

ORIGINAL RESEARCH

Prevention and management of osteoporotic fractures by non-physician health professionals: a systematic literature review to inform EULAR points to consider

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ABSTRACT

Objective To perform a systematic literature review (SLR) about the effect of non-pharmacological interventions delivered by non-physician health professionals to prevent and manage osteoporotic fractures.

Methods Eight clinical questions based on two criteria guided the SLR: (1) adults≥50 years at high risk of osteoporotic fracture and (2) interventions delivered by non-physician health professionals to prevent and manage osteoporotic fractures. Interventions focused on diagnostic procedures to identify risk of falling, therapeutic approaches and implementation strategies. Outcomes included fractures, falls, risk of falling and change in bone mineral density. Systematic reviews and randomised controlled trials were preferentially selected. Data were synthesised using a qualitative descriptive approach.

Results Of 15 917 records, 43 articles were included. Studies were clinically and methodologically diverse. We identified sufficient evidence that structured exercise, incorporating progressive resistance training delivered to people who had undergone hip fracture surgery, and multicomponent exercise, delivered to people at risk of primary fracture, reduced risk of falling. The effectiveness of multidisciplinary fracture liaison services in reducing refracture rate was confirmed. There was insufficient evidence found to support the effectiveness of nutrients and falls prevention programmes in this patient population.

Conclusion Despite study heterogeneity, our SLR showed beneficial effects of some interventions delivered by non-physician health professionals and the positive impact of multidisciplinary team working and patient educational approaches to prevent and manage osteoporotic fractures. These results informed a EULAR taskforce that developed points to consider for non-physician health professionals to prevent and manage osteoporotic fractures.

Key messages

What is already known about this subject?

Non-pharmacological interventions delivered by non-physician health professionals to prevent and manage osteoporotic fractures are increasingly important.

What does this study add?

- ► The literature about common non-pharmacological interventions delivered by non-physician health professionals to prevent and manage osteoporotic fractures in adults 50 years or older is synthesised and presented.
- ► Evidence about the effect of many nonpharmacological interventions delivered by nonphysician health professionals to reduce fragility fractures remains limited.

How might this impact on clinical practice?

► This systematic literature review informed a taskforce to develop EULAR points to consider for non-physician health professionals to prevent and manage fragility fractures in adults 50 years or older.

INTRODUCTION

By 2040, an estimated 319 million adults aged 50 years or more worldwide will be at high risk of osteoporotic fracture. While Asian populations will carry much of this burden, other nationalities, including European, will see risk rise. The morbidity, mortality and cost associated with osteoporotic fractures, and the availability of effective pharmacological treatments for prevention and management, highlight the importance of identification and treatment of 'high-risk' individuals. Yet,



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Alongside pharmacological agents, non-pharmacological interventions, such as exercise, fall prevention measures and adequate intake of key nutrients, are important in the prevention and management of osteoporosis. Two previous systematic reviews reported some evidence that interventions delivered by dietitians, nurses, physiotherapists and pharmacists, working alone or in multidisciplinary teams, can positively influence health-related outcomes for people with, or at risk of osteoporosis, including quality of life (QoL), calcium intake, medication compliance and bone mineral density (BMD) testing. 1112

Yet, despite evidence for the effectiveness of interventions provided by non-physician health professionals (HPs), implementation may be suboptimal in many countries. Arguably, there is scope for greater involvement of non-physician HPs in primary and secondary fracture prevention. Recent recommendations by the EULAR and European Federation of National Associations of Orthopaedics and Traumatology are available to guide physicians in the management of patients 50 years and older with a recent fragility fracture and prevention of subsequent fractures, ¹³ and updated European guidance exists to streamline healthcare for diagnosis and management of osteoporosis in postmenopausal women. ¹⁴ However, international recommendations for non-physician HPs are lacking.

To address this gap, a commissioned taskforce has developed the first EULAR points to consider for non-physician HPs in the prevention and management of fragility fractures in adults 50 years or older. A systematic literature review (SLR) was undertaken to inform the development of these points to consider.

METHODS

We aimed to identify and appraise the up-to date scientific literature about the effect of non-pharmacological interventions delivered by non-physician HPs to prevent and manage osteoporotic fracture in high-risk adults, age 50 years or more. High risk of osteoporotic fracture was categorised using BMD values for low bone mass (osteopenia) and osteoporosis specified by WHO, ¹⁵ and/or short-term probability of fracture. The definition we used for high-risk adults is detailed in table 1.

The aim of this SLR was to inform an international EULAR taskforce on a broad range of issues related to non-physician HPs' interventions. Non-physician HPs deliver different interventions in different countries. Therefore, we focused our review on interventions that could potentially be delivered by non-physician HPs, independent of whether a study was led by a non-physician HP or not.

A SLR for each of eight clinical questions (table 2), formulated and consensually agreed by the taskforce,

Table 1 Definitions used by the taskforce to identify studies that included individuals at high risk of osteoporotic fracture

Osteopenia	T score ≤-1.0 to -2.5 SD
Osteoporosis	T score ≤-2.5 SD
FRAX 10-year probability of a major* osteoporotic fracture	≥20% (age independent)
FRAX 10-year probability of hip fracture	≥3% (age independent)
FRAX NOGG threshold	40-90 years (age dependent)

T score, unit of SD from the mean for bone mineral density compared with a healthyyoung adult.

FRAX intervention thresholds vary between countries.

*A clinical spine, hip, forearm or humerus fracture.

FRAX, Fracture Risk Assessment Tool; NOGG, National

Osteoporosis Guideline Group.

was undertaken by a research fellow (NW) with guidance from the taskforce convenors (EH, JA) and a methodologist (TAS). The methods for each SLR, including the research question and inclusion/exclusion criteria, were agreed on and documented within a joint taskforce meeting. The taskforce comprised 2 patient research partners, 1 dietitian, 1 geriatrician and 1 nurse, 3 occupational therapists, 2 orthopaedic surgeons, 4 physiotherapists, 1 specialist in physical medicine and rehabilitation and 5 rheumatologists, drawn from 10 European countries.

The conduct of the review was informed by Cochrane principles. ¹⁶ A Participants, Interventions, Comparisons, Outcomes and Study design approach¹⁷ was adopted for each question followed by a systematic search across international electronic databases (Medline/PubMed, Embase and Cumulative Index to Nursing and Allied Health Literature (CINAHL) for relevant literature published between January 2007 and October 2017 (online supplementary file 1). Searches were based on two critieria: (1) adults≥50 years of age at high risk of primary or secondary osteoporotic fracture and (2) interventions delivered by non-physician HPs to prevent and manage osteoporotic fractures. Interventions included diagnostic procedures to identify risk of falling, therapeutic approaches (eg, structured exercise, education, falls prevention programmes) and implementation strategies. Key outcomes were fractures and falls (where the accepted definition of a fall was an unexpected event in which the participants come to rest on the ground, floor or lower level¹⁸). High risk of falling and change in BMD were included as surrogate end points. Fractures in adults age ≥50 years were assumed to be fragility fractures unless at the ankle, hands and feet, skull and face, ¹⁹ or as a result of high-intensity trauma.

Study selection

Following removal of duplicates, two review authors (NW and EH) independently selected eligible studies and achieved consensus on which articles to include.



Table 2	Clinical questions
1	Which diagnostic procedures, undertaken by non-physician health professionals (HPs), are recommended in the assessment of risk of falling in adults at high risk of primary or secondary osteoporotic fracture?
2	What is the effect (including cost-effectiveness and safety) of non-pharmacological treatments provided by non-physician HPs after osteoporotic fracture?
3	What is the effect (including cost-effectiveness and safety) of non-pharmacological treatments provided by non-physician HPs in adults at high risk of primary osteoporotic fracture?
4	What is the effect of strategies undertaken by non-physician HPs to implement recommendations for the prevention and management of osteoporotic fracture by potential stakeholders?
5	What is the effect of multi-disciplinary team care on health outcomes for persons at high risk of primary or secondary osteoporotic fracture?
6	What is the effect of interventions provided by non-physician HPs to enhance adherence to antiosteoporosis medicines in adults at high risk of primary or secondary osteoporotic fracture?
7	What is the remit of the rheumatology review as undertaken by non-physician HPs with respect to bone health across all rheumatic conditions?
8	What bone health education should non-physician HPs deliver to people with rheumatic disease, specifically younger adults (up to 50 years of age)?

Publications investigating interventions commonly undertaken by non-physician HPs were included even if the professional group delivering the intervention was not specifically stated or non-physician HPs were not sole providers. Articles were excluded if published in languages other than English. Systematic reviews and randomised controlled trials (RCTs) were preferentially selected, although (quasi) randomised and non-randomised studies were included. Systematic reviews with sufficient quality were considered to cover the time until their search ended. Studies with small sample sizes (<50 participants) were excluded.

Data extraction and quality assessment

Data, including research design, population characteristics, interventions and outcomes were extracted by the research fellow from all selected articles describing diagnostic procedures, therapeutic approaches and implementation strategies. Systematic reviews were evaluated using AMSTAR 2—A MeaSurement Tool to Assess systematic Reviews, ²⁰ while risk of bias (RoB) judgements about primary studies followed a domain-based assessment as recommended by the Cochrane collaboration.²¹ We characterised a 'partial Yes' response in a critical domain of AMSTAR 2 as a non-critical weakness. Risk of performance bias was considered unclear in studies in which blinding of participants and/or personnel was not feasible. Evidence was classified in accordance with the Oxford Centre for Evidence-based-Medicine 2011 Levels of Evidence, ²² but upgraded or downgraded in response to methodological strengths and weaknesses.

Data synthesis

Evidence about the effect of interventions was synthesised descriptively and rated using four categories: sufficient; some; insufficient; and insufficient evidence to determine, as described by Ryan *et al*²³ (see online supplementary file 1, table 1). Studies describing mixed

populations (participants with and without osteoporotic fracture) were allocated based on the proportion of participants with fracture, that is, if >50% of the population had at least one fragility fracture, the study was allocated to question 2; if \leq 50%, the study was allocated to question 3. If more than one published article reported data from a single cohort, the most up-to-date publication was included in the analysis.

RESULTS

The database searches yielded 15917 citations. Following removal of duplicates, we screened 11 195 titles and or abstracts. Two hundred and eighteen full-text articles were selected for review, of which 182 were rejected. Seven additional studies were identified from other sources, for example, the reference lists of selected publications. No articles were found to answer questions 7 and 8. Subsequently, 43 articles were included in data analysis and synthesis (figure 1).

Data were extracted from 1 review of systematic reviews, 17 systematic reviews, 1 narrative review, 20 RCTs, one quasi-RCT and 3 non-randomised studies. Meta-analyses for outcomes of interest were available in 9 papers, ^{24–32} with participant numbers from 116²⁴ to 19 519. ²⁵ Sample size of primary studies varied from 6229 participants ³³ to 70 participants. ³⁴ Four studies had a sample size of fewer than 100 participants. ^{34–37}

Overall confidence in systematic review findings was high in two reviews, ^{26 38} but low or critically low in the remainder (online supplementary file 1, table 2). Assessment of RoB of primary randomised studies showed that eight were at unclear RoB due to issues affecting methods of randomisation, while allocation concealment was unclear in over half of the studies. Nearly 50% of the included studies were at high or unclear risk of detection bias while seven studies were considered at risk of attrition bias. Recruitment and allocation concealment were

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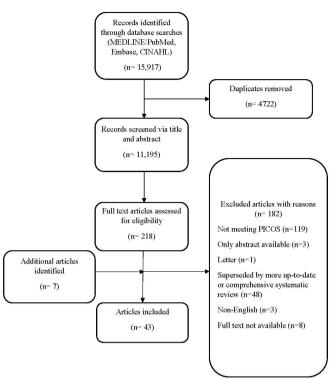


Figure 1 Flow diagram of articles included in the systematic literature review. PICOS, Participants, Interventions, Comparisons, Outcomes and Study design.

assessed as unclear in the non-randomised studies. Analysis was via intention to treat in 60% of the RCTs included in this SLR, although this was interpreted differently across studies. Eleven RCTs were adequately powered for the outcome of interest.

Clinical questions

Which diagnostic procedures, undertaken by non-physician HPs, are recommended in the assessment of risk of falling in adults at high risk of primary or secondary osteoporotic fracture?

Evidence about diagnostic procedures to assess risk of falls was extracted from one narrative review.³⁹ The Stopping Elderly Accidents, Deaths and Injuries algorithm incorporates a stepped approach to falls risk screening, assessment and intervention, and is recommended for use. Key initial screening questions help to identify people who have fallen in the past year, feel unsteady or are fearful of falling. Responses guide further assessment. Subsequent screening, if required, includes the Timed Up and Go Test, ⁴⁰ with the Four-Stage Balance Test, ⁴¹ the Five-Times Sit-to-Stand Test⁴² and other components of a multifactorial risk assessment if indicated. Recommended components include: a detailed falls history; medicines consumption and environmental and social factors associated with risk of falling; footwear and home hazards; evaluation of bodily systems, for example, via blood pressure monitoring; Fracture Risk Assessment Tool; and assessment of cognition and mental health. Although multiple tools are available to support the assessment of constituent factors associated with risk of falls, no specific tool is recommended, thereby reflecting the need for an individually tailored assessment.

What is the effect (including cost effectiveness and safety) of non-pharmacological treatments provided by non-physician HPs after osteoporotic fracture?

The evidence for this question clustered around (1) exercise, (2) nutrients including vitamin D plus calcium and oral nutritional supplements, (3) orthoses and (4) fall prevention programmes (table 3).

Exercise

Three meta-analyses and two RCTs contributed to the evidence synthesis about the effect of exercise on bone health-related outcomes in people who had experienced a vertebral fracture, ²⁷ any osteoporotic fracture ⁴³ or had undergone hip fracture surgery. ²⁸ ²⁹ ³⁵ Interventions included structured exercise of different types, ²⁸ balance training ⁴³ and progressive resistance exercise (PRE). ²⁹ ³⁵ Outcomes included factors associated with risk of falls, for example, mobility, knee-extension strength and balance.

After hip fracture surgery, structured exercise, in particular interventions incorporating PRE for 2-3 months, led to statistically significant improvements in mobility compared with usual care or no intervention (standardised mean difference (SMD)=0.501, 95% CI 0.297 to 0.705; p<0.001). Balance and leg strength were also favourably affected by the intervention, although one RCT showed that PRE, in addition to routine physiotherapy delivered between postoperative days 2 and 8, was not advantageous when compared with routine physiotherapy alone.³⁵ For people with vertebral fractures, structured exercise compared with usual daily activities reduced reports of pain and improved QoL, but did not improve risk of falling.²⁷ However, the number of trials and participants available for pooling in meta-analysis was small.

Nutrients including vitamin D plus calcium and oral nutritional supplements

The effect of vitamin D supplementation on fractures and falls in people with a history of osteoporotic fracture was investigated in a Cochrane review subgroup analysis²⁶ and one RCT. 44 Pooled data from 6134 participants (2737) taking daily vitamin D (800 IU) plus calcium (1000 mg) for a minimum of 12 months) showed no significant difference between the intervention and control groups for subsequent risk of hip fracture (risk ratio 1.02, 95% CI 0.71 to 1.47; p=0.26) or any fracture (risk ratio 0.93, 95% CI 0.79 to 1.10; p=0.84). Fracture outcomes were also unaffected by a single loading dose of vitamin D3 administered to older adults within 7 days of hip fracture surgery. 44 In this trial, participants received either cholecalciferol (250 000 IU) or a placebo injection in addition to supplementation with daily oral vitamin D (800 IU) and calcium (500 mg). Falls rate at 4 weeks was significantly lower in the intervention group compared with the

Table 3 Characteristics	of interv	Characteristics of intervention studies and their main fin	idings: non-pharmacological treatments provided after osteoporotic fracture	s provided after osteoporotic fracture	
Authors, country, setting if stated	Study design	Population characteristics; number of participants for outcomes of interest	Intervention; healthcare professional if stated	Main findings LoE	щ
i) Exercise					
Diong <i>et al</i> hospital and community ²⁸	MA	Patients after HF surgery; 13 studies (n=1903)	Structured exercise, mean (SD) dose 37 (31) h	Overall mobility was significantly better in the IG versus CG at 12 (6) weeks (SMD=0.35; 95% CI 0.12 to 0.58). Larger effects with PRE	
Lee et al hospital and community ²⁹	MA	Patients after HF surgery; 6 studies (n=420)	Progressive resistive exercise	Significant improvement in overall mobility in IG compared with CG 1 (SMD=0.501; 95% CI 0.297 to 0.705; p<0.001)	
Kronborg <i>et al</i> Denmark, inpatients ³⁵	RCT	Patients after HF surgery 1.Group 1 (n=45); 2. Group 2 (n=45)	 PRE+routine physiotherapy Routine physiotherapy Physiotherapists 	No significant between group difference in max. isometric knee-extension strength in the fractured limb in % of the non-fractured limb at d/c or postoperative day 10	
Liu <i>et al²⁷</i>	MA	Patients with OVF; three studies (n=128)	Exercise programmes	No influence on TUG (SMD=-0.36, 95% CI -0.96 to 0.24; p=0.24) 2	
Mikó e <i>t al</i> Hungary, community ⁴³	RCT	Women with OP fracture 1. Group 1 (n=49) 2. Group 2 (n=48)	 Balance training Usual care Physiotherapists 	Significantly greater improvement in balance and fewer falls at 12 2 months in the balance training group	
ii) Nutrients including vital	min D plu	ii) Nutrients including vitamin D plus calcium and oral nutritional supp	plements		
Avenell et al community ²⁶	A	Patients with a history of OP fracture; 4 studies (n=6134)	Vitamin D (800 IU) plus calcium (1000 mg) daily for a minimum of 12 months	No significant difference between IG and CG in incidence of HF (risk ratio=1.02, 95% Cl 0.71 to 1.47) or any new fracture (risk ratio=0.93, 95% Cl 0.79 to 1.10).	
Mak <i>et al</i> Australia inpatients ⁴⁴	RCT	Patients after HF surgery 1.Group 1 (n=106); 2. Group 2 (n=104)	Single dose of 250000 IU vitamin D3 Placebo	Statistically significant reduction in falls incidence in IG at 4 weeks. 2 No significant difference in fractures between groups at 4 weeks.	
Myint <i>et al</i> Hong Kong inpatient ⁴⁵	RCT	Patients after HF surgery 1.Group 1 (n=58); 2. Group 2 (n=58)	 Daily oral nutritional supplement for 28 days Usual care 	No significant between group difference in Elderly Mobility Scale 4 2 weeks postdischarge.	
iii) Orthoses					
Newman <i>et al</i> inpatient, outpatient and community ³⁸	SR	Patients with OVF; 12 studies (n=626)	Spinal orthoses	2/12 studies showed improvements in balance with orthoses 2	
de Morais Barbosa <i>et al</i> Brazil, community ³⁷	RCT	Women with OP ±fracture 1.Group 1 (n=44); 2. Group 2 (n=45)	Custom foot orthoses No intervention	Significant between group difference in TUG (p<0.001) and BBS 2 (p<0.001) favouring orthoses at 4 weeks	
iv) Falls prevention programmes	mmes				
Visschedijk et al inpatient and community ⁴⁶	SR	Patients with HF; 4 studies (n=221)	Home-based rehabilitation, community exercise programme, ambulatory training	2/4 studies showed a statistically significant reduction in fear of falling	
van Ooijen <i>et al</i> The Netherlands, rehabilitation centre ³⁴	RCT	Patients with HF 1.Group 1 (n=14); 2. Group 2 (n=16); 3. Group 3 (n=16)	 Treadmill training with visual context Conventional treadmill training Usual physical therapy Physical therapists 	No significant difference in fall rate between groups at 12 months. 2	Osteopo
				Gunitado	

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Table 3 Continued					
Authors, country, setting if stated	Study	Population characteristics; number of participants for outcomes of interest	Intervention; healthcare professional if stated	Main findings	LOE
Di Monaco <i>et al</i> Italy, rehabilitation hospital and community ⁴⁹	RCT	Women with HF 1. Group 1 (n=78) 2. Group 2 (n=75)	MDT programme +telephone call post d/c MDT programme Occupational therapist	 MDT programme +telephone call post 14.1% women in the IG and 13.3% in the CG sustained at least d/c MDT programme 2.34). 	2
Di Monaco <i>et al</i> Italy, community ⁵⁰	Quasi- RCT	Women with HF 1. Group 1 (n=45) 2. Group 2 (n=50)	 MDT programme +home visit post d/c MDT programme Occupational therapist 	Significantly lower proportion of fallers in IG at 6-month post d/c compared with CG (Adj OR 0.275; 95% CI 0.081 to 0.937; p=0.039)	2
Berggren <i>et al</i> Sweden inpatient and outpatient ⁵¹	RCT	Patients after HF surgery 1. Group 1 (n=102) 2. Group 2 (n=97)	Geriatric rehabilitation +home visit At 12 mo Care on orthopaedic ward the IG an Physiotherapists, occupational therapists p=0.063)	At 12 months, crude fall-incidence rate was 4.16/1000 days in the IG and 6.43/1000 days in CG (IRR 0.64, 95% CI 0.40 to 1.02; p=0.063)	0
Shyu <i>et al</i> Taiwan, inpatient RCT and community ⁵²	RCT	Patients after HF surgery 1. Group 1 (n=79) 2. Group 2 (n=81)	 Orthogeriatrics, rehabilitation +d/c plan Usual care Nurse, Physician, Physical Therapist 	29.6% of IG and 34.2% of CG had cognitive impairment. Only participants without cognitive impairment showed reduced fall occurrence (OR=0.47; 95% CI 0.25 to 0.86) at 2 years.	2

Adj. Adjusted; BBS, Berg Balance Scale; CG, control group; d/c, discharge; HF, hip fracture; IG, intervention group; IRR, incidence rate ratio; LoE, level of evidence; MA, meta-analysis; MDT, multidisciplinary team; OP, osteoporosis; OR, Odds ratio; OVF, osteoporotic vertebral fracture; PRE, progressive resistive exercise; RCT, randomised controlled trial; RR, risk ratio; RR Relative Risk; SMD, standardised mean difference; SR, systematic review; TUG, Timed Up and Go. placebo group (6.3% vs 21.2%; χ^2 =4.327; p=0.024), even though there was no statistically significant improvement in gait velocity.

Additionally, one small RCT investigated the effect of an oral nutritional supplement (containing 18–24g of protein and 500kcal) versus usual care on factors associated with risk of falls in older adults following hip fracture surgery. However, at 4weeks post discharge, there were no statistically significant differences in the Elderly Mobility Scale.

Orthoses

One systematic review of randomised and nonrandomised studies investigated the effect of spinal orthoses in the management of people with osteoporotic vertebral fracture (OVF).³⁸ Twelve studies with mainly small sample sizes and at RoB showed mixed results. No recommendations could be made about the use of spinal orthoses in people with an acute OVF (0-3 months), although complications from the use of rigid orthoses and casting, including falls and fractures, were reported. Three studies, incorporating 220 participants with a subacute OVF, reported wearing a semirigid brace for several hours a day for 6 months improved back extensor and abdominal strength, reduced postural sway and thoracic kyphosis angle compared with an inactive control group. Thoracolumbar corsets in women with no acute OVF but a history suggestive of fracture were not supported. A single trial, ³⁷ in which custom foot orthoses or no orthoses were worn by persons with a history of vertebral or non-vertebral osteoporotic fracture, reported a positive impact on balance favouring the intervention. However, this study was at high risk of detection bias.

Falls prevention programmes

One systematic review investigating fear of falling in patients following hip fracture included four studies comparing the effect of interventions such as home rehabilitation and community exercise with conventional care or a control group. 46 Two studies showed a statistically significant reduction in fear of falling, measured by the Falls Efficacy Scale, 47 48 although both had small sample sizes. An additional five studies 34 49-52 investigated the effect of single and multicomponent fall prevention interventions in older adults who had undergone hip fracture surgery. Data about falls occurring after discharge from hospital were collated during face-to-face or telephone interviews in four studies and by a daily calendar diary in one study. Follow-up took place between 4 and 24 months. All of the studies had relatively small sample sizes and three were at high risk of detection bias.

Of the single interventions, neither a brief telephone call targeted towards reducing falls made by an occupational therapist to participants postdischarge, ⁴⁹ nor a 6-week programme of treadmill walking focused towards visually guided stepping in relation to obstacles, ³⁴ resulted in a statistically significant reduction in the proportion of fallers or the rate of falls when compared

of selection bias.

Evidence for the effect of multicomponent interventions, incorporating inpatient geriatric care, rehabilitation and home assessment, and falls hazard reduction in older adults following hip surgery, also revealed mixed outcomes.^{51 52} One RCT based in Taiwan, in which participants received in-home rehabilitation for 3 months post discharge, reported a lower occurrence of falls in noncognitively impaired participants in the first 2 years after discharge compared with a control group (OR=0.47, 95% CI 0.25 to 0.86; p=0.014). ⁵² This benefit was not seen in participants with cognitive impairment. In contrast, Berggren et at 1 found no statistically significant difference in fall incidence between groups at 1 year following a similar multifactorial falls-prevention programme (incidence rate ratio (IRR) 0.64, 95% CI 0.40 to 1.02; p=0.063), although there was a trend favouring the intervention. In this study, postdischarge rehabilitation was provided if needed.

What is the effect (including cost effectiveness and safety) of nonpharmacological treatments provided by non-physician HPs in adults at high risk of primary osteoporotic fracture?

One systematic review,⁵³ three meta-analyses²⁴ ³⁰ ³¹ and three primary studies^{54–56} contributed evidence about exercise interventions. Two RCTs explored falls prevention programmes^{36 57} and two systematic reviews^{58 59} and one RCT⁶⁰ investigated nutrient supplementation. One systematic review explored patient education strategies⁶¹ (table 4).

Exercise

Evidence from seven publications was synthesised to investigate the effect of exercise on risk of falling, 30 31 53 BMD, ²⁴ ³⁰ ⁵³ incidence rate of fractures ⁵⁴ ⁵⁶ and falls. ⁵³ ⁵⁵ Available evidence from one meta-analysis³¹ suggests that multimodal exercise can reduce risk of falling in participants at high risk of primary osteoporotic fracture compared with a control group, through improvements in mobility (SMD=-0.56, 95% CI -0.81 to 0.32) and balance (SMD=0.5, 95% CI 0.27 to 0.74). Likewise, regular multimodal exercise incorporating weight-bearing aerobic exercise and resistance training undertaken for ≥1 year appears to confer positive benefits on BMD,⁵³ ⁵⁵ unlike whole-body vibration³⁰ and low impact mind-body conditioning exercise.²⁴

Two primary studies, 54 56 one randomised and one nonrandomised, reported fewer fractures in women with low bone mass undertaking regular long-term multimodal exercise at least twice a week compared with a control group. Korpelainen et al^{64} stated a fracture IRR of 0.68 (95% CI 0.34 to 1.32) following analysis of 7-year data collected from a national hospital discharge register

and hospital records, while Kemmler et $a\tilde{l}^{6}$ reported a rate ratio of 0.42 (95% CI 0.20 to 0.86) drawing on data gathered via questionnaires and interviews. The effect of exercise on falls incidence was variable. ⁵³ ⁵⁵ In one study, the number of fallers increased following a 12-month multimodal exercise intervention, although the mechanism for this is unclear.⁵⁵

Nutrients including vitamin D plus calcium and oral nutritional supplements

Publications described nutritional supplementation with vitamin D analogues, ⁵⁸ protein ⁵⁹ and vitamin K. ⁶⁰ Change in BMD was the primary outcome in all studies and was assessed between 9weeks and 48months. One study⁶⁰ reported fracture incidence as a secondary outcome. All study participants were women. Data synthesis showed that supplementation with vitamin D analogues (alfacalcidol and 2-methylene-19-nor-(20S)-1α,25-dihydroxyvi tamin D_o (2MD)) and daily vitamin K1 (5 mg), had no positive impact on BMD when assessed between 6 and 48 months. Evidence for the effect of protein interventions was limited and the findings were contradictory. Two high-quality RCTs included in a systematic review by Koutsofta et al⁵⁹ reported no significant change in BMD from daily consumption of dietary non-soy protein $(>90 \,\mathrm{g/day})$ or whey isolate supplement $(30.1 \,\mathrm{g}\,\mathrm{in}\,250 \,\mathrm{mg})$ supplement) for 24 months when compared with control groups. Results from three other RCTs in the review were conflicting. In one study, total body BMD reduced after 8 weeks of dietary supplementation, while in another, it increased at 24 months. The remaining RCT in the review reported improvement in total body BMD but not at other sites following 12-month supplementation with dietary protein and supplement (86g/day including 6g whey protein isolate). The sample size in all of these trials was small and the quality assessment rating was low.⁵⁹

Falls prevention programmes

Two RCTs, ^{36 57} one of which randomised over 1000 participants,⁵⁷ evaluated the effect of a multicomponent falls prevention programme compared with usual care on rate of falls in community dwelling older adults with osteoporosis, and/or other risk factors for fall and fracture. The Nijmegen Falls Prevention Programme, conducted over 5 and a half weeks, included training in falls techniques and correction of gait abnormalities, while the 12-month Chaos Clinic Falls Prevention Programme provided individualised interventions, for example, a medicines review and referral to other specialists. Exercise and education were key components in both programmes and dropout rates were low, suggesting good acceptability to participants.

Both studies reported a significantly lower fall rate in the intervention group compared with the control group at 12 months. Smulders et al³⁶ recorded a 39% reduction in falls per person years (IRR 0.61, 95% CI 0.40 to 0.94), while Palvanen et al⁵⁷ reported a 28% reduction in falls per 100 person years (IRR 0.72, 95% CI 0.61 to 0.86). In

Table 4 Characteristics of intervention studies and their main findings: non-pharmacological treatments provided to adults at high risk of primary osteoporotic fracture

Authors, country, setting if stated	Study design	Population characteristics; number of participants for outcomes of interest	Intervention; healthcare professional if stated	Main findings	LoE
i) Exercise					
de Kam <i>et al⁶³</i>	SR	Adults with osteoporosis/ osteopenia±a fracture nine trials (n=974)	Exercise compared with inactive control group or sham intervention	Exercising <1 year had no effect on BMD (3/4 studies) Exercising ≥1 year had positive effect on BMD/BMC (5/6 studies)	2
Luo <i>et al³⁰</i>	MA	Postmenopausal women with osteoporosis seven trials (n=287)	Whole body vibration therapy compared with usual care	No significant difference between groups in change in BMD (SMD=-0.06, 95% CI -0.22 to 0.11; p=0.05)	1
Wei et al ²⁴	MA	Postmenopausal women with osteoporosis two trials (n=116)	Wuqinxi exercise (mind/body conditioning) compared with usual care	No significant difference in lumbar spine BMD at 6 months between IG and CG (SMD 0.81, 95% CI -0.58 to 2.20 , $p=0.25$)	2
Varahra et al ³¹	MA	Adults with osteoporosis/ osteopenia±a fracture seven trials (n=614); five trials (n=406)	Multicomponent exercise compared with non-exercise, usual physical activity and education	SMD favoured IG for mobility (-0.56, 95% CI -0.81 to 0.32) and balance (0.5, 95% CI 0.27 to 0.74)	1
Korpelainen <i>et al</i> Finland, community ⁵⁴	RCT	Women with osteopenia 1.Group 1 (n=84); 2.Group 2 (n=76)	 Multimodal exercise for 12 months General health information and usual care 	17 fractures in the IG versus 23 fractures in CG at 7-year follow-up (IRR=0.68, 95% CI 0.34 to 1.32). Similar decrease in BMD in IG and CG	
Gianoudis <i>et al</i> Australia, community ⁵⁵	RCT	Adults with osteopenia/risk of falls 1.Group 1 (n=81); 2.Group 2 (n=81)	1.Multimodal exercise for 12 months+education 2.Usual care Exercise trainers	No significant difference in falls incidence between IG and CG at 1 year (IRR 1.22, 95% CI 0.71 to 2.04), p=0.46	2
Kemmler et al Germany community ⁵⁶	CCT NR	Women with osteopenia 1.Group 1 (n=59); 2.Group 2 (n=46)	1.Long-term multimodal exercise 2.Sedentary control group Certified trainers	13 fractures in the IG versus 24 fractures in the CG at 16-year follow-up (rate ratio=0.42; 95% CI 0.20 to 0.86; p=0.018)	3
ii) Nutrients including	vitamin D	plus calcium and oral nutrition	nal supplements		
Porter et al ⁵⁸	SR	Postmenopausal women with osteopenia three trials (n=254)	Supplementation with vitamin D analogues compared with placebo	No significant difference in mean % change in BMD in IG or CG when assessed between 6 and 12 months	1
Koutsofta et al ⁵⁹	SR	Postmenopausal women with osteoporosis five studies (n=677)	Non-soy protein (diet and/ or supplement) compared with a control group.	The effect of non-soy protein on BMD at different sites was mixed.	2
Cheung <i>et al</i> Canada, community ⁶⁰	RCT	Postmenopausal women with osteopenia 1.Group 1 (n=217); 2.Group 2 (n=223)	 Vitamin K (5 mg) daily Placebo 	No significant difference in BMD decrease at the LS or total hip between IG and CG at 2 years. IG, 6 fractures; CG, 11 fractures	1
iii) Falls prevention pro	ogramme	es			
Smulders <i>et al</i> The Netherlands, community ³⁶	RCT	Adults with osteoporosis +falls history 1.Group 1 (n=50); 2.Group 2 (n=46)	 Falls prevention programme lasting 5.5 weeks. Usual care Physical therapists, occupational therapists 	Fall rate at 12 months was 39% lower in the IG compared with the CG (IRR 0.61, 95% CI 0.40 to 0.94)	2
Palvanen et al Finland community ⁵⁷	RCT	Older adults at high risk of fracture 1.Group 1 (n=661); 2.Group 2 (n=653)	Individualised falls prevention programme Brochure Nurse, physiotherapist, physician	Significantly lower rate of falls at 12 months (IRR 0.72, 95% CI 0.61 to 0.86; p<0.001, NNT=3). Total number of fractures 33 (IG) versus 42 (CG) (IRR 0.77, 95% CI 0.48 to 1.23; p=0.276)	2
iv) Education					
Morfeld et al ⁶¹	SR	Patients with low bone mass four studies (n=2877)	Face-to-face patient education compared with no education or usual care	1/4 trials showed a significant between group difference in hip fracture incidence at 10-year follow-up.	2

BMC, bone mineral content; BMD, bone mineral density; CCT, controlled clinical trial; CG, control group; IG, intervention group; IRR, incidence rate ratio; LoE, level of evidence; LS, lumbar spine; MA, meta-analysis; NNT, number needed to treat; NR, non-randomised; RCT, randomised controlled trial; RR, relative risk; SMD, standardised mean difference; SR, systematic review.

this latter study, the number of fall induced injuries was significantly lower in the intervention group than the control group (IRR 0.74, 95% CI 0.61 to 0.89; p=0.002). However, risk of detection bias was high in this RCT due to a lack of blinding of the professionals collecting falls data and the method of falls recording.⁵⁷

Education

Evidence about the effect of patient education on bone health-related outcomes in people at risk of primary osteoporotic fracture came from one systematic review.61 Thirteen RCTs including 5912 participants investigated face-to-face group, or individual educational interventions delivered by HPs (nurses, community pharmacists, physicians, occupational therapists, dietitians, podiatrists and physiotherapists) working alone or in multidisciplinary teams to people at risk of primary fracture. Twelve of the 13 studies were judged to be at high risk of detection

The review highlighted inconsistent results across a range of outcomes. Less than half of the studies assessing initiation, receipt and use of pharmacological treatment for bone health showed a statistically significant difference between the intervention and control groups. However, knowledge about osteoporosis and intake of calcium and or vitamin D was significantly improved in the intervention group compared with a control group in ≥50% of studies. Only one of four RCTs reporting fractures showed a significant reduction in fracture incidence.⁶² In this study, participants in the intervention group received a weeklong programme of group and individual sessions with optional supervised gym sessions delivered by a multiprofessional team. Data about hip fracture incidence were collected at 10 years via a national hospital discharge register. Following adjustment for baseline differences the risk of hip fracture reduced by 55%.

What is the effect of strategies undertaken by non-physician HPs to implement recommendations for the prevention and management of osteoporotic fracture by potential stakeholders?

Five primary studies in various care settings contributed to the evidence synthesis about the effect of strategies to implement recommendations by stakeholders to prevent and manage osteoporotic fracture (table 5). These were grouped into three categories: (1) strategies to increase implementation of recommendations; (2) multidisciplinary team care and (3) interventions to enhance adherence to antiosteoporosis medicines.

Strategies to increase implementation of recommendations consisted of two or more components, these included: education and dissemination of educational materials, fall and fracture risk assessment, feedback through audit and evaluation, and a computer-aided decision support system. The three cluster RCTs³³ 63 64 were appraised as having unclear risk of other bias with respect to criteria particular to cluster trials, for example, baseline imbalances and loss of clusters.²¹

- Multisiciplinary team³² care was defined as care provided by two or more different care practitioners working together as/or supported by a multidisciplinary team. Selected publications focused on orthogeriatric inpatient care, 32 65 fracture liaison services (FLS)^{25 66} and care pathways for people following hip fracture.⁶⁷
 - Interventions to enhance adherence to antiosteoporosis medicines was supported by evidence that suggests vitamin D and/or calcium prescribing by stakeholders may be increased in people at risk of fracture following implementation of multicomponent interventions by non-physicians, such as nurses, pharmacists and multiprofessional teams. Cox et al³³ reported that supplements were 1.64 times more likely to be prescribed to care home residents in the intervention group (n=3315) over the control group (n=2322) (IRR 1.64, 95% CI 1.23 to 2.18; p<0.01), while Kennedy et al⁶³ stated an absolute improvement of approximately 15% in vitamin D and 7% in calcium prescribing for residents in long-term care following a 12-month multimodal education and quality improvement intervention. In one randomised study set in the community, ⁶⁸ treatment with calcium and vitamin D reportedly increased by 34% and 13%, respectively, although this study was at high risk of detection bias due to unblinded outcome assessors. One non-randomised study⁶⁹ showed that a pharmacist-implemented clinical decision support system increased coprescription of vitamin D with a bisphosphonate by 29% compared with a historical control group. However, the effect of strategies on prescription of antiosteoporosis medicines was inconclusive, with 50% of studies reporting benefit. 33 68 There was no statistically significant difference between intervention and control groups in fractures and falls.

What is the effect of multidisciplinary team care on health outcomes for persons at high risk of primary or secondary osteoporotic fracture?

Available evidence (see table 5) from one meta-analysis and one RCT suggests that collaborative orthogeriatric care can reduce risk of in-hospital and long-term mortality, and improve mobility, activities of daily living and QoL compared with an 'as needed' geriatrician consult requested by the surgeon,³² or routine orthopaedic care⁶⁵ in older adults admitted for hip fracture. An orthogeriatric model resulted in a 40% reduction in relative risk of death in hospital (relative risk 0.60, 95% CI 0.43 to 0.84) and a 17% reduction in risk of long-term mortality (relative risk 0.83, 95% CI 0.74 to 0.94). In addition, data from a single RCT showed improved mobility at 12 months in participants receiving orthogeriatric care compared with usual orthopaedic care. 32 However, multidisciplinary team care staff numbers (nurses, doctors and physiotherapists) per bed were higher in the geriatric unit than on the orthopaedic unit and the trial was at

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Authors, country, setting if stated	Study design	Population characteristics; number of participants for outcomes of interest	Intervention; healthcare professional if stated	Main findings	LoE
i) Implementation st	rategies to incre	i) Implementation strategies to increase implementation of recommer	ndations		
Cox <i>et al</i> UK, Care homes ³³	Cluster RCT	1. Group 1 (n=3315) 2. Group 2 (n=2322)	 Education+feedback No intervention Specialist osteoporosis nurses 	Significant increase in bisphosphonate prescription (IRR 1.5, 95% CI 1.00 to 2.24; p=0.05) and calcium and vitamin D prescription (IRR 1.64, 95% CI 1.23 to 2.18; p<0.01) in IG versus CG at 12 months	2
Kennedy <i>et al</i> Canada, Care homes ⁶³	Pilot cluster RCT	1. Group 1 (n=2185) 2. Group 2 (n=3293)	Education+action planning +feedback Fracture prevention toolkits Interdisciplinary care teams	Significant increase in vitamin D and calcium prescription from baseline to 12 months in IG versus CG; OR 1.82 (95% CI 1.12 to 2.96) and 1.33 (95% CI 1.01 to 1.74), respectively. No significant between group difference in prescribing osteoporosis medicines	α
Ciaschini <i>et al</i> Canada, community ⁶⁸	RCT	Adults at risk of future fracture 1. Group 1 (n=101) 2. Group 2 (n=100)	 Multifaceted intervention Usual care Nurses 	29/52 participants in IG versus 16/60 participants in CG taking osteoporotic medicines at 6 months (relative risk 2.09, 95% CI 1.29 to 3.40). Treatment with calcium and vitamin D increased by 34%–17%, respectively, in IG compared with CG.	2
Kilgore <i>et al</i> community ⁶⁴	Cluster RCT	1. Group 1 (n=330) 2. Group 2 (n=337)	Multicomponent Usual care Nurse	No significant difference between IG and CG in average proportion of eligible patients receiving osteoporosis medicines (IG: 19.1% vs UC; 15.7%, difference in proportions 3.4%, 95% CI –2.6 to 9.5%, p=0.252)	2
Baypinar et af ⁸⁹	Cohort study	1. Group 1 (n=60) 2. Group 2 (n=47)	 Clinical decision support alert No alert Pharmacists 	Coprescription of vitamin D or vitamin D analogues with a bisphosphonate increased by 29% (p=0.001) in the IG compared with the CG	ო
ii) MDT care					
Grigoryan e <i>t al</i> inpatients ³²	MA	Patients with hip fracture 9 studies (n=3333) and 11 studies (n=6305)	Orthogeriatric compared with standard care MDT	Orthogeriatric care 40% reduction in ST mortality (relative risk 0.60, 95% CI 0.43 to 0.84) and 17% reduction in LT mortality (relative risk 0.83, 95% CI 0.74 to 0.94)	-
Prestmo <i>et al</i> Norway, inpatients ⁶⁵	RCT	Patients with hip fracture 1.Group 1 (n=198) 2.Group 2 (n=199)	Orthogeriatric care Orthopaedic care MDT	Significant between group difference in SPPB in favour of orthogenatric care at 4 months (between group difference 0.74, 95% CI 0.18 to 1.30, p=0.010) and at 12 months (0.69, 95% CI 0.10 to 1.28, p=0.023).	2
Wu <i>et al</i> inpatients and outpatients ²⁵	MA	Patients with all fracture types 11 studies (n=19519) and 15 studies (n=16802)	FLS versus usual care/control MDT	FLS reduced absolute risk of refracture (ARR -0.05, 95% CI -0.08 to -0.03; NNT=20) RLS reduced absolute risk of mortality (ARR -0.03, 95% CI -0.05 to -0.01; NNT=33)	-
Wu et al inpatients and outpatients ⁶⁶	SR	Patients with all fracture types	FLS versus usual care or no treatment MDT	FLS implemented in HICs and MICs are cost effective across FLS model types	2
Leigheb et al inpatients and community ⁶⁷	SO	Patients with hip fracture	Care pathways and MCA versus usual care MDT	No significant reduction in short-term mortality Mixed effect on functional recovery	-
iii) Interventions to 6	enhance adheren	iii) Interventions to enhance adherence to antiosteoporosis medicines	w		
Hiligsman <i>et al⁷⁰</i>	SR	Adults using osteoporosis medicines 20 studies (n=14662)	Education; monitoring/supervision; drug regimens; electronic prescription; decision aid. Nurses, pharmacists, physicians, MDT, clinical personnel and health educators	9/12 studies showed statistically significant improvement in adherence to medicines in IG versus CG 5/13 studies showed improved persistence with an intervention	5

Continued

Table 5 Continued	per				
Authors, country, setting if stated	Study design	Population characteristics; number of participants for outcomes of interest	Intervention; healthcare professional if stated	Main findings	LoE
Kooij <i>et al</i> , The Netherlands, community pharmacies ⁷²	Cluster RCT	Participants starting bisphosphonates 1. Group 1 (n=379) 2. Group 2 (n=255)	Single telephone counselling call Usual care Pharmacist, trainee pharmacist, pharmacy technician	 Single telephone counselling call No significant between group difference in mean adherence rate. IG: 75.2% Usual care versus Pharmacist, frainee pharmacist, pharmacy UC: 73.3%. Counselling call only received by 137 participants in the IG echnician 	2
Stuurman-Bieze et al, The Netherlands, community pharmacies 71	Cohort study	Patients initiating osteoporosis medicines 1. Group 1 (n=495) 2. Group 2 (n=442)	 Counselling and monitoring service Usual care Pharmacists 	No statistically significant difference in non-adherence rate at 12 months. Significantly lower discontinuation rates in counselling and monitoring group (IG: 15.8% vs UC: 27.8%; p<0.001).	6

ARR, absolute risk reduction; CG, control group; ELS, fracture liaison services; HIC, high-income countries; IG, intervention group; IRR, incidence rate ratio; LOE, level of evidence; LT, long term; MA, meta-analysis; MCA, mutidisciplinary care approaches; MIC, middle-income countries; NNT, numbers needed to treat; OR, Odds ratio; RCT, randomised controlled trial; RR, relative risk; RR, risk ratio; SO, systematic overview; SPPB, short physical performance battery; ST, short-term; UC, usual care. unclear risk of detection bias due to only partial masking of assessors during follow-up. 65 The study also identified that comprehensive geriatric care was more cost effective than orthopaedic care, although a lack of baseline EO-5D-3L (3-level version of EuroQol 5 dimensions questionnaire) data precluded control of any baseline value

In contrast, Leighbeg *et al*⁶⁷ found no clear evidence of reduced mortality from their systematic overview of four secondary studies investigating the effect of care pathways and/or multidisciplinary team care approaches for people following hip fracture. However, diversity of study settings and difficulty with classification of studies in relation to the status of their interventions (care pathways or not care pathways) may have influenced the findings. Functional outcomes were investigated in three of the secondary studies with some evidence of improved functional recovery when interventions involving early mobilisation and intensive occupational and physical therapy input were provided in the acute setting.

The evidence for FLS suggests that this model of care delivered to people presenting with different types of minimal trauma fracture offers significant opportunity for improved bone health-related outcomes compared with no FLS or usual care. 25 Between 6 and 72 months, the absolute risk reduction in refracture rate in participants receiving FLS interventions compared with participants receiving no FLS intervention or usual care was -0.05 (95% CI -0.08 to -0.03), equating to about a 30% reduction in refracture rate. The absolute risk reduction in mortality over the same period was -0.03 (95% CI -0.05 to -0.01), equating to about a 20% drop. Synthesis of cost-effectiveness data shows that FLS implemented in high-income and middle-income countries are cost effective irrespective of the intensity of the model and the country of implementation. ⁶⁶ One study of a FLS in Australia, in which a nurse coordinator assessed bone health in patients≥50 years of age presenting with a minimal trauma fracture, and subsequently referred to an endocrinologist, reported improved Quality Adjusted Life Years (QALYs) by an estimated 0.054 per patient (Incremental Cost Effectiveness Ratio (ICER) \$A31749) when treatment was prescribed over 5 years. Similarly, a UK nurse-led FLS delivered to patients admitted to hospital with a hip fracture resulted in ICERs of £19955 and £20421 per QALY, thus falling within recommended ICER ranges. 66

What is the effect of interventions provided by non-physician HPs to enhance adherence to antiosteoporosis medicines in adults at high risk of primary or secondary osteoporotic fracture?

Synthesised evidence for the effect of interventions to enhance adherence to and/or persistence with antiosteoporosis medicines included one systematic review (14662 participants), ⁷⁰ one prospective cohort study ⁷¹ and one cluster RCT⁷² (table 5). Available evidence suggests that simplification of antiosteoporosis medication dosing regimens, incorporating less frequent dosing, electronic

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prescriptions and osteoporosis management services provided by pharmacists, which incorporate counselling and/or monitoring of prescription redemption, may favourably affect medication adherence and lower discontinuation rates, ^{70 71} although the amount of literature identified is limited. The effectiveness of educational interventions appears unclear.

DISCUSSION

This SLR has appraised evidence about the effect of non-pharmacological interventions delivered by nonphysician HPs to prevent and manage osteoporotic fractures in adults≥50 years at high risk of fracture. Our review showed positive effects of interventions to prevent and manage osteoporotic fracture despite heterogeneity of interventions, study designs and professions. An example is exercise. There is sufficient evidence that structured exercise, incorporating PRE, delivered to people following hip fracture surgery, reduces risk of falling. However, there is insufficient evidence to determine if structured exercise can reduce falls risk in people who have experienced OVF. In individuals at risk of primary osteoporotic fracture, there is sufficient evidence to support the delivery of multicomponent exercise for falls risk reduction and some evidence that regular multicomponent exercise interventions of at least 12 months duration may positively influence BMD.

There is currently insufficient evidence to support the effectiveness of nutrients including: daily supplementation with vitamin D plus calcium of older adults with a history of osteoporotic fracture; a single loading dose of vitamin D3 following hip fracture surgery to reduce future fractures and falls; vitamin D analogues and vitamin K in adults at risk of primary fracture on BMD, and protein supplementation on BMD or risk of falling in adults at risk of either primary or secondary fracture.

There is insufficient evidence to determine the effect of falls intervention initiatives on falls incidence in people at risk of primary or secondary osteoporotic fracture, or orthoses in reducing risk of falling. Educational interventions delivered to patients with low bone mass by healthcare professionals may be generally ineffective in reducing fracture incidence but there is some evidence that education, simplification of drug regimens and interventions by pharmacists may improve adherence to antiosteoporosis medicines.

Sufficient evidence exists to show that multidisciplinary orthogeriatric or FLS models of care reduce mortality and future fractures when offered to people who have experienced an osteoporotic fracture, and that FLS are cost effective. There is some evidence that hip fracture care pathways may reduce risk of falling. Finally, the evidence about strategies undertaken by healthcare professionals to increase uptake of recommendations for the treatment and management of osteoporosis by stakeholders, such as prescribing of vitamin D and calcium

and antiosteoporosis medicines, is insufficient to determine if they are, or are not, effective.

This review has several limitations. First, studies reporting falls and fractures as primary endpoints in populations at high risk of osteoporotic fracture are limited. Our definition of 'high risk', based solely on BMD values or an expression of short-term absolute risk of fracture, is likely to have excluded evidence about the effect of interventions on falls and fractures in other populations commonly considered at high risk of fracture, for example, older adults. Second, the aim of this SLR was to inform an international EULAR taskforce on a broad range of issues related to non-physician HPs' interventions. Non-physician HPs deliver different interventions in different countries. Therefore, we focused our review on interventions that could potentially be delivered by non-physician HPs independent of whether a study was led by a non-physician HP or not. The scope for further investigations into the role of the multidisciplinary team in treating osteoporotic fractures and using service link approaches was beyond the remit for this project, but deserves further inquiry. Third, our overall confidence rating of the results of the systematic reviews included in this SLR was based on reported evidence for domainspecific questions. Many of these systematic reviews were published prior to the publication of AMSTAR 2, and an absence of reporting may not reflect the review authors methods when conducting the review. Lastly, we were unable to answer questions 7 and 8 in our SLR. Despite these limitations, the process of reviewing, analysing and synthesising the identified evidence has been robust and followed EULAR guidelines for developing points to consider.

CONCLUSION

Existing evidence about the effect of non-pharmacological interventions on reducing fractures in people at high risk of osteoporotic fracture is limited. Despite study heterogeneity, our SLR showed beneficial effects of some interventions delivered by non-physician HPs and the positive impact of multidisciplinary team working and sound patient educational approaches to prevent and manage osteoporotic fractures. These results informed a EULAR taskforce that developed points to consider for non-physician HPs to prevent and manage osteoporotic fractures in adults 50 years or more.

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REFERENCES

- 1 Odén A, McCloskey EV, Kanis JA, et al. Burden of high fracture probability worldwide: secular increases 2010-2040. Osteoporos Int 2015;26:2243–8.
- 2 Hernlund E, Svedbom A, Ivergård M, et al. Osteoporosis in the European Union: medical management, epidemiology and economic burden. A report prepared in collaboration with the International osteoporosis Foundation (IOF) and the European Federation of pharmaceutical industry associations (EFPIA). Arch Osteoporos 2013;8:136.
- 3 Crandall CJ, Newberry SJ, Diamant A, et al. Comparative effectiveness of pharmacologic treatments to prevent fractures: an updated systematic review. Ann Intern Med 2014;161:711–23.
- 4 Yusuf AA, Cummings SR, Watts NB, et al. Real-World effectiveness of osteoporosis therapies for fracture reduction in post-menopausal women. Arch Osteoporos 2018;13:33.
- 5 Gallagher TC, Geling O, Comite F. Missed opportunities for prevention of osteoporotic fracture. *Arch Intern Med* 2002;162:450–6.
- 6 Parker D. An audit of osteoporotic patients in an Australian general practice. *Aust Fam Physician* 2013;42:423–7.
- 7 Khosla S, Cauley JA, Compston J, et al. Addressing the crisis in the treatment of osteoporosis: a path forward. J Bone Miner Res 2017;33:424–30
- 8 Howe TE, Shea B, Dawson LJ, et al. Exercise for preventing and treating osteoporosis in postmenopausal women. Cochrane Database Syst Rev 2011;32.

- 9 Hopewell S, Adedire O, Copsey BJ, et al. Multifactorial and multiple component interventions for preventing falls in older people living in the community. Cochrane Database Syst Rev 2018;7:CD012221.
- 10 Prentice A, Diet PA. Diet, nutrition and the prevention of osteoporosis. Public Health Nutr 2004;7:227–43.
- 11 Lai P, Chua SS, Chan SP. A systematic review of interventions by healthcare professionals on community-dwelling postmenopausal women with osteoporosis. *Osteoporos Int* 2010;21:1637–56.
- 12 Elias MN, Burden AM, Cadarette SM. The impact of pharmacist interventions on osteoporosis management: a systematic review. Osteoporos Int 2011;22:2587–96.
- 13 Lems WF, Dreinhöfer KE, Bischoff-Ferrari H, et al. EULAR/EFORT recommendations for management of patients older than 50 years with a fragility fracture and prevention of subsequent fractures. Ann Rheum Dis 2017;76:802–10.
- 14 Kanis JA, Cooper C, Rizzoli R, et al. European guidance for the diagnosis and management of osteoporosis in postmenopausal women. Osteoporos Int 2019;30:3–44.
- 15 World Health Organisation. Assessment of fracture risk and its application to screening for postmenopausal osteoporosis: report of a who Study Group. Geneva: World Health Organisation, 1994.
- 16 Higgins JPT, Green S. Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0. The Cochrane Collaboration, 2011.
- 17 Liberati A, Altman DG, Tetzlaff J, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. PLoS Med 2009;6:e1000100.
- 18 Lamb SE, Jørstad-Stein EC, Hauer K, et al. On behalf of the prevention of falls network Europe and outcomes consensus group. development of a common outcome data set for fall injury prevention trials: the prevention of falls network Europe consensus. J Am Geriatr Soc 2005;53:1618–22.
- 19 Prior JC, Langsetmo L, Lentle BC, et al. Ten-Year incident osteoporosis-related fractures in the population-based Canadian multicentre osteoporosis study — comparing site and age-specific risks in women and men. Bone 2015;71:237–43.
- 20 Shea BJ, Reeves BC, Wells G, et al. AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or nonrandomised studies of healthcare interventions, or both. BMJ 2017;358:j4008.
- 21 Higgins JPT, Altman DG, Sterne JAC. Chapter 8: Assessing risk of bias in included studies. In: Higgins JPT, Churchill R, Chandler J, eds. Cochrane Handbook for Systematic Reviews of Interventions Version 5.2.0. 2017.
- 22 OCEBM Levels of Evidence Working Group. "The Oxford 2011 Levels of Evidence". Oxford Centre for Evidence-Based Medicine. Available: http://www.cebm.net/index.aspx?o=5653 [Accessed 4 Apr 2019].
- 23 Ryan R, Santesso N, Lowe D, et al. Interventions to improve safe and effective medicines use by consumers: an overview of systematic reviews. Cochrane Database Syst Rev 2014;41:CD007768.
- 24 Wei X, Xu A, Yin Y, et al. The potential effect of Wuqinxi exercise for primary osteoporosis: a systematic review and meta-analysis. Maturitas 2015;82:346–54.
- Wu C-H, Tu S-T, Chang Y-F, et al. Fracture liaison services improve outcomes of patients with osteoporosis-related fractures: a systematic literature review and meta-analysis. Bone 2018a:111:92–100.
- 26 Avenell A, Mak JCS, O'Connell D. Vitamin D and vitamin D analogues for preventing fractures in post-menopausal women and older men. Cochrane Database Syst Rev 2014:CD000227.
- 27 Liu T, Sheng L, Huang Z. Influence of exercise intervention on pain, quality of life and functional mobility in patients with osteoporotic vertebral fractures: a systematic review and meta-analysis. *Int J Clin Exp Med* 2017;10:9864–70.
- 28 Diong J, Allen N, Sherrington C. Structured exercise improves mobility after hip fracture: a meta-analysis with meta-regression. Br J Sports Med 2016;50:346–55.
- 29 Lee SY, Yoon B-H, Beom J, et al. Effect of lower-limb progressive resistance exercise after hip fracture surgery: a systematic review and meta-analysis of randomized controlled studies. J Am Med Dir Assoc 2017;18:1096.e19–1096.e26.
- 30 Luo X, Zhang J, Zhang C, et al. The effect of whole-body vibration therapy on bone metabolism, motor function, and anthropometric parameters in women with postmenopausal osteoporosis. *Disabil Rehabil* 2017;39:2315–23.
- 31 Varahra A, Rodrigues IB, MacDermid JC, et al. Exercise to improve functional outcomes in persons with osteoporosis: a systematic review and meta-analysis. Osteoporos Int 2018;29:265–86.



- 32 Grigoryan KV, Javedan H, Rudolph JL. Orthogeriatric care models and outcomes in hip fracture patients: a systematic review and meta-analysis. J Orthop Trauma 2014;28:e49–55.
- 33 Cox H, Puffer S, Morton V, et al. Educating nursing home staff on fracture prevention: a cluster randomised trial. Age Ageing 2008;37:167–72.
- 34 van Ooijen MW, Roerdink M, Trekop M, et al. The efficacy of treadmill training with and without projected visual context for improving walking ability and reducing fall incidence and fear of falling in older adults with fall-related hip fracture: a randomized controlled trial. BMC Geriatr 2016;16:215.
- 35 Kronborg L, Bandholm T, Palm H, et al. Effectiveness of acute in-hospital physiotherapy with knee-extension strength training in reducing strength deficits in patients with a hip fracture: a randomised controlled trial. PLoS One 2017;12:e0179867.
- 36 Smulders E, Weerdesteyn V, Groen BE, et al. Efficacy of a short multidisciplinary falls prevention program for elderly persons with osteoporosis and a fall history: a randomized controlled trial. Arch Phys Med Rehabil 2010;91:1705–11.
- 37 de Morais Barbosa C, Barros Bértolo M, Marques Neto JF, et al. The effect of foot orthoses on balance, foot pain and disability in elderly women with osteoporosis: a randomized clinical trial. Rheumatology 2013;52:515–22.
- 38 Newman M, Minns Lowe C, Barker K. Spinal orthoses for vertebral osteoporosis and osteoporotic vertebral fracture: a systematic review. Arch Phys Med Rehabil 2016;97:1013–25.
- 39 Ambrose AF, Cruz L, Paul G. Falls and fractures: a systematic approach to screening and prevention. *Maturitas* 2015;82:85–93.
- 40 Podsiadlo D, Richardson S. The timed "Up & Go": a test of basic functional mobility for frail elderly persons. J Am Geriatr Soc 1991;39:142–8.
- 41 Rossiter-Fornoff JE, Wolf SL, Wolfson LI, et al. A cross-sectional validation study of the FICSIT common data base static balance measures. The Journals of Gerontology Series A: Biological Sciences and Medical Sciences
- 42 Paul SS, Canning CG, sit-to-stand F-repetition. Five-repetition sit-to-stand. *J Physiother* 2014;60:168.
- 43 Mikó I, Szerb I, Szerb A, et al. Effectiveness of balance training programme in reducing the frequency of falling in established osteoporotic women: a randomized controlled trial. Clin Rehabil 2017;31:217–24.
- 44 Mak JC, Mason RS, Klein L, et al. An initial loading-dose vitamin D versus placebo after hip fracture surgery: randomized trial. BMC Musculoskelet Disord 2016:17:336.
- 45 Myint MWW, Wu J, Wong E, et al. Clinical benefits of oral nutritional supplementation for elderly hip fracture patients: a single blind randomised controlled trial. Age Ageing 2013;42:39–45.
- 46 Visschedijk J, Achterberg W, Van Balen R, et al. Fear of falling after hip fracture: a systematic review of measurement instruments, prevalence, interventions, and related factors. J Am Geriatr Soc 2010:58:1739–48.
- 47 Tinetti ME, Richman D, Powell L. Falls efficacy as a measure of fear of falling. J Gerontol 1990;45:P239–43.
- 48 Hellström K, Lindmark B. Fear of falling in patients with stroke: a reliability study. *Clin Rehabil* 1999;13:509–17.
- 49 Di Monaco M, De Toma E, Gardin L, et al. A single postdischarge telephone call by an occupational therapist does not reduce the risk of falling in women after hip fracture: a randomized controlled trial. Eur J Phys Rehabil Med 2015;51:15–22.
- 50 Di Monaco M, Vallero F, De Toma E, et al. A single home visit by an occupational therapist reduces the risk of falling after hip fracture in elderly women: a quasi-randomized controlled trial. J Rehabil Med 2008:40:446–50.
- 51 Berggren M, Stenvall M, Olofsson B, et al. Evaluation of a fall-prevention program in older people after femoral neck fracture: a one-year follow-up. Osteoporos Int 2008;19:801–9.
- 52 Shyu Y-IL, Tsai W-C, Chen M-C, et al. Two-Year effects of an interdisciplinary intervention on recovery following hip fracture in older Taiwanese with cognitive impairment. Int J Geriatr Psychiatry 2012;27:529–38.

- 53 de Kam D, Smulders E, Weerdesteyn V, et al. Exercise interventions to reduce fall-related fractures and their risk factors in individuals with low bone density: a systematic review of randomized controlled trials. Osteoporos Int 2009;20:2111–25.
- 54 Korpelainen R, Keinänen-Kiukaanniemi S, Nieminen P, et al. Long-Term outcomes of exercise: follow-up of a randomized trial in older women with osteopenia. Arch Intern Med 2010;170:1548–56.
- 55 Gianoudis J, Bailey CA, Ebeling PR, et al. Effects of a targeted multimodal exercise program incorporating high-speed power training on falls and fracture risk factors in older adults: a community-based randomized controlled trial. J Bone Miner Res 2014:29:182–91.
- 56 Kemmler W, Bebenek M, Kohl M, et al. Exercise and fractures in postmenopausal women. final results of the controlled Erlangen fitness and osteoporosis prevention study (EFOPS). Osteoporos Int 2015;26:2491–9.
- 57 Palvanen M, Kannus P, Piirtola M, et al. Effectiveness of the chaos falls clinic in preventing falls and injuries of home-dwelling older adults: a randomised controlled trial. *Injury* 2014;45:265–71.
- 58 Porter J, Adderley M, Bonham M, et al. The effect of dietary interventions and nutritional supplementation on bone mineral density in otherwise healthy adults with osteopenia: A systematic review. Nutr Bull 2016;41:108–21.
- Koutsofta I, Mamais I, Chrysostomou S. The effect of protein diets in postmenopausal women with osteoporosis: systematic review of randomized controlled trials. J Women Aging 2019;31:117–39.
- 60 Cheung AM, Tile L, Lee Y, et al. Vitamin K supplementation in postmenopausal women with osteopenia (ECKO trial): a randomized controlled trial. PLoS Med 2008;5:e196.
- 61 Morfeld J-C, Vennedey V, Müller D, et al. Patient education in osteoporosis prevention: a systematic review focusing on methodological quality of randomised controlled trials. Osteoporos Int 2017;28:1779–803.
- 62 Pekkarinen T, Löyttyniemi E, Välimäki M. Hip fracture prevention with a multifactorial educational program in elderly community-dwelling Finnish women. *Osteoporos Int* 2013;24:2983–92.
- 63 Kennedy CC, Ioannidis G, Thabane L, et al. Successful knowledge translation intervention in long-term care: final results from the vitamin D and osteoporosis study (ViDOS) pilot cluster randomized controlled trial. *Trials* 2015;16:214.
- 64 Kilgore ML, Outman R, Locher JL, et al. Multimodal intervention to improve osteoporosis care in home health settings: results from a cluster randomized trial. Osteoporos Int 2013;24:2555–60.
- 65 Prestmo A, Hagen G, Sletvold O, et al. Comprehensive geriatric care for patients with hip fractures: a prospective, randomised, controlled trial. Lancet 2015;385:1623–33.
- 66 Wu C-H, Kao I-J, Hung W-C, et al. Economic impact and costeffectiveness of fracture liaison services: a systematic review of the literature. Osteoporos Int 2018b;29:1227–42.
- 67 Leigheb F, Vanhaecht K, Sermeus W, et al. The effect of care pathways for hip fractures: a systematic overview of secondary studies. Eur J Orthop Surg Traumatol 2013;23:737–45.
- 68 Ciaschini PM, Straus SE, Dolovich LR, et al. Community based intervention to optimize osteoporosis management: randomized controlled trial. BMC Geriatr 2010;10:60.
- 69 Baypinar F, Kingma HJ, van der Hoeven RTM, et al. Physicians' compliance with a clinical decision support system alerting during the prescribing process. J Med Syst 2017;41:96.
- 70 Hiligsmann M, Salas M, Hughes DA, et al. Interventions to improve osteoporosis medication adherence and persistence: a systematic review and literature appraisal by the ISPOR Medication Adherence & Persistence Special Interest Group. Osteoporos Int 2013:24:2907–18
- 71 Stuurman-Bieze AGG, Hiddink EG, van Boven JFM, et al. Proactive pharmaceutical care interventions decrease patients' nonadherence to osteoporosis medication. *Osteoporos Int* 2014;25:1807–12.
- 72 Kooij MJ, Heerdink ER, van Dijk L, et al. Effects of telephone counseling intervention by pharmacists (TelCIP) on medication adherence; results of a cluster randomized trial. Front Pharmacol 2016;7:2.