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CLINICIAN NOTE

EVIDENCE SUMMARY

Questions and evidence answers

Bones before they break · lecture preparation · 15 October 2026, revised 18 October 2026 · For discussion, not a prescription



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Bone loss speeds up from about a year before the last period. The decision to give a bone drug rests on fracture risk, not on irregular cycles alone. This sheet answers the questions most likely to come up, with a certainty grade for each answer.

HOW TO READ THE GRADES

- High or Moderate: randomised trials or a guideline built on them.
- Low or Very low: observational data, indirect trials, or small studies. Treat as a guide, not a rule.
- Expert consensus: a guideline says it, but no trial tests it directly.
- Grades are our reading of the cited sources (GRADE style), unless a guideline grade is quoted.

1. Screening — DXA

WHO TO SCAN AND WHEN

Q1. Does every woman with irregular periods need a DXA scan?

No. US and Indian guidance both use targeted case-finding, not a scan for every woman in the transition. USPSTF advises screening at 65 and in younger postmenopausal women with raised risk[1]. The Indian Menopause Society (IMS India 2026) says population DXA screening is not cost-effective in India and advises risk-based case-finding, with DXA where available[2].

CERTAINTY: MODERATE *USPSTF grade B; IMS India Grade B.*

Q2. Which women in the menopause transition should have a DXA?

IMS India 2026 lists women in the transition with a secondary cause of bone loss (endocrine, metabolic or drug-related), any fragility fracture, X-ray osteopenia or a vertebral compression fracture, and a baseline before starting a bone drug. After menopause it adds every woman more than 5 years past her last period, and earlier if she has risk factors[2].

Common risk factors in practice: glucocorticoids, early menopause or premature ovarian insufficiency, low body weight, a parent with hip fracture, smoking, heavy alcohol, rheumatoid arthritis and enzyme-inducing anti-epileptic drugs[2,3].

CERTAINTY: MODERATE *IMS India Grade B.*

Q3. Should FRAX be used for Indian women?

Yes, as a starting point, with care. The Indian FRAX model comes from a small North Indian cohort and likely underestimates risk[2]. ISBMR makes the same point and notes that Indian women fracture earlier than Western women[4]. Where DXA is not available, IMS India suggests OSTA (age and weight only) for first triage, then FRAX[2].

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[5]. Not Indian data; use as a guide.*

CERTAINTY: LOW *FRAX calibration for India is unvalidated.*

Q4. At what age should bone health come up in Indian women?

Average age at natural menopause in India is about 46.6 years, earlier than in many Western countries[6]. IMS India proposes 'Start at 35': awareness from 35 and screening for non-communicable diseases, including low bone mass, from 40[2].

OUTSIDE INDIA *Outside India: mean age at natural menopause was 48.8 years across 46 studies in 24 countries, lower in Asia, Africa and Latin America[7]. Not Indian data; use as a guide.*

CERTAINTY: LOW *IMS India grades the 'Start at 35' advice Grade C.*

2. Lifestyle — 800 mg+

CALCIUM, VITAMIN D, EXERCISE

Q5. How much calcium, and from food or tablets?

Food first. Average Indian intake is about 400 mg a day. IMS India sets a practical target of at least 800 mg a day from food, with supplements only for the gap[2]. The UK guideline also puts diet first and supplements only if intake is low[3].

Calcium for fracture prevention is weak evidence. In a systematic review, dietary calcium was not linked to fracture risk, and in the trials at lowest risk of bias, supplements made no difference[8].

CERTAINTY: LOW *Intake targets are consensus; fracture benefit is unproven in women with adequate diets.*

Q6. Should all perimenopausal women take vitamin D?

Correct deficiency; do not expect routine vitamin D to prevent fractures in women with normal levels. In VITAL, daily vitamin D3 did not lower fractures in healthy midlife and older adults not selected for deficiency (HR 0.98)[9]. Deficiency is common in South Asia, with a pooled prevalence of 68%[10]. IMS India recommends 1000 to 2000 IU a day for Indian adults and tests only women at risk[2].

> **OUTSIDE INDIA** *Outside India: in a worldwide review of 195 studies from 44 countries, 37.3% of studies reported a mean 25(OH)D below 50 nmol/L[11]. Not Indian data; use as a guide.*

CERTAINTY: MODERATE *Moderate for no benefit in replete adults; low for the Indian dose advice.*

Q7. What exercise helps bone?

Resistance and impact training, plus balance work. In the LIFTMOR trial (101 women with low bone mass, mean age 65), supervised high-intensity resistance and impact training raised spine BMD by 2.9% against a 1.2% fall in controls[12]. A Cochrane review found small BMD gains from exercise but could not show fewer fractures[13]. IMS India notes that brisk walking alone is not enough for bone[2].

CERTAINTY: LOW *BMD gains are shown; fracture reduction from exercise is not proven.*

3. Hormone therapy (MHT/HRT) — Prevents loss

WHO, WHEN AND WHY

Q8. Does menopausal hormone therapy protect bone?

Yes. In WHI, oestrogen plus progestin cut hip fractures (HR 0.66) and all fractures (8.6% vs 11.1%, HR 0.76) in women not selected for low bone density[14,15]. Oestrogen alone cut hip fractures too (HR 0.61)[16]. The 2025 Cochrane review rates the fall in clinical fractures with combined therapy as moderate certainty (RR 0.78)[17].

CERTAINTY: MODERATE *Benefit lasts while on treatment; it fades after stopping[18].*

Q9. Should MHT be started only for bone in a woman without symptoms?

Guidelines differ. USPSTF recommends against hormone therapy to prevent chronic disease, including fractures (grade D)[19]. The Menopause Society (NAMS 2022) says that under 60 or within 10 years of menopause the balance is favourable for symptoms and for preventing bone loss[20]. IMS India puts MHT as a first-line option for women at intermediate or high fracture risk within 10 years of menopause[2]. ESE 2025 treats MHT for chronic disease prevention as a contested question[21].

CERTAINTY: LOW *No trial has fracture as the reason for treatment in perimenopausal women.*

Q10. What about early menopause or premature ovarian insufficiency?

Women with menopause at or before 45 have higher risk of osteoporosis and fracture[2]. Hormone replacement is advised at least until the average age of natural menopause unless there is a contraindication[2].

CERTAINTY: MODERATE *Observational fracture data; consistent guideline advice.*

4. When to start a bone drug

T-score -2.5

WHAT CHANGES THE PLAN

Q11. Who needs an anti-osteoporosis drug?

IMS India lists three clear triggers: a fragility fracture, osteoporosis on DXA (T-score -2.5 or lower), or low bone mass with a FRAX 10-year risk above 3% for hip or above 20% for major osteoporotic fracture[2]. The UK guideline uses age-dependent FRAX thresholds[3].

A new fracture after 50 is a warning. A vertebral fracture raises the risk of another vertebral fracture about 5-fold[22].

CERTAINTY: HIGH *Drugs cut fractures in women with osteoporosis or prior fracture (placebo-controlled RCTs).*

Q12. Which drug first?

For most women, an oral bisphosphonate such as alendronate. In women with an existing vertebral fracture, alendronate roughly halved new vertebral fractures (8.0% vs 15.0%)[23]. Yearly zoledronate and six-monthly denosumab also cut vertebral and hip fractures[24,25]. IMS India allows MHT, a bisphosphonate or denosumab as first line in high-risk women within 10 years of menopause[2]. For very high risk, see the companion summary on sequential and combination therapy.

CERTAINTY: HIGH

Q13. Should a woman with osteopenia alone get a drug?

Usually no, unless FRAX risk is high. In FIT, alendronate did not significantly cut clinical fractures in women whose hip BMD was above the osteoporosis range[26]. Zoledronate every 18 months did cut fragility fractures in older women with osteopenia (HR 0.63, 15 treated to prevent one)[27]. In women aged 50 to 60, zoledronate at baseline and 5 years cut new vertebral fractures over 10 years (RR 0.56)[28].

CERTAINTY: MODERATE *The 50-60 trial is a single New Zealand RCT; X-ray (morphometric) vertebral fractures were the main outcome.*

5. Monitoring

1-5 years

FOLLOW-UP, BREAKS AND STOPPING

Q14. How often should DXA be repeated?

IMS India advises a repeat scan between 1 and 5 years, set by risk, on the same machine and at the same site[2].

EXPERT CONSENSUS *IMS India Grade B.*

Q15. Can a bisphosphonate be stopped after some years?

Review; do not stop by default. The UK guideline says routine 'drug holidays' are not supported by the evidence. In the extension trials, women who stayed on alendronate after 5 years, or on zoledronate after 3 years, had fewer vertebral fractures than those switched to placebo. Those who gain most from continuing have low hip BMD, a vertebral fracture, or a new fracture on treatment. Reassess with FRAX and BMD before any pause[3].

CERTAINTY: MODERATE

Q16. What is special about denosumab?

It must not be stopped without a plan. After stopping, vertebral fracture rates rose from 1.2 to 7.1 per 100 patient-years, and more women had multiple vertebral fractures[29]. Plan a switch to a bisphosphonate[3]. Details are in the companion summary on sequential and combination therapy.

CERTAINTY: MODERATE *Post hoc analysis of RCT data, but consistent across guidelines.*

6. How guidelines differ by region

SAME DATA, DIFFERENT EMPHASIS

REGION AND GROUP	SCREENING	MHT FOR BONE	DRUG THRESHOLD
UK: NOGG 2024[3]	Case-finding with FRAX; DXA when FRAX is near the threshold	An option; reduces fractures in unselected women; transdermal for clot risk	Age-dependent FRAX intervention thresholds
US: USPSTF 2025, 2022[1,19]	DXA at 65; younger if risk is raised (B)	Against for prevention alone (D)	Not covered
US: BHOF 2022, Endocrine Society 2019[22,30]	Risk-based	Not assessed for this document	Country-specific risk tool guides treatment
US: Menopause Society 2022[20]	Not its focus	Favourable under 60 or within 10 years for symptoms and bone-loss prevention	Not covered
Europe: ESE 2025[21]	Not its focus	Covers symptom care, POI and early menopause; treats MHT for chronic disease prevention as contested	Not covered
India: IMS India 2026, ISBMR 2021[2,4]	'Start at 35'; OSTA, then FRAX, then DXA	First-line option within 10 years of menopause at intermediate or high risk	Fracture, T-score -2.5, or FRAX hip >3% / MOF >20%

ACOG and EMAS/IOF guidance was not re-checked for this document; no verified source was added for them.

7. How the advice changed over time

FROM ROUTINE HRT TO RISK-BASED CHOICE

WHEN	WHAT HAPPENED	EFFECT ON PRACTICE (OUR INTERPRETATION)
Before 2002	HRT widely given for symptoms and to prevent heart disease and osteoporosis, largely on observational data[14].	Broad, long-term use.
2002	WHI oestrogen plus progestin arm stopped early: more breast cancer, heart events, strokes and clots; fewer hip and colorectal events[14].	Sharp fall in HRT use; bisphosphonates became the main bone drug.
2004	WHI oestrogen-alone arm stopped: more strokes, fewer hip fractures, no rise in breast cancer[16].	Oestrogen alone seen differently from combined therapy.
2013 and 2017	Long-term WHI follow-up: most risks and benefits faded after stopping; no change in deaths over 18 years; better balance at 50-59[18,31].	'Timing' idea: start near menopause, under 60.
2019	Worldwide meta-analysis: breast cancer risk rises with duration and persists after stopping[32].	More detail in consent about type and duration.
2022 to 2026	USPSTF D for prevention[19]; NAMS favourable under 60[20]; NOGG 2024[3]; ESE 2025[21]; IMS India 2026[2].	MHT is an individual choice; bone benefit counts, but prevention alone stays contested.

WHERE THE EVIDENCE IS WEAK

- No randomised trial has fracture as the main outcome in perimenopausal women. Most data come from women over 60 (WHI mean age 63)[17,31].
- Indian fracture-risk data are thin. FRAX India is uncalibrated, and the 'one in five perimenopausal women with vertebral fracture' figure comes from one hospital study, quoted by IMS India[2].

  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)[33]. Not Indian data; use as a guide.*

- Calcium and vitamin D: weak or no fracture benefit in women who are not deficient[8,9].
- ESE 2025 statements are based on its published summary only; the full guideline was not reviewed[21].
- NICE NG23 and NICE CG146 carry no PMID or DOI, so they are not in the numbered list.

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VERIFIED BY PMID AND DOI · VANCOUVER STYLE

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