based on TBS at the present time.

Findings from our systematic reviews showed that progressive resistance training can improve outcomes important to individuals living with osteoporosis, such as pain, physical functioning, and quality of life. However, our systematic reviews highlighted important knowledge gaps, such as the lack of compelling evidence on the effects of exercise in men with osteoporosis, and the absence of non-pharmacological options for the management of OVFs. Therefore, we generated consensus recommendations for the non-pharmacological management of OVFs, by adopting a Modified Delphi consensus process with participation bt over 30 healthcare professionals in Asia, Europe North America, and Oceania. Finally, we co-developed a virtually delivered education and training program for people with OVFs (VIVA) to implement such recommendations. VIVA was usable and acceptable to the patients, and the self-reported improvement in the perceived pain, as well as the increase self-confidence, are positive outcomes looking at the future implementation on a larger scale. Finally, a broad dissemination of the recommendations, and the creation of seminars and workshops for clinicians, would bridge some of the existing knowledge-to-practice gaps.

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Appendices

Appendix A
Study manual study 1

Study Manual

Index

1. Potential sources of error during lumbar spine densitometry

1.1 Is the DXA scan appropriate for BMD analysis?

YES: ≥ 2 contiguous vertebrae are appropriate for analysis.

NO: One of the following is present:

a. Only 1 vertebra is appropriate for analysis
b. ≥ 3 vertebrae with bone edges not clearly detectable
c. Patent incorrectly positioned
d. Heterotopic ossification across the first four lumbar vertebrae (L1-L4)
e. Extraneous calcified tissue interfering with BMD analysis at ≥ 3 vertebrae

f. Degenerative joint disease ≥ 3 vertebrae
g. Other potential sources of error that make the scan ineligible for analysis

The International Society of Clinical Densitometry recommends that at least 2 adjacent vertebrae must be appropriate for BMD analysis.[1] If only one vertebra is appropriate for analysis, the scan is not valid for BMD-based diagnosis and other sites should be considered instead. [1]

1.2 Should the DXA scan be re-analyzed?

YES: One of the following potential sources of errors was present and the interested vertebra/ae was/were not excluded from the original analysis:

a. ≥ 1 vertebra improperly numbered
b. ≥ 1 vertebra has outlier/unexpected BMD values
c. ≥ 1 vertebra with compression fracture has been included for BMD analysis
d. ≥ 1 vertebra with visible orthopaedic hardware of indication of previous surgical procedures has been included for BMD analysis
e. ≥ 1 vertebra with facet sclerosis or osteophytes has been included for BMD analysis
f. Extraneous calcified tissue interfering with BMD analysis at ≤ 2 vertebrae
g. Degenerative joint disease ≤ 2 vertebrae
h. Other potential sources of error that suggest that the scan is re-analyzed

NO: ≥ 2 contiguous vertebrae are appropriate for analysis and no other potential sources of errors are detected.

1.3 Should the TBS scan be re-analyzed?

YES: The region of interest was not properly identified.

NO: The region of interest was properly identified, and no artifacts interfere with the TBS measurement.

1.4 Should the DXA scan be removed from the dataset?

YES: The structural components of the vertebrae are not clearly visible or several artifacts interfere with BMD assessment.

NO: The structural components of the vertebrae are clearly visible and no artifacts interfere with BMD assessment.

1.5 Are vertebrae properly numbered?

YES: The first four lumbar vertebrae (L1-L4) are properly labeled as in Figure 1.

NO: Vertebrae were incorrectly labeled (e.g., T12 or L5 were included in the analysis).

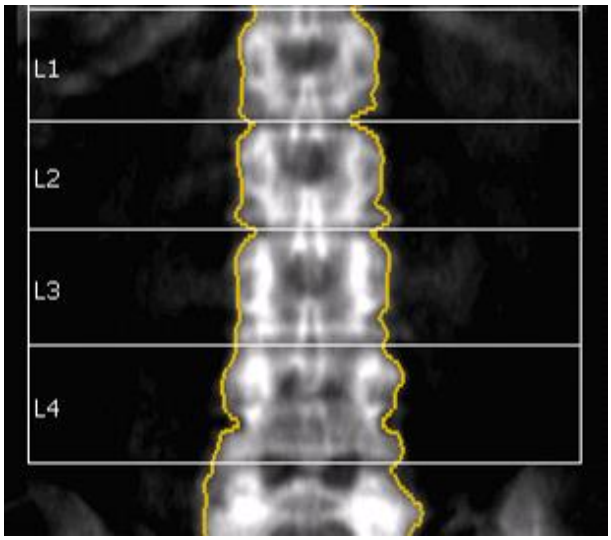

Figure 19 - Region of interest (ROI) at the lumbar spine for bone densitometry.

1.6 Are 2 contiguous vertebrae appropriate for analysis?

YES: There ≥ 2 contiguous vertebrae that do not present any potential sources of errors and that are appropriate for the measurement of BMD. Please check the box corresponding to each vertebra appropriate for BMD analysis.

NO: There are < 2 contiguous vertebrae that do not present any potential sources of errors and that are appropriate for the measurement of BMD.

1.7 Are there any regions or vertebrae that have outlier/unexpected BMD values?

YES: There is > 1 T-score difference between a vertebra and the adjacent vertebrae.[1] Please check the box corresponding to the vertebra with outlier BMD value.

NO: There is ≤ 1 T-score difference between a vertebra and the adjacent vertebrae.

1.8 Were bone edges clearly detectable?

YES: Vertebral borders are clearly visible in the scan.

NO: Vertebral borders are not entirely visible, and the identification of the borders of ≥ 1 vertebrae is ambiguous.

1.9 Do you think the patient was positioned correctly during the scan?

YES

NO: Please explain why the patient was not correctly positioned

1.10 Are there any changes in vertebral morphometry?

YES: Changes in vertebral morphometry are observable.

NO: No changes in vertebral morphometry are observable.

UNCLEAR: Changes in vertebral morphometry are suspected but not certain.

1.11 Are there any visible compression fractures?

YES: If a deformation is visible, please check the appropriate box corresponding to the location, and the boxes corresponding to the shape and the severity of the deformation, according to Figure 2.[2]

NO: No vertebral deformities are visible.

1.12 Are there any visible orthopaedic hardware or indication of previous surgical procedures?

YES: Please provide details about the visible hardware.

NO

1.13 Are facet sclerosis or osteophytes observable?

YES: If sclerosis or osteophytes are visible, please rate them according to the Kellgren and Lawrence scale:[3]

GRADE 1 (doubtful): doubtful joint space narrowing and possible osteophytic lipping

GRADE 2 (minimal): definite osteophytes and possible joint space narrowing

GRADE 3 (moderate): moderate multiple osteophytes, definite narrowing of joint space and some sclerosis and possible deformity of bone ends

GRADE 4 (severe): large osteophytes, marked narrowing of joint space, severe sclerosis and definite deformity of bone ends

NO: No observable fact sclerosis or osteophytes.

1.14 Are there any areas that present heterotopic ossification?

YES: Heterotopic bone formation is observable.

NO: No heterotopic bone.

1.15 Is degenerative joint disease observable anywhere in the scan (both within and outside the region of interest)?

YES: Please provide details if applicable

NO

1.16 Is scoliosis observable anywhere in the scan (both within and outside the region of interest)?

YES: Please provide details if applicable

NO

1.17 Is extraneous calcified tissue observable anywhere in the scan (both within and outside the region of interest)?

YES: Please provide details if applicable

NO

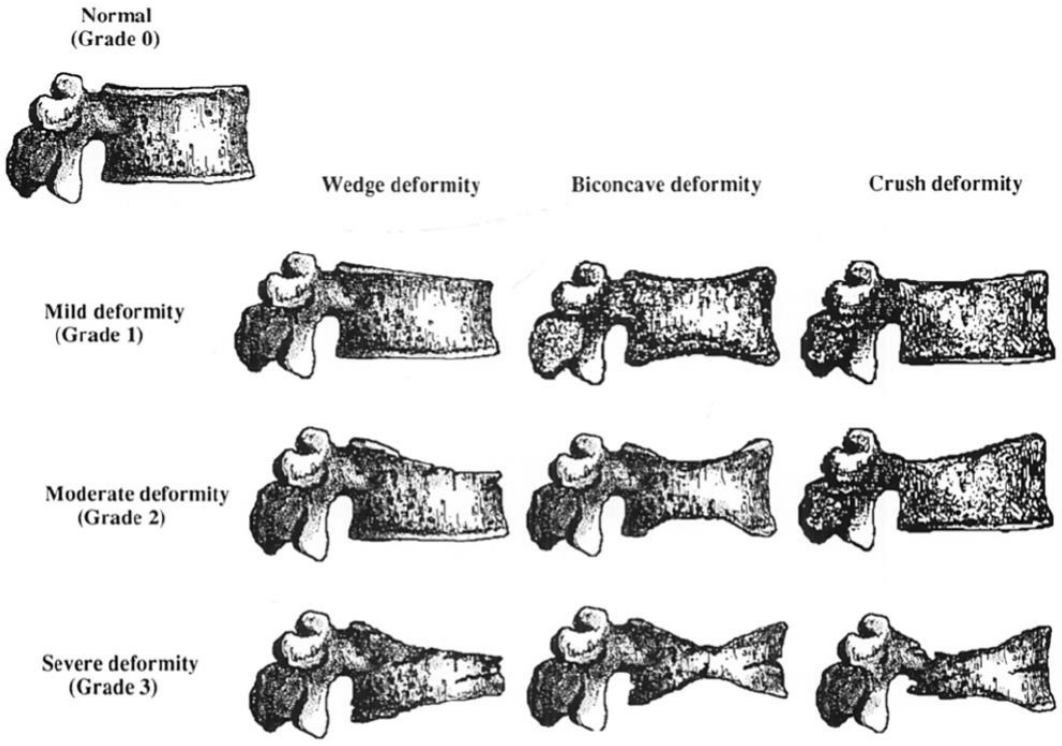

Figure 20 - Semiquantitative grading of vertebral deformity. From Genant et al (1993).[2]

References

1. Shuhart CR, Yeap SS, Anderson PA, Jankowski LG, Lewiecki EM, Morse LR, et al. Executive Summary of the 2019 ISCD Position Development Conference on Monitoring Treatment, DXA Cross-calibration and Least Significant Change, Spinal Cord Injury, Peri-prosthetic and Orthopedic Bone Health, Transgender Medicine, and Pediatrics. 2019;22(4):453–71.

2. Genant HK, Wu CY, van Kuijk C, Nevitt MC. Vertebral fracture assessment using a semiquantitative technique. 1993;8(9):1137–48.

3. Bonnick SL. Skeletal Anatomy in Densitometry. New York, USA: Humana Press; 2010.

Appendix B
Data collection form study 1

LUMBAR SPINE

		Comments
Is the scan appropriate for BMD analysis? (If not, please explain the reasons)	☐ Yes ☐ No	
Should the DXA scan be re-analyzed? (If yes, please explain the reasons)	☐ Yes ☐ No	
Should the TBS scan be re-analyzed? (If yes, please explain the reasons)	☐ Yes ☐ No	
Should the DXA scan be removed from the dataset? (If yes, please explain the reasons)	☐ Yes ☐ No	

Should the TBS scan be removed from the dataset? (If yes, please explain the reasons)	☐ Yes ☐ No	

		Comments
Are vertebrae properly numbered? (e.g., not labeling L5)	☐ Yes ☐ No	
Are 3 contiguous vertebrae appropriate for analysis? (Check the vertebrae that <u>are good</u> for analysis)	☐ Yes ☐ No **Check the vertebrae that are good for analysis:** ☐L1 ☐ L2 ☐ L3 ☐ L4	

Are there any regions or vertebrae that have outlier/unexpected BMD values? (Please check the vertebra or the region with <u>abnormal</u> BMD)	☐ Yes ☐ No **If yes, where was BMD inconsistent?** ☐ L1 ☐ L2 ☐ L3 ☐ L4 ☐ L1-L2 ☐ L1-L3 ☐ L1-L4 ☐ L2-L3 ☐ L2-L4 ☐ L3-L4	

Were bone edges clearly detectable?	☐ Yes ☐ No	
Do you think the patient was positioned correctly for the scan?	☐ Yes ☐ No	

		Comments
Are there any changes in vertebral morphometry?	☐ Yes ☐ No ☐ Unclear	

If yes:		**Comments**
Are there any visible compression fractures? (Please refer to the auxiliary document for the explanation of deformity types and severity grade)	☐ Yes ☐ No **If yes, location:** ☐ L1 ☐ L2 ☐ L3 ☐ L4 ☐ Multiple fractures	**If yes, deformity type:** ☐ Wedge ☐ Crush ☐ Biconcave ☐ Non-detectable **If so, severity Grade:** ☐ Grade 1 ☐ Grade 2 ☐ Grade 3 ☐ Non-detectable

Are there visible orthopaedic hardware or indication of previous surgical procedures?	☐ Yes ☐ No **If yes, location:** ☐ L1 ☐ L2 ☐ L3 ☐ L4	**If yes:** ☐ Laminectomy ☐ Hardware ☐ Other (specify):
Facet sclerosis or osteophytes (Please refer to the auxiliary document for the explanation of the Kellgren and Lawrence scale)	☐ Yes ☐ No **If yes, location:** ☐ L1 ☐ L2 ☐ L3 ☐ L4 ☐ Multiple fractures	**Severity Grade:** ☐ Grade 1 (doubtful) ☐ Grade 2 (minimal) ☐ Grade 3 (moderate) ☐ Grade 4 (severe)
Are there any areas that present heterotopic ossification?	☐ Yes ☐ No	

Are any of the following present anywhere in the scan?		**Comments**
Degenerative joint disease	☐ Yes ☐ No **If yes, location:** ☐ Thoracic spine ☐ Lumbar spine	
Scoliosis	☐ Yes ☐ No	
Extraneous calcified tissue	☐ Yes ☐ No **If yes, location:** ☐ Aorta ☐ Kidney ☐ Ovary ☐ Other (please specify)	

		Comments
Are there other potential sources of error? (If yes, please explain in the comments box)	☐ Yes ☐ No	

Assessor Printed Name:_____ ☐☐☐☐/☐☐/☐☐

Y Y Y Y M M D D

Assessor Signature:_____

Appendix C
Search strategy study 3

- **Total number of results:**

Total = 5880 results

Total after deduplication = 3606

Database breakdown

- 797: Cochrane Library (76 reviews, 721 trials)
- 1476: OVID MEDLINE
- 1789: OVID EMBASE
- 627: CINAHL
- 1191: Web of Science

- **Final search strategies:**
- **MEDLINE and EMBASE**

Search conducted by Jackie Stapleton on September 5, 2018

- MEDLINE: 1476 results
- EMBASE: 1789 results
- After duplicates removed: 2448 uploaded to Refworks

	Searches	Results
1	(osteopor* or osteopenia or low bone density or low bone mineral density or low bone mass or bone loss* or bone remodel$ing).ti,ab,kw.	241620
2	((fragility or spine or spinal or vertebra* or hip* or femoral neck or compression) adj2 fracture*).ti,ab,kw.	85248
3	exp osteoporosis/ or bone density/ or exp bone remodeling/ or exp hip fractures/ or spinal fractures/ or fractures, compression/ or osteoporotic fractures/	367527
4	1 or 2 or 3	462714
5	(older or elder or elderly or frail or senior* or middle age* or geriatric).ti,ab,kw.	1479583

6	middle aged/ or exp aged/	7975306
7	5 or 6	8601363
8	(Exercis* or Physical activit* or Physical fitness or Weight bearing or Load bearing or Axial bearing or Running or Dancing or Stair climb* or treadmill* or walk or walking or weight lifting or yoga or pilates).ti,ab,kw.	1070524
9	((Resistance or strength or strengthening or weight or high impact) adj2 (train* or exercis*)).ti,ab,kw.	46265
10	(Balance adj2 (exercis* or train*)).ti,ab,kw.	5378
11	exp exercise/ or exp sport/ or dancing/ or dance therapy/ or exp exercise therapy/ or weight bearing/ or osteoporosis/rh or walking/ or plyometric exercise/ or resistance training/ or yoga/ or postural balance/	816263
12	8 or 9 or 10 or 11	1410927
13	(Meta analys* or metaanalys*).ti,ab,kw.	300903
14	((Systematic or methodologi*) adj5 (review* or overview*)).ti,ab,kw.	305899
15	(Cochrane or Embase or Psyclit or Psychlit or Medline or pubmed).ab.	371844
16	(quantitativ* adj5 synthesi*).ti,ab,kw.	6082
17	((pooled or pooling) and analys*).ti,ab,kw.	131815
18	(randomized controlled trial* or Randomised controlled trial* or rct or clinical trial* or (allocated adj2 random*)).ti,ab,kw.	1109623

19	Randomized controlled Trials as Topic/ or Randomized controlled trial/ or Random allocation/ or Double blind method/ or single blind method/ or exp Clinical trial/ or exp clinical trials as topic/	2775433
20	13 or 14 or 15 or 16 or 17 or 18 or 19	3686891
21	4 and 7 and 12 and 20	3298
22	exp animals/ not humans/	16126373
23	21 not 22	2426
24	23 not (case reports or letter or editorial or comment).pt.	2400
25	24 use pmoz (MEDLINE results only)	1476
26	(osteopor* or osteopenia or low bone density or low bone mineral density or low bone mass or bone loss* or bone remodel$ing).ti,ab,kw.	241620
27	((fragility or spine or spinal or vertebra* or hip* or femoral neck or compression) adj2 fracture*).ti,ab,kw.	85248
28	exp osteoporosis/ or osteopenia/ or bone density/ or bone remodeling/ or bone atrophy/ or bone demineralization/ or fragility fracture/ or exp spine fracture/ or exp hip fracture/	353646
29	26 or 27 or 28	444574
30	(older or elder or elderly or frail or senior* or middle age* or geriatric).ti,ab,kw.	1479583
31	middle aged/ or exp aged/	7975306
32	30 or 31	8601363

33	(Exercis* or Physical activit* or Physical fitness or Weight bearing or Load bearing or Axial bearing or Running or Dancing or Stair climb* or treadmill* or walk or walking or weight lifting or yoga or pilates).ti,ab,kw.	1070524
34	((Resistance or strength or strengthening or weight or high impact) adj2 (train* or exercis*)).ti,ab,kw.	46265
35	(Balance adj2 (exercis* or train*)).ti,ab,kw.	5378
36	exp exercise/ or exp sport/ or dancing/ or dance therapy/ or exp kinesiotherapy/ or weight bearing/ or osteoporosis/rh or walking/ or plyometrics/ or resistance training/ or yoga/ or pilates/ or body equilibrium/	778429
37	33 or 34 or 35 or 36	1390141
38	(Meta analys* or metaanalys*).ti,ab,kw.	300903
39	((Systematic or methodologi*) adj5 (review* or overview*)).ti,ab,kw.	305899
40	(Cochrane or Embase or Psyclit or Psychlit or Medline or pubmed).ab.	371844
41	(quantitativ* adj5 synthesi*).ti,ab,kw.	6082
42	((pooled or pooling) and analys*).ti,ab,kw.	131815
43	exp meta analysis/ or systematic review/	348676
44	(randomized controlled trial* or Randomised controlled trial* or rct or clinical trial*).ti,ab,kw.	1064645
45	(allocated adj2 random*).ti,ab,kw.	61422
46	randomized controlled trial/ or exp randomization/ or random allocation/ or double blind method/ or single blind method/ or exp clinical trial/ or exp clinical trials as topic/	2778184

47	38 or 39 or 40 or 41 or 42 or 43 or 44 or 46	3699005
48	29 and 32 and 37 and 47	3247
49	(exp animals/ or exp invertebrate/ or animal experiment/ or animal model/ or animal tissue/ or animal cell/ or nonhuman/) and (human/ or normal human/ or human cell/)	35991235
50	(exp animals/ or exp invertebrate/ or animal experiment/ or animal model/ or animal tissue/ or animal cell/ or nonhuman/) not 49	10475345
51	48 not 50	3236
52	51 not (case study/ or letter/ or abstract report/ or editorial.pt. or note.pt.)	3195
53	52 use oemezd (EMBASE results only)	1789
54	25 or 53	3265
55	remove duplicates from 54 (removes duplicates from MEDLINE and EMBASE results)	2448

Line 25 = MEDLINE results (1476 results)

Line 53 = EMBASE results (1789 results)

Line 55 = Deduplication of OVID results resulted in 2448 uploaded to Refworks

- **CINAHL**

Search conducted by Jackie Stapleton on August 31, 2018

#	Query	Results
S6	S1 AND S2 AND S3 AND S4 Limiters – Peer reviewed	(627)

S17	S13 AND S14 AND S15 AND S16	674
S16	((MH "Meta Analysis") OR (MH "Systematic Review")) OR TX (meta analy* OR metaanaly*) OR TX ((systematic or methodologi*) N5 (review or overview)) OR AB (Cochrane or Embase or Psyclit or Psychlit or Medline or pubmed) OR TX quantitativ* N5 synthesi* OR TX ((pooled or pooling) and analys*) OR TX (randomized controlled trial* or randomised controlled trial* or rct) OR TX (allocat* random* OR placebo* OR random* allocate* OR randomi* control* trial*) OR TX clinical N1 trial* OR ((MH "random assignment") OR (MH "clinical trials+"))	Display
S15	((MH "Exercise+") OR (MH "Sports+") OR (MH "Dancing+") OR (MH "Dance Therapy") OR (MH "Therapeutic Exercise+") OR (MH "Weight-Bearing") OR (MH "Walking+") OR (MH "Resistance Training") OR (MH "Muscle Strengthening+") OR (MH "yoga") OR (MH "pilates") OR (MH "balance training, physical") OR (MH "balance, postural")) OR TX (Exercis* or Physical activit* or Physical fitness or Weight bearing or Load bearing or Axial bearing or Running or Dancing or Stair climb* or treadmill* or walk or walking or weight lifting or yoga or pilates) OR TX ((Resistance or strength or strengthening or weight or “high impact”) N2 (train* or exercis*)) OR TX (Balance adj2 (exercis* or train*))	Display
S14	((MH "Middle Age") OR (MH "Aged+") OR (MH "Aging") OR (MH "Rehabilitation, Geriatric")) OR TX (older or elder or elderly or frail or senior* or middle age* or geriatric or "old age")	Display

S13	(MH "Osteoporosis+") OR (MH "Bone Density") OR (MH "Bone Remodeling+") OR (MH "hip fractures+") OR (MH spinal fractures+") OR TX (osteopor* or osteopenia or low bone density or low bone mineral density or low bone mass or bone loss* or bone remodeling or bone remodelling) OR TX ((fragility or spine or spinal or vertebra* or hip* or femoral neck or compression) N2 fracture*)	Display

- **Web of Science**

Search conducted by Jackie Stapleton on September 5, 2018

et	Results	Save History / Create AlertOpen Saved History
# 6	1,191	#4 AND #3 AND #2 AND #1 **Refined by: DOCUMENT TYPES:** (ARTICLE OR PROCEEDINGS PAPER OR REVIEW) *Indexes=SCI-EXPANDED, SSCI Timespan=1900-2018*
# 5	1,216	#4 AND #3 AND #2 AND #1 *Indexes=SCI-EXPANDED, SSCI Timespan=1900-2018*
# 4	906,167	TS=("Meta analys*" or "metaanalys*") OR TS=("systematic" NEAR/2 ("review" or "overview")) OR TS=(("pooled" OR "pooling") AND "analys*") OR TS=("randomized controlled trial*" OR "randomised controlled trial*" OR "rct" OR "clinical trial*" OR "random allocat*") *Indexes=SCI-EXPANDED, SSCI Timespan=1900-2018*
# 3	670,641	TS=("Exercis*" or "Physical activit*" or "Physical fitness" or "Weight bearing" or "Load bearing" or "Axial bearing" or "Running" or "Dancing" or "Stair climb*" or "treadmill*" or "walk" or "walking" or "weight lifting" or "yoga" or "pilates") OR TS=(("Resistance" or "strength" or "strengthening" or "weight" OR "high impact") NEAR/2 (train* or exercis*)) OR TS=(Balance NEAR/2 (exercis* or train*)) *Indexes=SCI-EXPANDED, SSCI Timespan=1900-2018*

# 2	**727,390**	TS=("older" OR "elder" or "elderly" or "frail" or "senior*" or "middle age*" or "geriatric") *Indexes=SCI-EXPANDED, SSCI Timespan=1900-2018*
# 1	**171,349**	TS=("osteopor*" or "osteopenia" or ("low" NEAR/2 ("bone density" OR "bone mineral density" or "bone mass")) or bone loss* or "bone remodeling" or "bone remodeling") OR TS=(("fragility" OR "spine" OR "spinal" OR "vertebra*" or "hip" OR "compression") NEAR/2 "fracture*") *Indexes=SCI-EXPANDED, SSCI Timespan=1900-2018*

- **Cochrane Library**

Search conducted by Jackie Stapleton on September 11, 2018

#1	osteopor* or osteopenia or low bone density or low bone mineral density or low bone mass or bone loss* or bone remodeling or bone remodeling or ((fragility or spine OR spinal OR vertebra* or hip* or femoral) NEAR/2 fracture*)	20372
#2	MeSH descriptor: [Osteoporosis] explode all trees	3683
#3	MeSH descriptor: [Bone Density] explode all trees	4370
#4	MeSH descriptor: [Bone Remodeling] explode all trees	2408
#5	MeSH descriptor: [Hip Fractures] explode all trees	1404
#6	MeSH descriptor: [Spinal Fractures] explode all trees	637
#7	MeSH descriptor: [Fractures, Compression] explode all trees	110
#8	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7	21833
#9	older or old or elder or elderly or frail or senior* or middle age* or geriatric	391545
#10	MeSH descriptor: [Middle Aged] explode all trees	1387
#11	MeSH descriptor: [Aged] explode all trees	1669
#12	#9 OR #10 OR #11	391609
#13	Exercis* or Physical activit* or Physical fitness or Weight bearing or Load bearing or Axial bearing or Running or Dancing or Stair climb* or treadmill* or walk or walking or ((Resistance or strength or strengthening or weight) NEAR/2 (train* or exercise*)) or weight lifting or yoga or pilates or (Balance NEAR/2 (exercis* or train*))	107204
#14	MeSH descriptor: [Exercise] explode all trees	20663
#15	MeSH descriptor: [Sports] explode all trees	13867
#16	MeSH descriptor: [Dance Therapy] explode all trees	70
#17	MeSH descriptor: [Dancing] explode all trees	147
#18	MeSH descriptor: [Exercise Therapy] explode all trees	11203
#19	MeSH descriptor: [Weight-Bearing] explode all trees	941
#20	MeSH descriptor: [Walking] explode all trees	4899
#21	MeSH descriptor: [Resistance Training] explode all trees	2623

#22	MeSH descriptor: [Yoga] explode all trees	544
#23	MeSH descriptor: [Postural Balance] explode all trees	2251
#24	#14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23	33322
#25	#8 AND #12 AND #24	797

797 results

- 76 Cochrane Reviews
- 721 Trials

Appendix D
Search strategy study 4

PubMed

#1 exercise [mesh] OR exercis* [tiab] OR yoga [tiab] OR pilates [tiab] OR "exercise therap*" [tiab] OR "physical activit*" [tiab] OR "exercise movement techniques" [tiab] OR "resistance training" [tiab] OR "weight lifting" [mesh] OR "exercise therapy" [mesh] OR "exercise movement techniques" [mesh] OR "physical fitness" [MeSH] OR lifting effort[tiab] OR stretching[tiab] OR swimming[tiab]

#2 posture [tiab] OR "spinal curvature" [tiab] OR "hyperkypho*" [tiab] OR kypho* [tiab] OR "skeletal alignment" [tiab] OR "kyphosis" [mesh]

#3 "elderly" [tiab] OR "older adult*" [tiab] OR senior* [tiab] OR "older people" [tiab] OR "middle age*" [tiab] OR "aged" [mesh] OR "middle aged" [mesh] OR old age[tiab] OR geriatric* [tiab]

Final Search: #1 AND #2 AND #3

Cumulative Index to Nursing and Allied Health Literature Search

#1 MH ("exercise" OR "therapeutic exercise") OR TX (exercis* OR pilates OR yoga OR "physical activit*" OR "exercise movement techniques" OR "resistance training" OR "weight lifting" OR lifting effort OR stretching OR swimming)

#2 TX posture OR "spinal curvature" OR hyperkypho* OR kypho* OR "skeletal alignment"

#3 MH ("aged" OR "middle age" OR "frail elderly") OR TX (elderly OR "older adult*" OR "old age" OR "older people" OR senior* OR "middle age*" OR geriatric*)

Final Search: S1 AND S2 AND S3

Embase search

#1 kyphosis/

#2 posture.tw

#3 spinal curvature.tw

#4 skeletal alignment.tw

#5 hyperkypho*.tw

OR kypho*.tw

#6 1 or 2 or 3 or 4 or 5

#7 exercise/ or aerobic exercise/ or anaerobic exercise/ or aquatic exercise/ or arm exercise/ or breathing exercise/ or dynamic exercise/ or endurance training/ or isokinetic exercise/ or muscle exercise/ or pilates/ or plyometrics/ or resistance training/ or static exercise/

#8 exercis*.tw

#9 physical activity/ or lifting effort/ or stretching/ or swimming/ or weight lifting/

OR resistance training.tw OR weight lifting.tw OR physical fitness.tw OR lifting effort.tw OR stretching.tw OR swimming.tw

#10 yoga.tw

#11 7 or 8 or 9 or 10

#12 aged/

#13 older adult*.tw

#14 middle aged/

#15 senior*.tw

OR elderly.tw OR older people.tw OR middle age*.tw OR old age.tw OR geriatric*.tw

#16 12 or 13 or 14 or 15

Final Search: #6 and #11 and #16

Cochrane search

#1 Exercis* or "Physical activit*" or "Physical fitness" or ((Resistance or strength or strengthening or weight) NEAR/2 (train*)) or "weight lifting" or yoga or pilates or (Balance NEAR/2 (train*)) OR "lifting effort" OR stretching OR swimming

#2 MeSH descriptor: [Exercise] explode all trees
#3 MeSH descriptor: [Yoga] explode all trees
#4 MeSH descriptor: [Exercise Therapy] explode all trees

#5 MeSH descriptor: [Exercise movement techniques] explode all trees
#6 MeSH descriptor: [Resistance Training] explode all trees
#7 MeSH descriptor: [Weight Lifting] explode all trees
#8 MeSH descriptor: [Physical Fitness] explode all trees

#9 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8

#9 postur* or “spinal curvature*” or hyperkypho* or kypho* or “skeletal alignment”

#10 MeSH descriptor: [Posture] explode all trees

#11 MeSH descriptor: [Spinal Curvatures] explode all trees

#12 MeSH descriptor: [Kyphosis] explode all trees

#13 #9 OR #10 OR #11 OR #12

#14 “older adult*” OR “older people” or “old age” or elder* or frail or senior* or “middle age*” or geriatric*

#15 MeSH descriptor: [Middle Aged] explode all trees

#16 MeSH descriptor: [Aged] explode all trees

#17 #14 OR #15 OR #16

#18 #12 AND #13 AND 17

Web of Science

#1 TS=(postur* or “spinal curvature*” or hyperkypho* or kypho* or “skeletal alignment”)

#2 TS=("older adult*" or elder* or “older people” or “old age” or frail or senior* or "middle age*" or geriatric*)
Indexes=SCI-EXPANDED

Appendix E
Supplementary material study 5

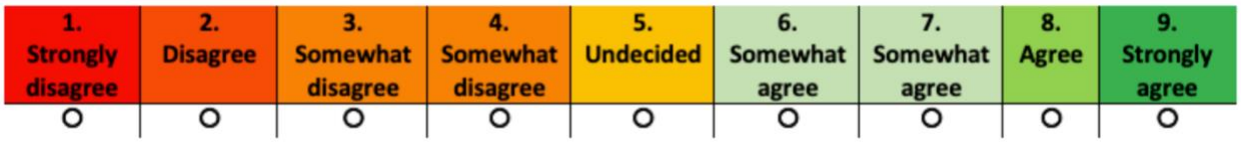

Figure S1. Agreement rating scale used by the panelists to rate their agreement with each question.

Table S1. Modified Delphi survey for the first round. The first column reports the statements that were presented in the survey, the second the mean percentage agreement for each question. Based on panel size (n = 31), consensus upon each statement was reached if the rating of no more than 9 panelists was outside the 3-point region containing the median. The minimum percentage agreement for each statement of the first round was 71%. The statements where a consensus was not reached are reported in bold.

Statements	Percentage agreement
1. Individuals with vertebral fracture should:	
a. Avoid prolonged or continuous bed rest. Some people have severe pain immediately after the fracture, and a few days of bed rest might be indicated, but limit the duration of prolonged or continuous bed rest as much as possible.	77.42%
b. Temporarily avoid heavy physical exertion (e.g., during work, daily life or exercise), lifting, or activities that exacerbate pain during the 12-week period following fracture; examples include carrying groceries, lifting pets or children, yard work. When to resume will depend on the severity of fracture(s) and symptoms. Resume activities involving heavy physical exertion gradually.	90.32%
c. Receive education on pain expectation, for example: that, for most people, pain and activity tolerance will get better over time, but it may take 3 months or longer; and that they can gradually start or resume exercise and physical activities of daily life, leisure, or work as pain diminishes.	93.55%
d. Receive education that having a spine fracture increases the risk of having another fracture, and that they must be referred to a fracture liaison service or their physician to learn about treatment strategies (including medications, fall prevention, etc.) to prevent further fractures.	100%
2. In the acute and chronic stages after a vertebral fracture, healthcare professionals are encouraged to use "how to" language rather than only suggesting activity restrictions, and to be mindful of choosing words carefully, to promote optimism rather than create fear and activity avoidance. Health care professionals can provide examples of activities that should be modified or avoided (e.g., bend at your hips instead of rounding your back, get someone to lift heavy objects for you instead of doing it yourself).	96.67%
3. Strategies to manage back pain and discomfort (in acute or chronic stages) associated with vertebral fracture include:	
a. Assessment by a healthcare professional for pain-related psychological risk factors (e.g., pain catastrophizing, pain-related fear, anxiety, social isolation, low mood) that could increase the risk of persistent pain and disability (e.g., using STarT Back Screening Tool -	93.33%

	https://startback.hfac.keele.ac.uk/ or any validated tools) and, if present, consider referral to a health professional (e.g., physical therapist, occupational therapist, psychologist) who has expertise in pain and psychological factors.	
b.	Avoiding prolonged sitting and, and when sitting, do so with attention to posture during sitting, as well as getting in and out of the seated position. If prolonged sitting is necessary, for example at work, get up and move around every 30 minutes and consider consulting an ergonomist about alternative strategies, such as perched sitting or standing desks.	76.67%
c.	**Lying supine on the floor, bed, or firm surface, with feet flat on surface and knees bent, to unload the spine, encourage spinal extension and stretch pectoral and front shoulder muscles. Individuals with hyperkyphosis can use one or more pillows under the head. While there is no RCT evidence to support this statement, there is a prior consensus process encouraging this approach. A frequency of 2-4 times per day for 15-20 minutes each bout has been suggested**	**70.00%**
d.	Education on movements to avoid or modify (e.g., rapid, repetitive, weighted, sustained or end-range flexion or twisting of the spine) and on strategies to reduce loads on the spine (e.g., hip hinge, step-to-turn, getting up and moving around every 30 minutes) during physical activities of daily life, leisure, and work. Where possible, refer to a physical therapist for assessment and education, or suggest free resources for education, to get detail on the types of movements to modify or avoid.	96.67%
e.	Pacing or "graded activity" to help facilitate increased activity tolerance, or to avoid doing too much too soon.	100%
f.	**Self-application of cold or heat for sore or painful areas**	**56.67%**
4.	**Bracing is not recommended for individuals with vertebral fracture**	**50.00%**
5.	When the therapeutic goal is to improve respiratory function, individuals with acute or chronic vertebral fractures can be taught diaphragmatic breathing exercises (e.g., in the supine position supine with knees bent and feet flat on lying surface, cueing focus on lower rib expansion and diaphragm contraction on inhale through nose, and exhaling through pursed lips with focus on lower ribs moving in, pelvic-floor and deep abdominal muscle contraction). Progression involves practicing breathing exercises during sitting or standing.	93.33%
6.	Ideally in consultation with a physical therapist or exercise physiologist, individuals with a vertebral fracture should initiate an individualized exercise program focusing on goals such as improving back extensor endurance, spinal mobility, physical functioning and balance; the exercise program can be introduced within 4-12 weeks after vertebral fracture, as tolerated, or when acute fracture-related pain has diminished, or after 12 weeks, based on patient preference and clinician judgement. Referring to a physical therapist or exercise physiologist is recommended so that exercises can be phased in and tailored in accordance with the patient's needs, health conditions, abilities, fracture type and symptoms, and time post-fracture (e.g., start with focus on teaching body mechanics, individualized selection and phasing in of exercises). When access to physiotherapy or exercise physiologist is not possible, refer patients to print or online resources from a national osteoporosis society. Example exercises to consider are provided below, derived from clinical trials of exercise for people with vertebral fracture.	93.33%
a.	**Shoulder press**	**70.00%**
b.	**Supine thoracic extension with one arm flexed at 180 degrees**	**56.67%**
c.	**Supine hip and leg extension, "pressing" into ground/bed or extending through leg e.g., leg lengthener**	**60.00%**
d.	**Supine gentle head press**	**56.67%**
e.	**Supine lying over rolled up towel placed lengthways along the back**	**56.67%**

f.	**Head to wall**	**66.67%**
g.	**Bridging in supine**	**66.67%**
h.	**Trunk extension**	**60.00%**
i.	**Advanced: quadruped thoracic extension stretch, birddog (arm only, leg only, then progress to alternate arm & leg at once)**	**53.33%**
j.	**Supine shoulder flexion**	**63.33%**
k.	**Scapula retraction**	**63.33%**
l.	**Wall push-ups**	**63.33%**
7.	When pain has diminished and the fracture has healed (~12 weeks post fracture), individuals with vertebral fracture should initiate an exercise program, ideally in consultation with a physical therapist or exercise physiologist, and informed by a baseline assessment so that it can be tailored to the patient. The exercise program should include progressive balance training and functional or muscle strength training, focusing on form first and then progressing to moderate intensity (i.e., 70-80% of estimated 1 repetition maximum (RM), or 8-12 RM, determined during baseline assessment - an estimated 1 RM is suggested as the safety of 1 RM testing has not been established).	83.33%
	There is evidence that progressive resistance training may address activity limitations and improve physical functioning in individuals with vertebral fracture. There are very little data on the effects of exercise on BMD in this population. Functional or muscle strength training should target muscles of upper and lower extremities, back extensor muscles and stabilizers of shoulder or pectoral girdle. When selecting exercises, consider fall risk and the loads on the spine (e.g., modify or avoid rapid, repetitive, weighted, sustained or end-range flexion or twisting of the spine). Clinical judgement is required regarding the selection of exercises, especially ones that involve overhead movements, or hip and lower back extension (e.g., bridging) in the presence of lumbar spine fractures	90.00%
a.	**Horizontal press. Examples: Push-up (wall, counter, floor); exercise band chest press.**	**66.67%**
b.	**Vertical press. Examples: Shoulder press (seated or standing with band or weights), Incline chest press, shoulder flexion and reach in supine**	**60.00%**
c.	**Horizontal Pull. Examples: seated row, scapular retraction, or protraction.**	**56.67%**
d.	**Vertical Pull. Examples: Lat pull down**	**56.67%**
e.	Lower body exercises. Examples: squat; half squat or sit to stand; supine bridging; hip extension; hip adduction; step up or climbing steps; lunges. (76.67%)	76.67%
f.	Balance exercises. Examples: walking forwards, backwards, and sideways while changing direction; avoiding and stepping over obstacles; getting down to and up off the floor; standing on one leg while doing movements with the other leg; standing on different types of surfaces; reaching out sideways; anticipatory adjustments; tandem or single leg standing	80.00%
8.	For individuals with fear-related beliefs (e.g., fear of pain, fractures, falling, movement, etc.), in addition to an exercise program as described in the previous page, consider education on coping techniques, body awareness, spine safe movement strategies, and movements to modify or avoid, being mindful of choosing words carefully to avoid creating fear and activity avoidance	96.67%
9.	Patients often have questions about whether they can participate in certain physical activities of leisure or daily life (e.g., lifting, yoga, golf, running, Pilates). If the patient has a history or a strong preference to perform an activity, the activity should be encouraged if it can be performed safely, or modified; however, the patient is encouraged to discuss their options with a health care provider. Factors that may affect decision-making include the patient's physical health, functional status, and history of the activity, as well as time since fracture and time on therapy.	96.67%

10. Some individuals may experience chronic pain after the fracture has healed (>12 weeks post fracture) and may not be thriving. Consider whether the patient would benefit from a referral to an interdisciplinary pain management clinic or psychologist that specializes in the biopsychosocial management of pain, or, to a physician for the medical management of pain.	90.00%
11. Research in younger people suggest that certain cognitive behavioral techniques may be effective for addressing body image concerns, but they have not been tested in older adults, or in individuals with body image issues specific to vertebral fractures. When body image is a concern at any stage post-vertebral fracture, health professionals could consider using education or approaches informed by cognitive behavioral therapy to enhance self-esteem and improve the perception of body image	83.33%
12. When weight management or early satiety are a concern for individuals at any stage post-vertebral fracture, consider the following strategies to ensure adequate intake:	
a. Referral to dietitian	93.33%
b. **Weight monitoring**	**66.67%**
c. Assess and educate regarding recommended daily intake of calcium and vitamin D	96.67%
d. Consider how functional impairments may impact food-related activities (e.g. bending over in the kitchen, standing in the kitchen, shopping etc.), and develop a plan to address this, or refer to an occupational therapist.	90.00%
e. Recommend smaller but more frequent meals throughout the day, additional snacks or finger foods.	80.00%
f. **Food fortification by means of natural foods (e.g., oil, cream, butter, eggs) and/or specific nutrient preparations (e.g., protein powder).**	**63.33%**
g. **Texture-modified foods if oral consumption is energy consuming or dysphagia is present**	**66.67%**
h. Create an eating environment that supports food intake (e.g., preparation of appealing food)	80.00%
i. Increasing variety in diet, considering individual food preferences	76.67%
A physical therapy assessment can include an assessment of spinal range of motion. Is it appropriate to assess lateral and forward flexion of the spine, and rotation, in someone with a vertebral fracture, or should it be avoided or modified, and if it should be modified, how would you do it?	Free text answer
Self-limited forward reach is used to assess balance, either alone or as part of a battery like the Berg Balance Test. Choose a statement that reflects your opinion on the safety of forward reach to assess balance in people with osteoporotic vertebral fractures.	
• Avoid the forward reach test in people with vertebral fractures as the potential risk is not worth it.	n = 4
• The forward reach test is safe and appropriate for individuals with vertebral fractures.	n = 2
• The forward reach test is safe in some scenarios and not others, as follows: <free text box>	n = 11
• Unsure	n = 13
	Free text answer
How do I determine when it is safe to begin a progressive exercise program with a patient after a vertebral fracture?	Free text answer
A resistance or strength training exercise prescriptions is often based on an assessment of a person's estimated 1 repetition maximum or other measures of capacity. How should we assess capacity and use the information from the assessment to prescribe resistance exercise intensity in individuals with vertebral fractures?	Free text answer
If you were dealing with a patient who had a history of participating in resistance exercise, and they had a vertebral fracture, how would you guide their return to activity? How would you assess and prescribe resistance exercises and exercise intensity in that person?	Free text answer
Are there specific resistance exercises (e.g., squats, deadlifts, overhead presses) or other types of exercise or physical activity that should be avoided or modified (and how to modify) in individuals with vertebral fractures	Free text answer

Patients are often given advice not to lift things, or bend or twist the spine. Others argue that flexion and twisting are necessary to maintain spinal mobility, and impossible to avoid, even if you are trying to maintain a neutral spine. What would your advice to a person with vertebral fracture be when it comes to lifting, bending or twisting?	Free text answer
Are there any other assessments or interventions that should be discussed in the non-pharmacological, non-surgical management of individuals with vertebral fractures? If so, describe them and why they should be considered, with references if you have any	Free text answer

Table S2. Modified Delphi survey for the second round. The first column reports the statements that were presented in the survey, the second the mean percentage agreement for each question. Based on panel size (n = 27), consensus upon each statement was reached if the rating of no more than 8 panelists was outside the 3-point region containing the median. The minimum percentage agreement for each statement of the second round was 70%. Consensus was reached on every statement.

Statements	Percentage agreement
or painful areas can be performed if it helps to manage pain, with education on when and how to safely	100%
st or occupational therapist to perform an assessment of fall risk and physical functioning, or a home	96.30%
namic, or soft orthoses) is not recommended for individuals with vertebral fractures. Some people ly after fracture, can benefit from using braces intermittently in the acute stage, if it means reducing nobilize or resume activities. However, evidence from clinical trials is heterogeneous and of very low Bracing should not be used routinely, and should not be used at all in subacute or chronic stages post-	80.00%
herapist or exercise physiologist, individuals with a vertebral fracture should initiate an individualized n as improving back extensor endurance, spinal mobility, physical functioning, and balance. The exercise program can be introduced within 4-12 weeks after vertebral fracture, as tolerated, or when acute fracture-related pain has diminished, or after 12 weeks, based on patient preference and clinician judgement. Referring to a physical therapist or exercise physiologist is recommended so that exercises can be phased in and tailored in accordance with the patient's needs, health conditions, abilities, fracture type and symptoms, and time post-fracture (e.g., start with focus on teaching body mechanics, individualized selection and phasing in of exercises). When access to physiotherapy or exercise physiologist is not possible, refer patients to print or online resources from a national osteoporosis society. Example exercises to consider are provided below, derived from clinical trials of exercise for people with vertebral fracture. There is a comment box at the end for you to comment or make suggestions.	
a. Supine thoracic extension e.g., gentle chest lift, shoulder flexion like “arm lengthener” exercise. Individuals with severe hyperkyphosis may require pillows to support the head and neck. Individuals with acute mid-thoracic compression fracture should not perform this exercise until the fracture has healed or the exercise does not exacerbate pain.	86.36%
b. Bridging in supine, with care to avoid thoracic flexion. Ensure patient can perform thoracic extension without pain prior to progression to bridging. May need to be avoided in individuals with acute lumbar fractures.	85.71%
c. Supine hip and leg extension, “pressing” into ground, bed, or firm surface or extending through leg (e.g., leg lengthener); individuals with acute lumbar compression fractures should avoid this exercise.	90.00%
d. Supine gentle head press	85.71%

e.	Lying in supine over a rolled-up towel placed lengthways along the back, to unload the spine, encourage spinal extension and stretch pectoral and front shoulder muscles. In the presence of hyperkyphosis, use one or more pillow under head for hyperkyphosis to support head and neck.	85.00%
f.	Head to wall	95.24%
g.	Supine scapula retraction. Progress to sitting position if pain-free.	100%
h.	Supine shoulder flexion, only within pain-free range of motion.	95.45%%
i.	Wall push-ups	80.95%
j.	Advanced: modified birddog using a chair to provide support and increase balance, perform alternate arm flexions, then alternate leg extensions. If pain-free and able to maintain balance, progress to alternate arm and leg at once.	83.33%

gressive exercise program at moderate or higher intensity? When pain has diminished and the fracture dividuals with vertebral fracture should initiate a progressive exercise program consistent with national osis society guidelines. Patients should, ideally, consult a physical therapist or exercise physiologist, so r a baseline assessment and tailored to the patient. 96.00%

How should a patient start a progressive exercise program? Start with instruction on body mechanics, functional or gentle exercises, with a focus on form, and exercise tolerance. If a person was practicing strength training prior to fracture and wishes to return to training, the physical therapist or exercise physiologist should review the exercise program that the patient was previously doing and modify or replace exercises that cannot be done with good form or that exacerbate pain.

The exercise program should include progressive balance training and functional or muscle strength training. Progress exercise intensity when pain has improved during daily activities (usually within 6-12 weeks after fracture), and the patient can perform gentle or low intensity exercises with good form with no pain exacerbation. Progress resistance exercise intensity gradually (e.g., no more than 10% increase in volume per week) to moderate intensity (i.e., 65-80% of estimated 1 repetition maximum (RM), or 8-12 RM, determined during baseline assessment - an estimated 1 RM, with a few repetitions in reserve, or rating of perceived exertion strategy is suggested as the safety of 1 RM testing has not been established).

There is evidence that progressive resistance training may address activity limitations and improve physical functioning in individuals with vertebral fracture. There are very little data on the effects of exercise on BMD in this population. Functional or muscle strength training should target muscles of upper and lower extremities, back extensor muscles and stabilizers of shoulder or pectoral girdle. When selecting exercises, consider fall risk and the loads on the spine (e.g., modify or avoid rapid, repetitive, weighted, sustained or end-range flexion or twisting of the spine). Clinical judgement is required regarding the selection of exercises, especially ones that involve overhead movements.

ining exercises that have been included in prior studies are listed below. There is a comment box at gestions.

a.	Horizontal press, for example: push up (wall, counter, floor); exercise band chest press	85.00%
b.	vertical press, for example: shoulder press (standing with band, tubing, or weights); incline chest press (standing with band, tubing, or weights); shoulder flexion and reach in supine	85.00%
c.	horizontal pull, for example: - standing or seated row (with band, tubing, or weights); scapular retraction and protraction	89.47%
d.	vertical pull, for example: lat pull down (with band, tubing, or weights)	77.78%
e.	lower body, for example: squat, half squat, sit to stand; supine bridging; hip extension; hip abduction; step up or climbing step; lunges	85.00%
f.	balance, for example: walking forwards, backwards, and sideways while changing direction; avoiding and stepping over obstacles; getting down to and up off the floor; standing on one leg	100%

while doing movements with the other leg - single leg stance at the kitchen counter with eyes closed; standing on different types of surfaces; reaching out sideways; anticipatory adjustments; tandem or single leg standing	
re sometimes considered risky for people with one or more vertebral fractures, including: deadlift, leep squats, spinal flexion movements in yoga, golf, ball sports, or anything involving sudden, end- or end-range spinal twisting. Some exercises, like yoga, squats, overhead presses, and modified t can perform them with good alignment, or if they could be modified to be safer, ideally supervised	95.83%
re-existing back or radicular pain, decreased mobility due to pain, increase or sudden worsening of tness of breath might indicate a new fracture or progression of an existing fracture, and the need for l back to physician.	96.00%
l follow national guidelines or their health care provider's recommendations related to protein, calcium ead to inadequate intake of nutrients and calories, and loss of bone and muscle. When weight rn for individuals at any stage post-vertebral fracture, consider the strategies below to ensure adequate There is a comment box at end for you to comment or make suggestions.	
a. Weight monitoring	91.67%
b. Food fortification by means of natural foods (e.g., eggs, oil, avocado, milk powder, nuts, nut butters), or specific nutrient preparations (e.g., protein powder, energy bars).	90.48%
c. Texture-modified foods if oral consumption is energy consuming or dysphagia is present	94.24%
n should be avoided in people with an acute vertebral fracture or multiple fractures. If the fracture has ıssessment with the potential risk, and whether you can assess functional mobility via observation of bed or chair). If it is necessary to assess spinal range of motion, consider a modified version, or cue d. Do not continue if the movement is painful.	95.83%
f-limited forward reach (i.e., to assess balance) should be avoided in all people with vertebral painful fractures. Others think that it may be safe in some scenarios. Factors that might influence whether shoulder flexion to 90 degrees is pain free, if you can ensure they are not reaching forward and a spotter, if standing balance is not impaired, if there is no fracture-related pain, or if it is relevant for task they are having difficulty with.	95.83%
t things, or bend or twist the spine. However, lifting things, forward bending, and twisting the spine are often impossible to completely avoid in the daily life. Tips on safe movement for patients include: • Consult a physical or occupational therapist on safe movement during activities of leisure or daily life; • Bend at the hips, knees and ankles rather than rounding the back. • Rather than twisting the torso, use a step-to turn, so that the trunk, knees and toes face the same direction. • When holding objects out front, hold them close to the body, and when holding something in hands at sides of body, split and distribute the weight evenly across both hands (e.g., carrying shopping bags). • Use slow and controlled movements rather than sudden movements. • Look for print or online resources from a national osteoporosis society.	96.00%

Table S3. Demographics characteristics of the panelists for the first and second round.

	First round (n = 31)	First round (n = 27)
Age (mean ± SD, median, range)	55 ± 11 years, 57 years, range 30-73 years	54 ± 12 years, 57 years, range 30-70 years
Gender (n, %)	Female (n = 18, 58%) Male (n = 13, 42%)	Female (n = 20, 74%) Male (n = 7, 26%)
Ethnicity (n, %)	White (n = 26, 84%)	White (n = 21, 78%)

	Asian (n = 4, 13%) Hispanic (n = 1, 3%)	Asian (n = 4, 15%) Hispanic (n = 1, 4%) Prefer not to say (n = 1, 4%)
Occupation (n, %)	Physiotherapist (n = 10, 32%) Rheumatologist (n = 5, 16%) Geriatrician (n = 4, 13%) Family Physician (n =2, 7%) Internist (n = 1, 3%) Orthopaedic surgeon (n = 1, 3%) Endocrinologist (n = 1, 3%) Kinesiologist (n = 1, 3%) Certified exercise physiologist (n = 1, 3%) Other (n = 5, 16%)	Physiotherapist (n = 9, 33%) Geriatrician (n = 5, 19%) Rheumatologist (n = 4, 15%) Family Physician (n =1, 4%) Other (n = 8, 30%)
Years of practice (mean ± SD, median,)	27 ± 13 years, 25 years, range: 1-49 years	22 ± 14 years, 20 years, range: 1-49 years

Table S4. Exercises to consider when acute pain has diminished (usually starting within 4-12 weeks after the vertebral fracture).

Therapeutic goal	Example exercises
Improving back extensor endurance and spinal mobility: Start with supine exercises	Supine shoulder press
	Gentle head press
	Hip and leg extension, “pressing” into ground, bed, or firm surface or extending through leg (e.g., leg lengthener) NOTE. Individuals with acute lumbar compression fractures should avoid this exercise.
	Supine thoracic extension (e.g., gentle chest lift, shoulder flexion like "arm lengthener" exercise) NOTE. Individuals with severe hyperkyphosis may require pillows to support the head and neck. Individuals with acute mid-thoracic compression fracture should not perform this exercise until the fracture has healed or the exercise does not exacerbate pain.
	Supine lying over rolled up towel placed lengthways along the back to unload the spine, encourage spinal extension, and stretch pectoral and front shoulder muscles NOTE. In the presence of hyperkyphosis, use one or more pillow under head to support head and neck.
Improving back extensor endurance and spinal mobility: Intermediate	Head to wall in the standing position
	Bridging in supine, with care to avoid thoracic flexion NOTE. Ensure patient can perform thoracic extension without pain prior to progression to bridging. May need to be avoided until after 12 weeks after lumbar fractures.
	Trunk extension in prone position
Improving back extensor endurance and spinal mobility:	Modified birddog (i.e., using a chair to provide support and increase balance, perform alternate arm flexions, then alternate leg extensions)

Advanced	NOTE. If pain-free and able to maintain balance, progress to alternate arm and leg at once.
Improving shoulder mobility and stabilizing pectoral girdle	Supine shoulder flexion NOTE. Only within pain-free range of motion.
	Scapular retraction (e.g., sitting position with hands behind head and elbows pointing to sides)
	Wall push-ups NOTE. May progress to kitchen counter or floor.

Table S5 Exercises to consider after the vertebral fracture has healed (usually 12 weeks after the fracture).

Therapeutic goal	Example exercises
Improving chest, triceps, and shoulder strength: Horizontal press	Push-up (wall, counter, floor) Exercise band chest press
Improving chest, triceps, and shoulder strength: Vertical press	Shoulder press (seated or standing with band or weights) Incline chest press Shoulder flexion and reach in supine
Improving shoulder and upper back strength: Horizontal pull	Seated row Scapular retraction, protraction
Improving upper back strength: Vertical pull	Lat pull down
Improving lower back and lower body strength	Squat, half squat or sit to stand Supine bridging Hip extension Hip abduction Step up or climbing steps Lunges
Improving balance	Walking forwards, backwards, and sideways while changing direction Avoiding and stepping over obstacles Getting down to and up off the floor Standing on one leg while doing movements with the other leg Standing on different types of surfaces Reaching out sideways, anticipatory adjustments Tandem or single leg standing