Fracture prevention in postmenopausal women

Search date January 2002

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QUESTIONS

INTERVENTIONS

See glossary, p 1101

Key Messages

- **Alendronate** One systematic review and one subsequent RCT have found that alendronate versus placebo significantly reduces vertebral and non-vertebral fractures over 1–4 years.
- **Calcitonin** One large RCT found that calcitonin versus placebo significantly reduced the incidence of new vertebral fractures over 5 years. One systematic review found limited evidence about the effects of calcitonin versus placebo, no treatment, calcium, or calcium plus vitamin D.
- **Calcium alone** One RCT found that in women with existing fractures calcium versus placebo significantly reduced the incidence of new vertebral or non-vertebral fractures over 3 years, but found no significant difference in new fractures in women without existing fractures. Another RCT found no significant difference with calcium versus placebo in the proportion of women who had one or more new fractures over 2–4 years.
- **Calcium plus vitamin D** One RCT in elderly women in nursing homes has found that calcium plus vitamin D3 versus placebo significantly reduced the incidence of non-vertebral fractures over 18 months to 3 years. Another RCT found no significant difference in the incidence of vertebral fractures over 3 years with calcium plus vitamin D3 versus placebo, but it may have been underpowered to exclude a clinically important difference.

Clin Evid 2002;8:1089–1102.

- **Etidronate** One systematic review has found that etidronate versus placebo, calcium, or calcium plus vitamin D significantly reduces vertebral fractures over 2 years. One systematic review has found no significant difference in non-vertebral fractures over 2 years with etidronate versus placebo, versus calcium, or versus calcium plus vitamin D.
- **Hip protectors** RCTs in elderly nursing home residents found that hip protectors versus no hip protectors significantly reduced the incidence of hip fracture over 9–19 months, but found no significant difference in the incidence of pelvic fracture.
- **Hormone replacement therapy** RCTs found no significant difference with hormone replacement therapy versus placebo in the proportion of women who sustained vertebral fractures. One systematic review found that hormone replacement therapy versus placebo significantly reduced the proportion of women with non-vertebral fractures. Pooled estimates from observational studies found an increased risk of endometrial cancer and breast cancer when oestrogen was used for over 8 years, and found that hormone replacement therapy increased the risk of venous thromboembolism.
- **Risedronate** One large RCT in women with one or more existing fractures found that risedronate versus placebo reduced non-vertebral fractures over 3 years, but another large RCT found no significant difference. One large RCT in women aged over 70 years has found that risedronate versus placebo significantly reduces the incidence of hip fracture over 3 years. Two large RCTs in women with one or more existing fractures have found that risedronate versus placebo significantly reduces the incidence of vertebral fracture over 3 years. Observational evidence suggests that risedronate may be associated with significant increase in the occurrence of pulmonary cancer.
- **Tiludronate** One large RCT in women with low bone mineral density with and without one or more existing fracture found no significant difference with tiludronate versus placebo in the incidence of vertebral fractures over 3 years.
- **Vitamin D alone** One large RCT found no significant difference with vitamin D3 versus placebo in the incidence of non-vertebral fracture over 3 years. One systematic review found that calcitriol versus placebo significantly reduced the incidence of vertebral fractures during the third year of treatment.
- **Environmental manipulation; exercise; pamidronate** RCTs found insufficient evidence about the effects of these interventions in preventing vertebral and non-vertebral fractures.

DEFINITION A fracture is a break or disruption of bone or cartilage. Symptoms and signs may include immobility, pain, tenderness, numbness, bruising, joint deformity, joint swelling, limb deformity, and limb shortening. Diagnosis is usually based on a typical clinical picture combined with results from an appropriate imaging technique.

INCIDENCE/ PREVALENCE The lifetime risk of fracture in white women is 20% for the spine, 15% for the wrist, and 18% for the hip.[1]

AETIOLOGY/ RISK FACTORS Fractures usually arise from trauma. Risk factors include those associated with an increased tendency to fall (such as ataxia, drug and alcohol intake, loose carpets), age, osteoporosis, bony metastases, and other disorders of bone.

PROGNOSIS Fractures may result in pain, short or long term disability, haemorrhage, thromboembolic disease (see thromboembolism, p 209), shock, and death. Vertebral fractures are associated with pain, physical impairment, muscular atrophy, changes in body shape,

loss of physical function, and lower quality of life. About 20% of women die in the first year after a hip fracture, representing an increase in mortality of 12–20% compared with women of similar age and no hip fracture. Half of elderly women who had been independent become partly dependent after hip fracture. One third become totally dependent.

AIMS	To prevent fractures, with minimal adverse effects from treatment.
OUTCOMES	Incidence of hip, wrist, and vertebral fractures.
METHODS	*Clinical Evidence* update search and appraisal January 2002. We also hand searched journals of bone diseases and carried out manual searches using the bibliographies of review articles published after 1985. Some of the RCTs identified provide results generalised to fracture per person/year or overall fractures. These results provide an idea of the group effect of an intervention, but not of its effects on the incidence of fracture in an individual. Data on multiple fractures in one person clearly differ from data on multiple people experiencing a single fracture. Regulatory authorities and scientific groups have recommended that the results of studies evaluating new chemical entities are expressed in terms of the proportion of people experiencing new fractures.[2]

QUESTION What are the effects of treatments to prevent fractures in postmenopausal women?

OPTION BISPHOSPHONATES

Olivier Bruyere and Jean-Yves Reginster

One systematic review and one subsequent RCT have found that alendronate versus placebo significantly reduces vertebral and non-vertebral fractures over 1–4 years. One systematic review has found that etidronate versus placebo, calcium, or calcium plus vitamin D significantly reduces vertebral fractures over 2 years, but has found no significant difference in non-vertebral fractures. Two large RCTs in women with one or more existing fracture have found that risedronate versus placebo significantly reduces the incidence of new vertebral fracture over 3 years. One of the RCTs found that risedronate versus placebo reduced non-vertebral fractures over 3 years, but the other found no significant difference. One large RCT in women aged over 70 years has found that risedronate versus placebo significantly reduces the incidence of hip fracture over 3 years. Observational evidence suggests that risedronate may be associated with significant increase in the occurrence of pulmonary cancer. One large RCT in women with low bone mineral density with and without one or more existing fractures found that tiludronate versus placebo significantly reduced the incidence of non-vertebral fractures. It found no significant difference with tiludronate versus placebo in the incidence of vertebral fractures over 3 years, but may have been too small to detect a clinically important difference. One small RCT found no significant difference with pamidronate versus placebo in the incidence of vertebral fracture per patient year.

Benefits: **Alendronate:** We found one systematic review[3] and one subsequent RCT.[4] The systematic review (search date 1998, 7 RCTs, 10 287 postmenopausal women aged 39–85 years) found that

alendronate versus placebo significantly reduced vertebral fractures (RR 0.54, 95% CI 0.45 to 0.66) and non-vertebral fractures (RR 0.81, 95% CI 0.72 to 0.92). It found a non-significant reduction of hip fractures over 1–4 years (RR 0.64, 95% CI 0.40 to 1.01; results presented graphically).[3] One large subsequent RCT (3658 women with vertebral fracture or osteoporosis) compared alendronate (5–10 mg/day) versus placebo for 3–4 years.[4] It found that alendronate versus placebo significantly reduced non-vertebral fractures, including hip fractures, over 3 years (all non-vertebral: RR 0.73, 95% CI 0.61 to 0.87; hip: RR 0.47, 95% CI 0.2 to 0.79; no further data provided) and both clinical and radiologic vertebral fractures over 3 years (radiologic vertebral: RR 0.52, 95% CI 0.42 to 0.66; no further data provided).[4] **Etidronate:** We found one systematic review (search date 1998, 13 RCTs, 1010 women) comparing etidronate versus placebo, calcium, or calcium plus vitamin D.[5] It found that etidronate versus placebo significantly reduced vertebral fractures over 2 years (9 RCTs: 32/538 [6%] *v* 54/538 [10%]; RR 0.60, 95% CI 0.41 to 0.88), but found no significant difference in non-vertebral fractures (7 RCTs: 48/433 [11%] *v* 49/434 [11%]; RR 0.98, 95% CI 0.68 to 1.42).[5] **Pamidronate:** We found no systematic review but found one RCT (48 women with osteoporosis) comparing pamidronate (150 mg/day) versus placebo for 2 years.[6] It found no significant difference with pamidronate versus placebo in the incidence of vertebral fracture per patient year (13/100 *v* 24/100; P = 0.07; see methods, p 1091). **Risedronate:** We found no systematic review but found three RCTs.[7–9] The first RCT (2458 women < 85 years with at least 1 vertebral fracture) compared oral risedronate (2.5 mg/day or 5 mg/day) versus placebo for 3 years.[7] After 1 year the 2.5 mg dose of risedronate was discontinued as 5 mg was found to be more effective. It found that risedronate 5 mg versus placebo significantly reduced the incidence of new vertebral fractures over 3 years (Kaplen-Meier survival data 11% with risedronate *v* 16% with placebo; RR 0.59, 95% CI 0.43 to 0.82) and non-vertebral fractures (Kaplen-Meier survival data 5% with risedronate *v* 8% with placebo; RR 0.6, 95% CI 0.39 to 0.94).[7] The second RCT (1226 women with 2 or more existing vertebral fractures) compared risedronate 2.5 mg or 5 mg daily versus placebo for 3 years.[8] After 2 years the 2.5 mg dose of risedronate was discontinued as 5 mg was found to be more effective. It found that risedronate 5 mg versus placebo significantly reduced the proportion of women with new vertebral fractures over 3 years (Kaplan-Meier survival data 18% *v* 29%; RR 0.51, 95% CI 0.36 to 0.73), but found no significant difference in the proportion of women with osteoporosis related non-vertebral fractures (Kaplan-Meier survival data 8.9% with risedronate *v* 16% with placebo; RR 0.67, 95% CI 0.44 to 1.04).[8] The third RCT (9331 women > 70 years) compared risedronate 2.5 mg or 5 mg versus placebo.[9] It found that risedronate significantly reduced the proportion of women who had hip fracture over 3 years (Kaplan-Meier survival data 3% with risedronate *v* 4% with placebo; RR 0.7, 95% CI 0.6 to 0.9; see comment below). **Tiludronate:** We found no systematic review. We found one RCT (1805 women with low vertebral bone mineral density and at least 1 existing vertebral fracture and 488 women with

low bone mineral density and no existing fracture) comparing tiludronate 50 mg or 200 mg daily versus placebo for the first 7 days of each month for 3 years.[10] It found no significant difference with tiludronate versus placebo in the incidence of vertebral fractures over 3 years, but may have been too small to detect a clinically important difference (20% with tiludronate 50 mg *v* 19% with placebo; RRR −8%, 95% CI −35 to +19%; 19.2% with tiludronate 200 mg *v* 18.9% with placebo; RRR −1.4%, 95% CI −27 to +25%; no raw data provided). It found that tiludronate 200 mg/day versus tiludronate 50 mg/day or versus placebo reduced the incidence of non-vertebral fractures (6% with tiludronate 200 mg/day *v* 9% with tiludronate 50 mg *v* 12% with placebo; no further data provided).

Harms: **Alendronate:** Observational evidence suggests that oral alendronate is associated with oesophageal erosions and ulcerative oesophagitis. However, one RCT[11] identified by the review[3] (where people took alendronate with 180–240 mL water on arising in the morning and remained upright for at least 30 min after swallowing the tablet and until the first food of the day had been ingested) found no significant difference in oesophagitis with alendronate versus placebo. **Risedronate:** One observational study found limited evidence suggesting that the gastrointestinal safety of risedronate appears to be in the same range as alendronate.[12] One non-systematic review (10 phase III studies) found limited evidence that risedronate versus placebo may be associated with a significant increase in the occurrence of pulmonary cancer (3.9/1000 people/year of exposure with risedronate 2.5 mg/day *v* 1.9/1000 patients/year of exposure with risedronate 5 mg/day *v* 1.2/1000 patients/year of exposure with placebo; significance not stated; see comment below).[13]

Comment: **Risedronate:** In the third RCT, risedronate versus placebo reduced the risk of hip fracture by 60% in women aged 70–79 years with osteoporosis and baseline vertebral fractures.[9] However, this subgroup included only 1128/6197 women in the trial and, although the RCT found an overall 30% reduction in the relative risk of hip fracture, this reduction was not significant either in women aged 70–79 years without existing vertebral fracture, or in women over the age of 80 with at least one clinical risk factor for hip fracture.[9] The non-systematic review assessing the harms of risedronate[13] did not provide a source of reference and the methods of the phase III studies identified are unclear.

OPTION CALCIUM AND VITAMIN D ALONE OR IN COMBINATION

Olivier Bruyere and Jean-Yves Reginster

One RCT found that in women with existing fractures calcium versus placebo significantly reduced the incidence of new vertebral or non-vertebral fractures over 3 years, but found no significant difference in new fractures in women without existing fractures. Another RCT found no significant difference with calcium versus placebo in the proportion of women who had one or more new fracture over 2–4 years. One large RCT identified by a systematic review found no significant difference with vitamin D3 versus placebo in the incidence of non-vertebral fracture over 3 years. One systematic review found that calcitriol versus placebo

significantly reduced the incidence of vertebral fractures during the third year of treatment. One RCT has found that calcium plus vitamin D3 versus placebo significantly reduces the incidence of non-vertebral fractures over 18 months to 3 years. Another RCT found no significant difference in the incidence of vertebral fractures over 3 years with calcium plus vitamin D3 versus placebo, but it may have been underpowered to exclude a clinically important difference.

Benefits:

Calcium versus placebo: We found no systematic review but found two RCTs.[14,15] The first RCT (78 women) comparing elemental calcium (calcium lactate–gluconate plus calcium carbonate) 1 g/day versus placebo found no significant difference in the proportion of women who had one or more new fractures over 2–4 years, but may have been too small to exclude a clinically important difference (2/38 [5%] *v* 7/40 [17%]; RR 0.30, 95% CI 0.06 to 1.36).[14] The second RCT (197 women) compared oral calcium carbonate (1.2 g/day) versus placebo for a mean 3 years in women aged over 60 years with or without existing fractures (see comment below).[15] It found that in women with existing fractures (94 women, mean age 74.9 years) calcium versus placebo significantly reduced the proportion of women who had vertebral and non-vertebral fractures over a mean 3 years (15/53 [28%] *v* 21/41 [51%]; RR 0.55, 95% CI 0.33 to 0.93), but found no significant difference in the incidence of vertebral and non-vertebral fractures in women without existing fractures (103 women, mean age 72.4; 12/42 [28%] with calcium *v* 13/61 [21%] with placebo; RR 1.34, 95% CI 0.68 to 2.64).[15] **Vitamin D or vitamin D analogue versus placebo:** We found one systematic review (search date 2000, 3 RCTs).[16] The first RCT (2578 people; 1916 women, 662 men, mean age 80 years, living at home; see comment) found no significant difference with vitamin D3 versus placebo in the incidence of hip fracture (58/1284 [4.5%] *v* 48/1280 [3.7%]; RR 1.20, 95% CI 0.83 to 1.75) or any non-vertebral fracture over 3 years (135/1284 [10%] *v* 122/1280 [9%]; RR 1.10 95% CI 0.87 to 1.39). The review identified two small RCTs (68 women aged ≥ 54 years) comparing calcitriol (1,25 dihydroxy vitamin D) versus placebo. It found that calcitriol versus placebo significantly reduced the incidence of new vertebral fractures over 3 years (8/34 [23%] *v* 17/34 [50%]; RR 0.49, 95% CI 0.25 to 0.95). **Vitamin D or vitamin D analogue versus calcium:** We found one systematic review[16] that identified one RCT (622 women)[17] comparing calcitriol versus calcium (see comment below). It found that calcitriol significantly reduced the frequency of new vertebral fractures during the third year of treatment (12/213[6%] *v* 44/219 [20%]; RR 0.28, 95% CI 0.15 to 0.52; see comment below). **Calcium plus vitamin D versus placebo:** We found one systematic review (search date 2002, 2 RCTs, 3715 people).[16] One of the RCTs (3270 mobile elderly women, age range 69–106 years, living in 180 nursing homes) found that calcium plus vitamin D3 versus placebo significantly reduced the incidence of hip fractures (80/1387 [6%] *v* 110/1403 [8%]; RR 0.74, 95% CI 0.60 to 0.91) and all non-vertebral fractures (160/1387 [11%] *v* 215/1403 [15%]; RR 0.75, 95% CI 0.62 to 0.91) over 18 months. This difference remained significant after 3 years' treatment (hip fracture: 137/1176 [12%] *v* 178/1127 [16%]; RR 0.74, 95% CI 0.60 to 0.91; all

non-vertebral fracture: 255/1176 [22%] *v* 308/1127 [27%]; RR 0.72, 95% CI 0.60 to 0.84). The other RCT (246 women, 199 men, mean age 71 years, living at home; see comment) found no significant difference with calcium plus vitamin D versus placebo in the incidence of hip fractures over 3 years (0/187 [0%] *v* 1/202 [0.5%]; RR 0.36, 95% CI 0.01 to 8.78), but may have been underpowered to exclude a clinically important difference. It found that calcium plus vitamin D significantly reduced overall non-vertebral fractures (11/187 [6%] *v* 26/202 [13%]; RR 0.46, 95% CI 0.23 to 0.90).[16]

Harms: The systematic review found that vitamin D or vitamin D analogues versus placebo or calcium significantly increased hypercalcaemia (5 RCTs, 1009 people; 22/498 [4.4%] *v* 18/511 [3.5%]; RR 1.71, 95% CI 1.01 to 2.89).[16]

Comment: In the RCT comparing calcium versus placebo in subgroups of women with and without existing fractures, randomisation was not stratified according to existing fracture status and there was an unequal number of women taking calcium or placebo in each subgroup.[15] In the RCT[17] comparing calcitriol versus placebo, identified by the review,[16] the rate of vertebral fractures in the calcitriol group did not change over time. The statistical difference in fracture rates observed between the groups may have occurred because people taking calcium had an increase in fracture incidence during the third year of the trial.[17] The results of the RCT should be interpreted with caution as they are not intention to treat, and there was a high withdrawal rate, particularly in the third year. This RCT did not have a central x ray reading facility for the assessment of vertebral fractures.[17] Although some RCTs included both men and women at risk of hip fracture,[16] it is likely that the results are generalisable to postmenopausal women.

OPTION CALCITONIN

Olivier Bruyere and Jean-Yves Reginster

One large RCT found that calcitonin versus placebo significantly reduced the incidence of new vertebral fractures over 5 years. One systematic review found limited evidence about the effects of calcitonin versus placebo, no treatment, calcium, or calcium plus vitamin D.

Benefits: We found one systematic review[18] and one subsequent RCT.[19] The systematic review (search date 1997, 14 RCTs, 7 RCTs in peri-menopausal women with crush fractures or osteoporosis, 7 RCTs in men and women with osteoporosis or taking corticosteroids, 1309 people, exact proportions of women and men not specified; see comment) compared calcitonin (salcatonin) versus placebo, no treatment, calcium, or calcium plus vitamin D (see comment below).[18] It found that fewer people developed vertebral or non-vertebral fractures with calcitonin versus no calcitonin, but the difference was not significant (vertebral fractures: 166/1190 [14%] people with calcitonin *v* 96/554 [17%] with no calcitonin; RR 0.80, 95% CI 0.64 to 1.01; non-vertebral fractures; RR 0.48, 95% CI 0.20 to 1.15; no raw data provided).[18] One subsequent RCT (1108 postmenopausal women with osteoporosis receiving calcium

1000 mg/day and vitamin D 400 IU/day) compared salmon calcitonin nasal spray (100, 200, or 400 IU) daily versus placebo for 5 years.[19] It found that calcitonin 200 IU versus placebo significantly reduced the proportion of women with new vertebral fractures over 5 years (51/287 [18%] with calcitonin 200 IU *v* 70/270 [26%] with placebo; RR 0.67, 95% CI 0.47 to 0.97). The difference remained significant in women with one to five existing vertebral fractures at baseline (60/203 [30%] *v* 40/207 [19%]; RR 0.64, 95% CI 0.43 to 0.96). It found no significant difference in the risk of vertebral fractures with calcitonin 100 IU or 400 IU versus placebo.[19]

Harms: The systematic review gave no information on harms.[18] The subsequent RCT found that nasal spray calcitonin versus placebo significantly increased nasal congestion, nasal discharge, or sneezing (22% *v* 15%: $P < 0.01$; no raw data provided).[19]

Comment: The systematic review commented that its conclusions are limited because many of the RCTs identified did not report the occurrence of fractures, were not double blinded, and only two of the RCTs identified were of over 2 years duration.[18] Although the review included some RCTs in both men and women at risk of hip fracture, it is likely that the results are generalisable to postmenopausal women.[18]

OPTION ENVIRONMENTAL MANIPULATION

John Edwards

We found no RCTs assessing environmental manipulation alone. One RCT in men and women aged over 70 years found no significant difference in the fracture rate over 4 years with health visitor care versus control.

Benefits: We found no systematic review and no RCTs assessing environmental manipulation alone (see glossary, p 1101). We found one RCT (674 men and women > 70 years; similar proportions of women and men; see comment) comparing health visitor care (aimed at assessing nutritional deficiencies, reducing smoking and alcohol intake, improving muscle tone and fitness, assessing medical conditions and use of medication, and improving home environment, such as lighting) versus control (not specified).[20] It found no significant difference with health visitor versus control in the incidence of new fractures over 4 years (16/350 [5%] *v* 14/324 [4%]; RR 1.06, 95% CI 0.52 to 2.13).

Harms: The RCT gave no information on harms.[20]

Comment: Although the RCT included both men and women at risk of hip fracture, it is likely that the results are generalisable to postmenopausal women.[20]

OPTION EXERCISE

John Edwards

Three RCTs found no significant difference in the incidence of falls resulting in fracture over 1 year with exercise versus control.

Benefits: We found one systematic review (search date 2001) that identified three RCTs comparing the effects of exercise versus control in preventing falls resulting in fracture.[21] The review did not perform a meta-analysis because of heterogeneity of methods and interventions between the trials. The first RCT identified by the review (165 postmenopausal women living in the community who had fractured an upper limb in the previous 2 years) compared advice to walk briskly for up to 40 minutes three times weekly versus advice to carry out upper limb exercises. It found no significant difference in the incidence of falls resulting in fracture after 1 year (2/81 [2%] with brisk walking *v* 3/84 [4%] with upper limb exercises; RR 0.69, 95% CI 0.12 to 4.03). The second RCT identified by the review (77 women and 22 men, aged > 65 years, living in the community; see comment) compared a home based exercise programme (balance and strength exercises plus walking) versus no exercise programme for 14 weeks. It found no significant difference in the incidence of falls resulting in fracture over 44 weeks (1/45 [2%] with exercise *v* 0/48 [0%] with no exercise; RR 3.20, 95% CI 0.13 to 76.48). The third RCT (162 women, 78 men, aged > 75 years; see comment) found no significant difference with a home exercise programme (balance and strength exercises plus walking) versus usual care over 1 year (2/121 [2%] with home exercise *v* 7/119 [6%] with usual care; RR 0.28, 95% CI 0.06 to 1.33).[21]

Harms: One of the RCTs found that brisk walking versus control increased the number of falls (15/100 person/years, 95% CI 1.4 to 29) (see methods of fracture prevention in postmenopausal women, p 1091).[21] This result should be interpreted with caution as falls are subject to memory bias.

Comment: Most of the RCTs identified by the review examined falls rather than fractures as the main outcome of interest.[21] Although two of the RCTs included both men and women at risk of hip fracture, it is likely that the results are generalisable to postmenopausal women.

OPTION HIP PROTECTORS

John Edwards

RCTs in elderly nursing home residents found that hip protectors versus no hip protectors significantly reduced the incidence of hip fracture over 9–19 months, but found no significant difference in the incidence of pelvic fracture.

Benefits: **Non-vertebral fractures:** We found one systematic review[22] and two subsequent RCTs.[23,24] The systematic review (search date 2000) identified six RCTs (3412 people, predominantly women, see comment) assessing the effects of hip protectors versus no hip protectors on hip fractures.[22] It could not perform a meta-analysis of all of the RCTs because some of the RCTs used cluster randomisation and others randomised individuals. In the RCTs that randomised individuals, it found that hip protectors versus no hip

protectors significantly reduced the incidence of hip fractures over 9–19 months (3 RCTs, 202 people, 90–100% women in 2 RCTs, proportion of women and men not stated in 1 RCT; 4/111 [4%] *v* 15/91 [16%]; RR 0.22, 95% CI 0.09 to 0.57).[22] The first subsequent RCT (164 elderly women) found that hip protectors versus control significantly reduced hip fractures over a mean 377 days (1/88 [1%] *v* 8/76 [10%]; RR 0.11, 95% CI 0.01 to 0.84).[23] The second subsequent RCT (64 women and 8 men in a nursing home) found no significant difference with hip protectors versus no hip protectors in hip fractures over 1 year (1/36 [3%] *v* 7/36 [19%]; RR 0.14, 95% CI 0.02 to 1.10), but it may have been too small to exclude a clinically important difference (see comment).[24] **Pelvic fractures:** The review identified three RCTs.[22] It could not perform a meta-analysis because of methodological differences between the trials. All three RCTs included men and women (see comment). The first RCT (1801 people aged > 75 years, 77–79% women) identified by the review found no significant difference in the incidence of pelvic fractures over a mean 11–15 months with hip protectors versus no hip protectors (2/653 [0.3%] *v* 12/1148 [1%]; RR 0.29, 95% CI 0.07 to 1.31). The second RCT identified by the review (665 people aged > 69 years living in a nursing home, 70% women) found no significant difference in the incidence of pelvic fractures over 11 months (0/247 [0%] *v* 2/418 [0.5%]; RR 0.34, 95% CI 0.02 to 7.01). The third RCT identified by the review (64 men and 8 women, aged 71–96 years living in a nursing home) found no significant difference with hip protectors versus no hip protectors in pelvic fractures over 12 months, but may have been too small to exclude a clinically important difference (0/36 [0%] hip protector *v* 2/36 [5%]; RR 0.20, 95% CI 0.01 to 4.03).[22]

Harms: **Non-hip or non-pelvic fractures and injuries:** One of the RCTs identified by the review (665 people) found that more people had non-hip fractures over 11 months with hip protectors versus no hip protectors, but the difference was not significant (15/247 [6.1%] *v* 25/418 [6.0%]; RR 1.02, 95% CI 0.55 to 1.89). Another small RCT identified by the review found no significant difference in the incidence of non-hip fractures with hip protectors versus no hip protectors (2/35 [5.7%] *v* 0/24 [0%]; RR 3.47, 95% CI 0.17 to 69.27). A third RCT identified by the review (1801 people) also found no significant difference in the proportion of people with lower limb or other non-hip fractures over a mean 11–15 months with hip protectors versus no hip protectors (23/653 [3.5%] *v* 59/1148 [5%]; RR 0.69, 95% CI 0.43 to 1.10). The first subsequent RCT found no significant difference in the incidence of non-hip fractures over a mean 377 days with hip protectors versus no hip protectors (2/88 [2.3%] *v* 0/76 [0%]).[23] **Falls:** One of the RCTs identified by the review found that more people fell on the hip with hip protectors versus no hip protectors, but the difference was not significant (8/101 [7.9%] *v* 1/40 [2.5%]; RR 3.17, 95% CI 0.41 to 24.5). The first subsequent RCT found no significant difference in the proportion of people sustaining one or more falls over a mean 377 days (40/88 [45%] *v* 28/76 [37%]; RR 1.23, 95% CI 0.85 to 1.79). The other five RCTs identified by the review and the second subsequent RCT found no difference in the incidence of falls with hip protectors versus no hip protectors, but gave no information on the proportion of people who