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CLINICIAN NOTE

EVIDENCE SUMMARY

Fracture risk and how to reduce it in perimenopause

Bones before they break · lecture preparation · 15 October 2026 · For discussion, not a prescription



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Fracture risk around the menopause is low in absolute terms and rises with age. The question for this age group is how to spend a small absolute benefit wisely. Relative risk cuts look large; the absolute numbers below keep them in proportion.

How big is the risk?

Absolute terms

BASELINE NUMBERS FROM TRIAL PLACEBO GROUPS

GROUP (PLACEBO ARM)	FRACTURE OUTCOME	RATE
WHI, women 50-79 with a uterus, about 5.6 years [1]	Any fracture	11.1%
New Zealand women aged 50-60, T-score 0 to -2.5, 10 years [2]	New vertebral fracture on X-ray	11.1%
FREEDOM, women 60-90 with osteoporosis, 3 years [3]	Vertebral / hip	7.2% / 1.2%
HORIZON, mean age 73 with osteoporosis, 3 years [4]	Vertebral / hip	10.9% / 2.5%

Indian data: hip fractures occur about a decade earlier than in Western women [5]. One hospital study quoted by IMS India found vertebral fractures in about one in five women aged 40 to 49; this is a single-centre figure and should not be taken as population prevalence [5].

OUTSIDE INDIA *Outside India: in 15,570 Europeans aged 50 to 79, about 12% of women had a vertebral deformity on X-ray, range 6% to 21% by centre (EVOS) [6]. Not Indian data; use as a guide.*

CERTAINTY: LOW *No Indian population fracture incidence for perimenopausal women was found.*

NO INDIAN DATA *No Indian data; outside-India figure: in New Zealand women aged 50 to 60, 11.1% of the placebo group had a new vertebral fracture on X-ray over 10 years [2]. In WHI (US, ages 50 to 79), 11.1% of the placebo group had any fracture over about 5.6 years [1]. Use as a guide.*

What raises risk

THE RISK FACTORS THAT MATTER

- A previous fragility fracture. A vertebral fracture raises the risk of another about 5-fold and of other fractures 2- to 3-fold [7].
- Low BMD. Each standard deviation fall in BMD roughly doubles fracture risk [5].
- Early menopause or premature ovarian insufficiency [5].
- Glucocorticoids, aromatase inhibitors, enzyme-inducing anti-epileptic drugs and other medicines [5,8].
- Low body weight. Women with lower BMI lose bone faster through the transition [9].

What lowers risk: lifestyle

Small

BMD GAINS, FRACTURE BENEFIT UNPROVEN

MEASURE	BEST EVIDENCE	EFFECT	CERTAINTY
Resistance and impact training	LIFTMOR RCT, n=101 [10]	Spine BMD +2.9% vs -1.2%	Low (BMD only)
Any exercise	Cochrane, 43 RCTs [11]	Small BMD gains; no fracture reduction shown	Low
Calcium	Systematic review [12]	No effect in lowest-bias trials	Low
Vitamin D (not deficient)	VITAL RCT [13]	No fewer fractures (HR 0.98)	Moderate

Lifestyle still matters. It keeps muscles strong, prevents falls and costs little. But it should not delay a drug when risk is high.

What lowers risk: hormone therapy

HR 0.76

WHI AND COCHRANE

TRIAL	OUTCOME	RESULT	ABSOLUTE EFFECT
WHI oestrogen + progestin [1,14]	Hip fracture; all fractures	HR 0.66; 8.6% vs 11.1% (HR 0.76)	5 fewer hip fractures per 10,000 women per year
WHI oestrogen alone [15]	Hip; total fractures	HR 0.61; HR 0.70	6 fewer hip fractures per 10,000 women per year
Cochrane 2025 [16]	Clinical fracture (combined)	RR 0.78	Moderate certainty

The same WHI arm showed 8 more breast cancers, 8 more strokes, 8 more pulmonary emboli and 7 more heart events per 10,000 women per year [14]. Bone benefit is real but small in absolute terms, which is why most guidelines do not use MHT for bone alone in women without symptoms [17].

CERTAINTY: MODERATE

What lowers risk: bone drugs

NNT 15

BISPHOSPHONATES AND DENOSUMAB

DRUG AND TRIAL	WOMEN	RESULT
Alendronate, FIT 1 [18]	Low BMD plus vertebral fracture	New vertebral fracture 8.0% vs 15.0%; hip RH 0.49
Alendronate, FIT 2 [19]	Low BMD, no vertebral fracture	Clinical fractures cut 36% only if T-score -2.5 or lower (NNT 15); no benefit above it
Zoledronate, HORIZON [4]	Osteoporosis, mean age 73	Vertebral 3.3% vs 10.9%; hip 1.4% vs 2.5%
Zoledronate, 18-monthly [20]	Osteopenia, 65 and over	Fragility fracture HR 0.63; NNT 15 over 6 years
Zoledronate, 2 doses [2]	Aged 50-60, T-score 0 to -2.5	New vertebral fracture RR 0.56 over 10 years
Denosumab, FREEDOM [3]	Osteoporosis, 60-90	Vertebral 2.3% vs 7.2%; hip 0.7% vs 1.2%

The 2025 zoledronate trial is the only fracture trial focused on women aged 50 to 60. Two infusions, five years apart, cut new vertebral fractures. It is one trial, its main outcome was X-ray vertebral fracture, and it has not yet shaped guidelines [2].

Stopping denosumab without a follow-on drug raises vertebral fractures to 7.1 per 100 patient-years [21].

CERTAINTY: HIGH *High for women with osteoporosis; moderate for osteopenia and the 50-60 group.*

Putting it together

A PRACTICAL ORDER

SUGGESTED ORDER FOR A PERIMENOPAUSAL WOMAN

- Everyone: food calcium, vitamin D repletion, resistance and balance training, no smoking, low alcohol [5].
- Symptoms and under 60 or within 10 years: MHT treats symptoms and protects bone [22].
- Fragility fracture, T-score -2.5 or high FRAX: start a bone drug, usually a bisphosphonate [5,8].
- Osteopenia only: decide on FRAX, not T-score alone [5,19].
- Denosumab: always plan the switch before stopping [21].

WHERE THE EVIDENCE IS WEAK

- No trial with fracture as the primary outcome in perimenopausal women except the single 2025 zoledronate trial [2].
- No Indian fracture incidence data for this age group; FRAX India is uncalibrated [5].

NO INDIAN DATA *No Indian data; outside-India figure: in New Zealand women aged 50 to 60, 11.1% of the placebo group had a new vertebral fracture on X-ray over 10 years [2]. In WHI (US, ages 50 to 79), 11.1% of the placebo group had any fracture over about 5.6 years [1]. Use as a guide.*

OUTSIDE INDIA *Outside India: FRAX was built from 9 population cohorts and checked in 11 more. Clinical risk factors plus hip BMD gave a hip-fracture gradient of risk of 4.2 per SD at age 50 (Kanis 2007) [23]. Not Indian data; use as a guide.*

- Exercise and calcium reduce bone loss more clearly than they reduce fractures [11,12].

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VERIFIED BY PMID AND DOI · VANCOUVER STYLE

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