




## 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 non-pharmacological interventions delivered by non-physician 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.<sup>1</sup> 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,<sup>2–4</sup> highlight the importance of identification and treatment of ‘high-risk’ individuals. Yet,

current healthcare provision is insufficient and many people at high risk of osteoporotic fracture are neither identified nor receive treatment.<sup>5–7</sup>

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.<sup>8–10</sup> 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.<sup>11 12</sup>

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,<sup>13</sup> and updated European guidance exists to streamline healthcare for diagnosis and management of osteoporosis in postmenopausal women.<sup>14</sup> 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,<sup>15</sup> 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 $\leq -1.0$ to $-2.5$ SD |
| Osteoporosis   | T score $\leq -2.5$ SD           |
| FRAX 10-year probability of a major* osteoporotic fracture | $\geq 20\%$ (age independent)    |
| FRAX 10-year probability of hip fracture                   | $\geq 3\%$ (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 healthy young 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.<sup>16</sup> A Participants, Interventions, Comparisons, Outcomes and Study design approach<sup>17</sup> 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 criteria: (1) adults  $\geq 50$  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 level<sup>18</sup>). High risk of falling and change in BMD were included as surrogate end points. Fractures in adults age  $\geq 50$  years were assumed to be fragility fractures unless at the ankle, hands and feet, skull and face,<sup>19</sup> 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,<sup>20</sup> while risk of bias (RoB) judgements about primary studies followed a domain-based assessment as recommended by the Cochrane collaboration.<sup>21</sup> 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,<sup>22</sup> 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*<sup>23</sup> (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 ≤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

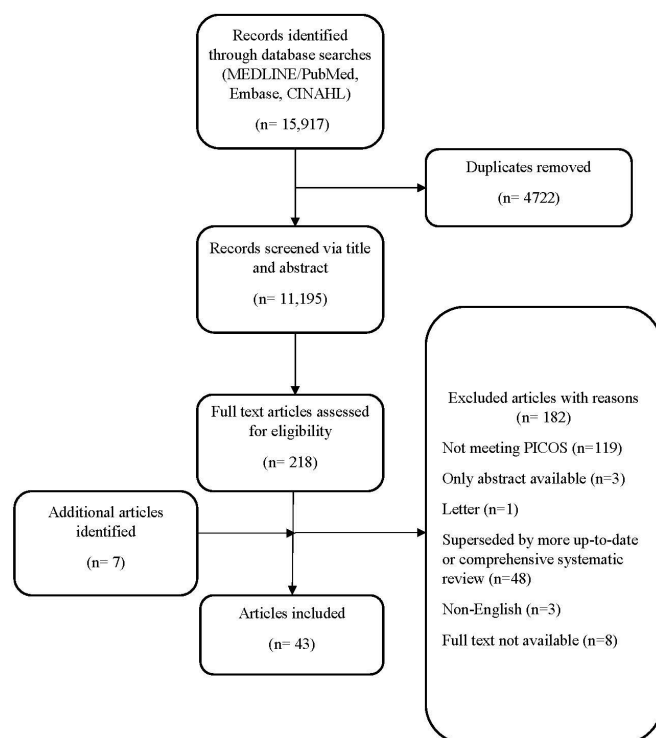
The database searches yielded 15 917 citations. Following removal of duplicates, we screened 11 195 titles and or abstracts. Two hundred and eighteen full-text articles were selected for review, of which 182 were rejected. Seven additional studies were identified from other sources, for example, the 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,<sup>24–32</sup> with participant numbers from 116<sup>24</sup> to 19 519.<sup>25</sup> Sample size of primary studies varied from 6229 participants<sup>33</sup> to 70 participants.<sup>34</sup> Four studies had a sample size of fewer than 100 participants.<sup>34–37</sup>

Overall confidence in systematic review findings was high in two reviews,<sup>26 38</sup> 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



Figure 1



**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.<sup>39</sup> 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,<sup>40</sup> with the Four-Stage Balance Test,<sup>41</sup> the Five-Times Sit-to-Stand Test<sup>42</sup> and other components of a multi-factorial 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,<sup>27</sup> any osteoporotic fracture<sup>43</sup> or had undergone hip fracture surgery.<sup>28 29 35</sup> Interventions included structured exercise of different types,<sup>28</sup> balance training<sup>43</sup> and progressive resistance exercise (PRE).<sup>29 35</sup> 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;  $p<0.001$ ).<sup>29</sup> 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.<sup>35</sup> 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.<sup>27</sup> 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 analysis<sup>26</sup> and one RCT.<sup>44</sup> 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.<sup>44</sup> 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 intervention studies and their main findings: non-pharmacological treatments 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 |
|--|--------------|---|---|---|-----|
| <b>i) Exercise</b>   |              |   |   |   |     |
| Diong <i>et al</i> hospital and community <sup>28</sup>                                | 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                                | 1   |
| Lee <i>et al</i> hospital and community <sup>29</sup>                                  | MA           | Patients after HF surgery; 6 studies (n=420)                                | Progressive resistive exercise  | Significant improvement in overall mobility in IG compared with CG (SMD=0.501; 95% CI 0.297 to 0.705; p<0.001)  | 1   |
| Kronborg <i>et al</i> Denmark, inpatients <sup>35</sup>                                | RCT          | Patients after HF surgery<br>1. Group 1 (n=45); 2. Group 2 (n=45)           | 1. PRE+routine physiotherapy<br>2. Routine physiotherapy<br>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 | 2   |
| Liu <i>et al</i> <sup>27</sup>   | 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 <i>et al</i> Hungary, community <sup>43</sup>                                     | RCT          | Women with OP fracture<br>1. Group 1 (n=49)<br>2. Group 2 (n=48)            | 1. Balance training<br>2. Usual care<br>Physiotherapists  | Significantly greater improvement in balance and fewer falls at 12 months in the balance training group   | 2   |
| <b>ii) Nutrients including vitamin D plus calcium and oral nutritional supplements</b> |              |   |   |   |     |
| Avenell <i>et al</i> community <sup>26</sup>   | MA           | 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% CI 0.71 to 1.47) or any new fracture (risk ratio=0.93, 95% CI 0.79 to 1.10).     | 1   |
| Mak <i>et al</i> Australia inpatients <sup>44</sup>                                    | RCT          | Patients after HF surgery<br>1. Group 1 (n=106); 2. Group 2 (n=104)         | 1. Single dose of 250 000 IU vitamin D3<br>2. Placebo   | Statistically significant reduction in falls incidence in IG at 4 weeks. No significant difference in fractures between groups at 4 weeks.                            | 2   |
| Myint <i>et al</i> Hong Kong inpatient <sup>45</sup>                                   | RCT          | Patients after HF surgery<br>1. Group 1 (n=58); 2. Group 2 (n=58)           | 1. Daily oral nutritional supplement for 28 days<br>2. Usual care   | No significant between group difference in Elderly Mobility Scale 4 weeks postdischarge.  | 2   |
| <b>iii) Orthoses</b>   |              |   |   |   |     |
| Newman <i>et al</i> inpatient, outpatient and community <sup>38</sup>                  | SR           | Patients with OVf; 12 studies (n=626)                                       | Spinal orthoses   | 2/12 studies showed improvements in balance with orthoses   | 2   |
| de Moraes Barbosa <i>et al</i> Brazil, community <sup>37</sup>                         | RCT          | Women with OP ±fracture<br>1. Group 1 (n=44); 2. Group 2 (n=45)             | 1. Custom foot orthoses<br>2. No intervention   | Significant between group difference in TUG (p<0.001) and BBS (p<0.001) favouring orthoses at 4 weeks   | 2   |
| <b>iv) Falls prevention programmes</b>   |              |   |   |   |     |
| Visser <i>et al</i> inpatient and community <sup>46</sup>                              | 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   | 2   |
| van Ooijen <i>et al</i> The Netherlands, rehabilitation centre <sup>34</sup>           | RCT          | Patients with HF<br>1. Group 1 (n=14); 2. Group 2 (n=16); 3. Group 3 (n=16) | 1. Treadmill training with visual context<br>2. Conventional treadmill training<br>3. Usual physical therapy<br>Physical therapists | No significant difference in fall rate between groups at 12 months.   | 2   |

Continued

Table 3 Continued

| Authors, country, setting if stated   | Study design | 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 <sup>49</sup> | RCT          | Women with HF<br>1. Group 1 (n=78)<br>2. Group 2 (n=75)                     | 1. MDT programme +telephone call post d/c<br>2. MDT programme<br>Occupational therapist                             | 14.1% women in the IG and 13.3% in the CG sustained at least 1 fall during 6-month follow-up (relative risk 1.06, 95% CI 0.48 to 2.34).  | 2   |
| Di Monaco <i>et al</i> Italy, community <sup>50</sup>                             | Quasi-RCT    | Women with HF<br>1. Group 1 (n=45)<br>2. Group 2 (n=50)                     | 1. MDT programme +home visit post d/c<br>2. MDT programme<br>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 <sup>51</sup>               | RCT          | Patients after HF surgery<br>1. Group 1 (n=102)<br>2. Group 2 (n=97)        | 1. Geriatric rehabilitation +home visit<br>2. Care on orthopaedic ward<br>Physiotherapists, occupational therapists | 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)   | 2   |
| Shyu <i>et al</i> Taiwan, inpatient and community <sup>52</sup>                   | RCT          | Patients after HF surgery<br>1. Group 1 (n=79)<br>2. Group 2 (n=81)         | 1. Orthogeriatrics, rehabilitation +d/c plan<br>2. Usual care<br>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%;  $\chi^2=4.327$ ;  $p=0.024$ ), 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.<sup>45</sup> However, at 4 weeks post discharge, there were no statistically significant differences in the Elderly Mobility Scale.

### Orthoses

One systematic review of randomised and non-randomised studies investigated the effect of spinal orthoses in the management of people with osteoporotic vertebral fracture (OVF).<sup>38</sup> 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,<sup>37</sup> 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.<sup>46</sup> Two studies showed a statistically significant reduction in fear of falling, measured by the Falls Efficacy Scale,<sup>47 48</sup> although both had small sample sizes. An additional five studies<sup>34 49–52</sup> 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,<sup>49</sup> nor a 6-week programme of treadmill walking focused towards visually guided stepping in relation to obstacles,<sup>34</sup> resulted in a statistically significant reduction in the proportion of fallers or the rate of falls when compared



with a control group. In contrast, a single home visit undertaken by an occupational therapist<sup>50</sup> led to a lower proportion of fallers in the intervention group compared with a control group (OR 0.275, 95% CI 0.081 to 0.937;  $p=0.039$ ). However, this was a quasi-RCT at unclear risk 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.<sup>51 52</sup> One RCT based in Taiwan, in which participants received in-home rehabilitation for 3 months post discharge, reported a lower occurrence of falls in non-cognitively impaired participants in the first 2 years after discharge compared with a control group (OR=0.47, 95% CI 0.25 to 0.86;  $p=0.014$ ).<sup>52</sup> This benefit was not seen in participants with cognitive impairment. In contrast, Berggren *et al*<sup>51</sup> 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 non-pharmacological treatments provided by non-physician HPs in adults at high risk of primary osteoporotic fracture?

One systematic review,<sup>53</sup> three meta-analyses<sup>24 30 31</sup> and three primary studies<sup>54-56</sup> contributed evidence about exercise interventions. Two RCTs explored falls prevention programmes<sup>36 57</sup> and two systematic reviews<sup>58 59</sup> and one RCT<sup>60</sup> investigated nutrient supplementation. One systematic review explored patient education strategies<sup>61</sup> (table 4).

#### Exercise

Evidence from seven publications was synthesised to investigate the effect of exercise on risk of falling,<sup>30 31 53</sup> BMD,<sup>24 30 53</sup> incidence rate of fractures<sup>54 56</sup> and falls.<sup>53 55</sup> Available evidence from one meta-analysis<sup>31</sup> 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  $\geq 1$  year appears to confer positive benefits on BMD,<sup>53 55</sup> unlike whole-body vibration<sup>30</sup> and low impact mind-body conditioning exercise.<sup>24</sup>

Two primary studies,<sup>54 56</sup> one randomised and one non-randomised, 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*<sup>54</sup> 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 al*<sup>56</sup> 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.<sup>53 55</sup> In one study, the number of fallers increased following a 12-month multimodal exercise intervention, although the mechanism for this is unclear.<sup>55</sup>

#### Nutrients including vitamin D plus calcium and oral nutritional supplements

Publications described nutritional supplementation with vitamin D analogues,<sup>58</sup> protein<sup>59</sup> and vitamin K.<sup>60</sup> Change in BMD was the primary outcome in all studies and was assessed between 9 weeks and 48 months. One study<sup>60</sup> 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)-1 $\alpha$ ,25-dihydroxyvitamin D<sub>3</sub> (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 al*<sup>59</sup> reported no significant change in BMD from daily consumption of dietary non-soy protein ( $>90$  g/day) or whey isolate supplement (30.1 g in 250 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 (86 g/day including 6 g whey protein isolate). The sample size in all of these trials was small and the quality assessment rating was low.<sup>59</sup>

#### Falls prevention programmes

Two RCTs,<sup>36 57</sup> one of which randomised over 1000 participants,<sup>57</sup> 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 al*<sup>36</sup> recorded a 39% reduction in falls per person years (IRR 0.61, 95% CI 0.40 to 0.94), while Palvanen *et al*<sup>57</sup> 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 |
|--|--------------|--|---|---|-----|
| <b>i) Exercise</b>   |              |  |   |   |     |
| de Kam <i>et al</i> <sup>53</sup>  | 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)<br>Exercising ≥1 year had positive effect on BMD/BMC (5/6 studies)  | 2   |
| Luo <i>et al</i> <sup>30</sup>   | 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 <i>et al</i> <sup>24</sup>   | 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 <i>et al</i> <sup>31</sup>   | 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 <sup>54</sup>                              | RCT          | Women with osteopenia 1.Group 1 (n=84); 2.Group 2 (n=76)                                 | 1. Multimodal exercise for 12 months<br>2. 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  | 2   |
| Gianoudis <i>et al</i> Australia, community <sup>55</sup>                              | RCT          | Adults with osteopenia/risk of falls 1.Group 1 (n=81); 2.Group 2 (n=81)                  | 1.Multimodal exercise for 12 months+education<br>2.Usual care<br>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 <i>et al</i> Germany community <sup>56</sup>                                   | CCT NR       | Women with osteopenia 1.Group 1 (n=59); 2.Group 2 (n=46)                                 | 1.Long-term multimodal exercise<br>2.Sedentary control group<br>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   |
| <b>ii) Nutrients including vitamin D plus calcium and oral nutritional supplements</b> |              |  |   |   |     |
| Porter <i>et al</i> <sup>58</sup>  | 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 <i>et al</i> <sup>59</sup>   | 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 <sup>60</sup>                                    | RCT          | Postmenopausal women with osteopenia 1.Group 1 (n=217); 2.Group 2 (n=223)                | 1. Vitamin K (5 mg) daily<br>2. 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   |
| <b>iii) Falls prevention programmes</b>  |              |  |   |   |     |
| Smulders <i>et al</i> The Netherlands, community <sup>36</sup>                         | RCT          | Adults with osteoporosis +falls history 1.Group 1 (n=50); 2.Group 2 (n=46)               | 1. Falls prevention programme lasting 5.5 weeks.<br>2. Usual care<br>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 <i>et al</i> Finland community <sup>57</sup>                                  | RCT          | Older adults at high risk of fracture 1.Group 1 (n=661); 2.Group 2 (n=653)               | 1. Individualised falls prevention programme<br>2. Brochure<br>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   |
| <b>iv) Education</b>   |              |  |   |   |     |
| Morfeld <i>et al</i> <sup>61</sup>   | 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.<sup>57</sup>

### 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.<sup>61</sup> 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 bias.

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  $\geq 50\%$  of studies. Only one of four RCTs reporting fractures showed a significant reduction in fracture incidence.<sup>62</sup> 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 RCTs<sup>33 63 64</sup> 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.<sup>21</sup>

- Multidisciplinary team<sup>32</sup> 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,<sup>32 65</sup> fracture liaison services (FLS)<sup>25 66</sup> and care pathways for people following hip fracture.<sup>67</sup>
- 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 al*<sup>63</sup> 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 al*<sup>63</sup> 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,<sup>68</sup> 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 study<sup>69</sup> 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.<sup>33 68</sup> 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,<sup>32</sup> or routine orthopaedic care<sup>65</sup> 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.<sup>32</sup> 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

**Table 5** Characteristics of intervention studies and their main findings: implementation strategies to increase implementation of recommendations; multidisciplinary team (MDT) care; interventions to enhance adherence to antiosteoporosis medicines

| Authors, country, setting if stated   | Study design      | Population characteristics; number of participants for outcomes of interest         | Intervention; healthcare professional if stated   | Main findings   | LoE |
|---|-------------------|---|---|---|-----|
| <b>i) Implementation strategies to increase implementation of recommendations</b> |                   |   |   |   |     |
| Cox <i>et al</i> UK, Care homes <sup>63</sup>                                     | Cluster RCT       | 1. Group 1 (n=3315)<br>2. Group 2 (n=2322)  | 1. Education+feedback<br>2. No intervention<br>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 <sup>63</sup>                             | Pilot cluster RCT | 1. Group 1 (n=2185)<br>2. Group 2 (n=3293)  | 1. Education+action planning +feedback<br>2. Fracture prevention toolkits<br>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.<br>No significant difference in prescribing osteoporosis medicines | 2   |
| Ciaschini <i>et al</i> Canada, community <sup>68</sup>                            | RCT               | Adults at risk of future fracture<br>1. Group 1 (n=101)<br>2. Group 2 (n=100)       | 1. Multifaceted intervention<br>2. Usual care<br>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 <sup>64</sup>                                      | Cluster RCT       | 1. Group 1 (n=330)<br>2. Group 2 (n=337)  | 1. Multicomponent<br>2. Usual care<br>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 <i>et al</i> <sup>69</sup>   | Cohort study      | 1. Group 1 (n=60)<br>2. Group 2 (n=47)  | 1. Clinical decision support alert<br>2. No alert<br>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  | 3   |
| <b>ii) MDT care</b>   |                   |   |   |   |     |
| Grigoryan <i>et al</i> inpatients <sup>32</sup>                                   | MA                | Patients with hip fracture<br>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)   | 1   |
| Prestmo <i>et al</i> Norway, inpatients <sup>65</sup>                             | RCT               | Patients with hip fracture<br>1. Group 1 (n=198)<br>2. Group 2 (n=199)              | 1. Orthogeriatric care<br>2. Orthopaedic care<br>MDT  | Significant between group difference in SPPB in favour of orthogeriatric 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 <sup>25</sup>                          | MA                | Patients with all fracture types<br>11 studies (n=19 519) and 15 studies (n=16 802) | FLS versus usual care/control<br>MDT  | FLS reduced absolute risk of refracture (ARR -0.05, 95% CI -0.08 to -0.03; NNT=20)<br>FLS reduced absolute risk of mortality (ARR -0.03, 95% CI -0.05 to -0.01; NNT=33)   | 1   |
| Wu <i>et al</i> inpatients and outpatients <sup>66</sup>                          | SR                | Patients with all fracture types  | FLS versus usual care or no treatment<br>MDT  | FLS implemented in HICs and MICs are cost effective across FLS model types  | 2   |
| Leigheb <i>et al</i> inpatients and community <sup>67</sup>                       | SO                | Patients with hip fracture  | Care pathways and MCA versus usual care<br>MDT  | No significant reduction in short-term mortality<br>Mixed effect on functional recovery   | 1   |
| <b>iii) Interventions to enhance adherence to antiosteoporosis medicines</b>      |                   |   |   |   |     |
| Hilligsmann <i>et al</i> <sup>70</sup>  | SR                | Adults using osteoporosis medicines<br>20 studies (n=14 662)                        | Education; monitoring/supervision; drug regimens; electronic prescription; decision aid.<br>Nurses, pharmacists, physicians, MDT, clinical personnel and health educators | 9/12 studies showed statistically significant improvement in adherence to medicines in IG versus CG<br>5/13 studies showed improved persistence with an intervention  | 2   |

Continued

Table 5 Continued

| 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 <sup>72</sup>          | Cluster RCT  | Participants starting bisphosphonates<br>1. Group 1 (n=379)<br>2. Group 2 (n=255)      | 1. Single telephone counselling call<br>2. Usual care<br>Pharmacist, trainee pharmacist, pharmacy technician | No significant between group difference in mean adherence rate. IG: 75.2% versus UC: 73.3%. Counselling call only received by 137 participants in the IG                                     | 2   |
| Stuurman-Bieze <i>et al.</i> , The Netherlands, community pharmacies <sup>71</sup> | Cohort study | Patients initiating osteoporosis medicines<br>1. Group 1 (n=495)<br>2. Group 2 (n=442) | 1. Counselling and monitoring service<br>2. Usual care<br>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). | 3   |

ARR, absolute risk reduction; CG, control group; FLS, 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, multidisciplinary care approaches; MIC, middle-income countries; NNT, numbers needed to treat; OR, Odds ratio; RCT, randomised controlled trial; RR, relative risk; 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.<sup>65</sup> The study also identified that comprehensive geriatric care was more cost effective than orthopaedic care, although a lack of baseline EQ-5D-3L (3-level version of EuroQol 5 dimensions questionnaire) data precluded control of any baseline value imbalances.

In contrast, Leighbeg *et al.*<sup>67</sup> 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.<sup>25</sup> 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.<sup>66</sup> 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) \$A31 749) 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 £19 955 and £20 421 per QALY, thus falling within recommended ICER ranges.<sup>66</sup>

#### 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 (14 662 participants),<sup>70</sup> one prospective cohort study<sup>71</sup> and one cluster RCT<sup>72</sup> (table 5). Available evidence suggests that simplification of antiosteoporosis medication dosing regimens, incorporating less frequent dosing, electronic



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,<sup>70 71</sup> 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 non-physician HPs to prevent and manage osteoporotic fractures in adults  $\geq 50$  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 domain-specific 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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