# In the name of God

# Management of osteoporosis in Chronic kidney disease

Asghar Haji Abbasi MD

**Guilan University for Medical Sciences**

**25** Dec 2025

# Introduction

- **Osteoporosis remains one of the most prevalent, disabling, and yet undertreated chronic diseases of ageing.**
- **Osteoporosis is characterized by low bone mass, increased bone fragility, and increased susceptibility to fracture .**
- **It is associated with substantial morbidity, mortality, and economic costs.**
- **Despite effective therapies, fewer than 20% of patients with fragility fractures receive appropriate pharmacologic treatment.**

***Lancet* 2025; 406: 2003–16**

# Introduction

- Osteoporosis remains one of the most prevalent, disabling, and yet undertreated chronic diseases of ageing.

**Worldwide, 1 in 3 women and 1 in 5 men older than 50 years of age experience osteoporotic fractures in their lifetime.**

**JAMA 2025**

- Despite effective therapies, fewer than 20% of patients with fragility fractures receive appropriate pharmacologic treatment.

*Lancet* 2025; 406: 2003–16

# Undertreatment of osteoporosis

## Probable reasons for undertreatment of osteoporosis include:

- **Fear of adverse effects**
- **Scarcity of awareness of osteoporosis**

**( both among healthcare professionals and affected individuals)**

- **Poor coordination of healthcare systems involved in the care of people**

**The problem is compounded by poor adherence to therapy, which has been particularly well documented for oral bisphosphonates.**

**Lancet Jan 2019**

# *Fearing Drugs' Rare Side Effects, Millions Take Their Chances With Osteoporosis*

- **Millions of Americans are missing out on a chance to avoid debilitating fractures from weakened bones.**

- **Researchers say, because they are terrified of exceedingly rare side effects from drugs that can help them.**

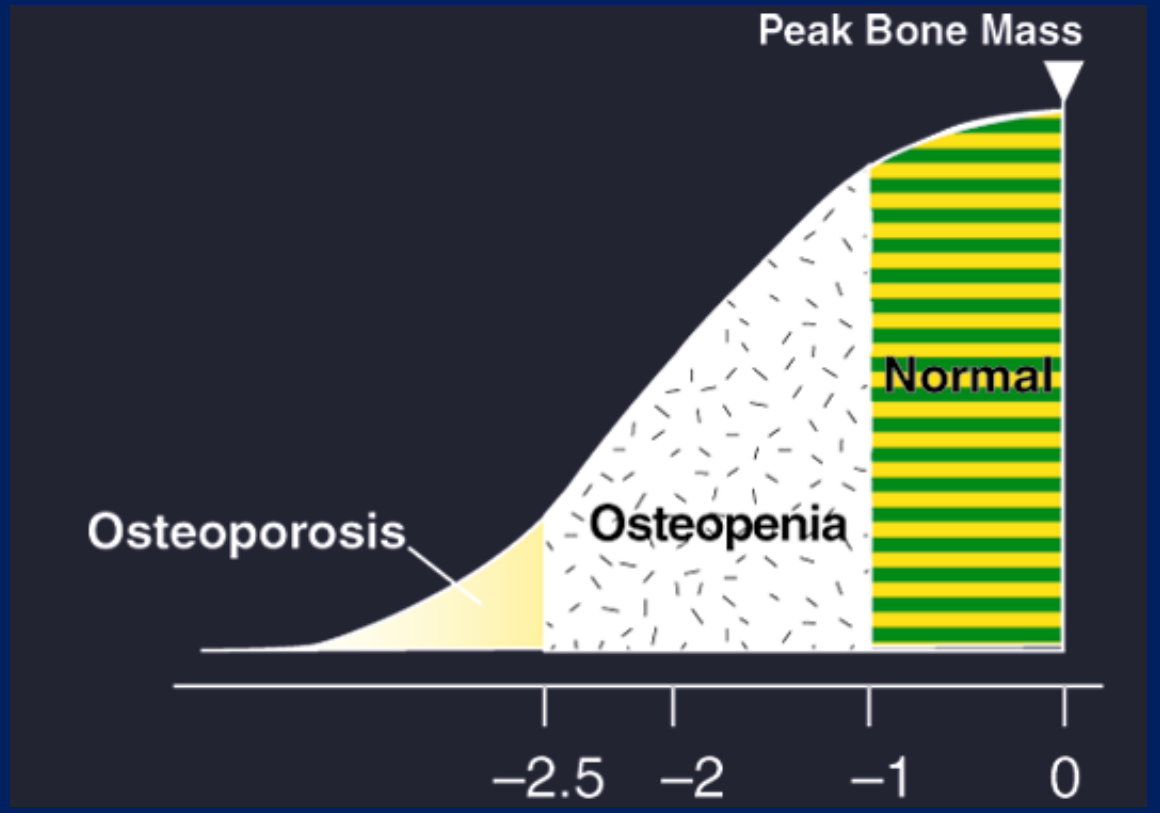
**By Gina Kolata** June 1, 2016. The ***newyork*** times

# Definition of osteoporosis

**In 2000, the National Institutes of Health (NIH) defined osteoporosis as :**

**"A skeletal disorder characterized by compromised bone strength predisposing to increased fracture risk."**

- **However, an operational definition of T-scores less than 2.5 SD below the mean young adults' values is adopted to define osteoporosis .**




*Osteoporos Int* 33, 2259–2274 (2022)

# Bone Strength
# NIH Consensus Statement 2000

**Bone Strength** = **Bone Quality** and **Bone Density**

1. Architecture
2. Turnover
3. Damage Accumulation
4. Mineralization
5. Matrix quality

BMD = grams/cm$^2$

# Conceptual shift: from BMD to fracture risk

- Osteoporosis management is no longer about bone density alone, but absolute fracture risk.
- Up to 70% of fractures occur in patients without a T-score ≤ –2.5, reinforcing the need for tools beyond DXA.
- FRAX remains the cornerstone, incorporating clinical risk factors with or without femoral neck BMD.
- Vertebral fractures—often silent—must be actively sought; any vertebral fracture confers high future fracture risk, regardless of BMD.

JAMA June 2025

# Conceptual shift: from BMD to fracture risk

- **Osteoporosis management is no longer about bone density alone, but absolute fracture risk.**

**Adjuncts such as trabecular bone score (TBS), emerging FRAXplus adjustments may refine risk estimation, but clinical judgement remains essential.**

***Lancet* 2025; 406: 2003–16**

- **Vertebral fractures—often silent—must be actively sought; any vertebral fracture confers high future fracture risk, regardless of BMD.**

**JAMA June 2025**

# Goals and targets in long-term osteoporosis therapy

## Treatment goals

- **Keep the patient free of fragility fracture or at least reduce the fracture risk as much as possible**

- **Avoid long-term adverse effects of bone medication**

## Treatment targets

- **Improve bone structure and density to a level associated with low fracture risk**

- **Preserve bone architecture and strength**

- **Control comorbidities and fall risk as well as individual risk factors**

**Nature Reviews Endocrinology 2023**

# Vitamin D and Calcium

- **Vitamin D supplementation alone does not reduce fractures in vitamin D–replete populations.**
- **Combined calcium plus vitamin D shows modest fracture reduction, but Dietary calcium is preferred.**
- **Excess supplementation may increase cardiovascular risk.**
- **Vitamin K2 shows possible BMD benefit, but fracture data remain inconsistent .**

*Lancet* 2025; 406: 2003–16

# Who should we treat?

**Pharmacologic therapy is recommended for:**

- **Prior hip, vertebral, or multiple fractures, regardless of BMD**
- **T-score ≤ –2.5**
- **High FRAX risk (≥20% major osteoporotic fracture or ≥3% hip fracture)**

**JAMA June 2025**

# pharmacological treatments in men
## (a systematic review and meta-analysis)

**Through a systematic review and meta-analysis including 21 RCTs, we have established that:**

- **Medications used in the management of OP in women , appear to be similarly beneficial in men with osteoporosis.**

- **Therefore, the algorithm for the management of OP in men could be identical to that recommended for the management of OP in women.**

Aging Clinical and Experimental Research (2023) 35:1789–1806

# Treatment options for Osteoporosis

## Antiresorptive treatments :

- Bisphosphonates, Denosumab, Selective Estrogen Receptor Modulators (SERMs), and Estrogen.

## Bone-forming treatments:

- Teriparatide and Abaloparatide

## Dual-action treatment :

- Romosozumab

Nature Reviews Endocrinology 2023

# Antiresorptives

- **Bisphosphonates and denosumab remain first-line worldwide.**

**Denosumab is highly effective and convenient, but two critical safety messages:**

**1. Severe hypocalcaemia risk in advanced CKD.**

**2. Rebound bone loss and vertebral fractures upon discontinuation.**

*Lancet* 2025; 406: 2003–16

# Denosumab must never be stopped without a transition plan

- Never stop abruptly

- Transition to bisphosphonate

**Ideally to intravenous zoledronic acid—sometimes requiring repeated dosing.**

- Prevent rebound bone loss & fractures

*Lancet* 2025; 406: 2003–16

# Anabolic Therapy

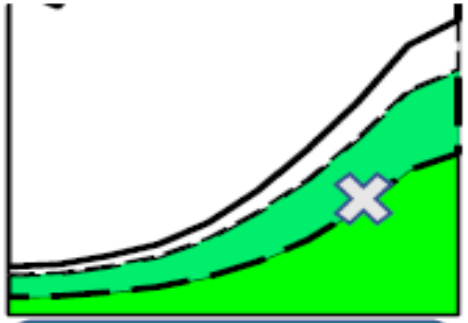
**Robust evidence confirms anabolic agents are superior to antiresorptives for:**

- **Rapid fracture-risk reduction**
- **Greater BMD gains**

- **Romosozumab, teriparatide, and abaloparatide outperform bisphosphonates and denosumab in high-risk patients.**

- **The optimal sequence is clear: Anabolic first → antiresorptive consolidation.**
- **Romosozumab should be avoided in patients with recent MI or stroke, though real-world cardiovascular risk appears low.**

*Lancet* 2025; 406: 2003–16

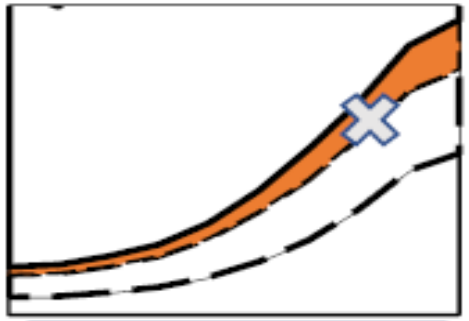


**Low risk**

Optimize calcium and vitamin D status

Risk appropriate exercise

Reassurance, lifestyle advice. Consider MHT and SERMs

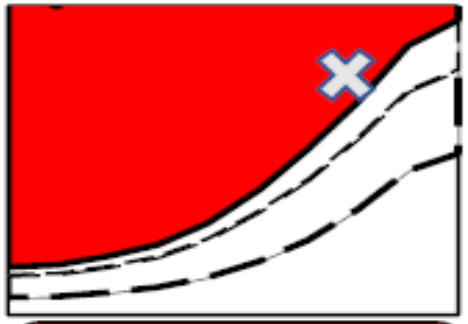


**High risk**

Optimize calcium and vitamin D status

Risk appropriate exercise and falls prevention

Consider oral bisphosphonate or other inhibitor of bone resorption*



**Very high risk**

Optimize calcium and vitamin D status

Risk appropriate exercise and falls prevention

**Consider anabolic agent followed by inhibitor of bone resorption*. Consider LOEP**

**Osteoporos Int (2020) 31:1–12**

# When selecting drug treatments to prevent fractures in postmenopausal women, and men age≥50 years

- **Start treatment promptly following a fragility fracture .**

- **Because the risk of re-fracture is highest immediately after a fracture and the risk remains elevated.**

- **Consider referral of very high-risk patients to an osteoporosis specialist in secondary care for assessment and consideration of parenteral treatment .**

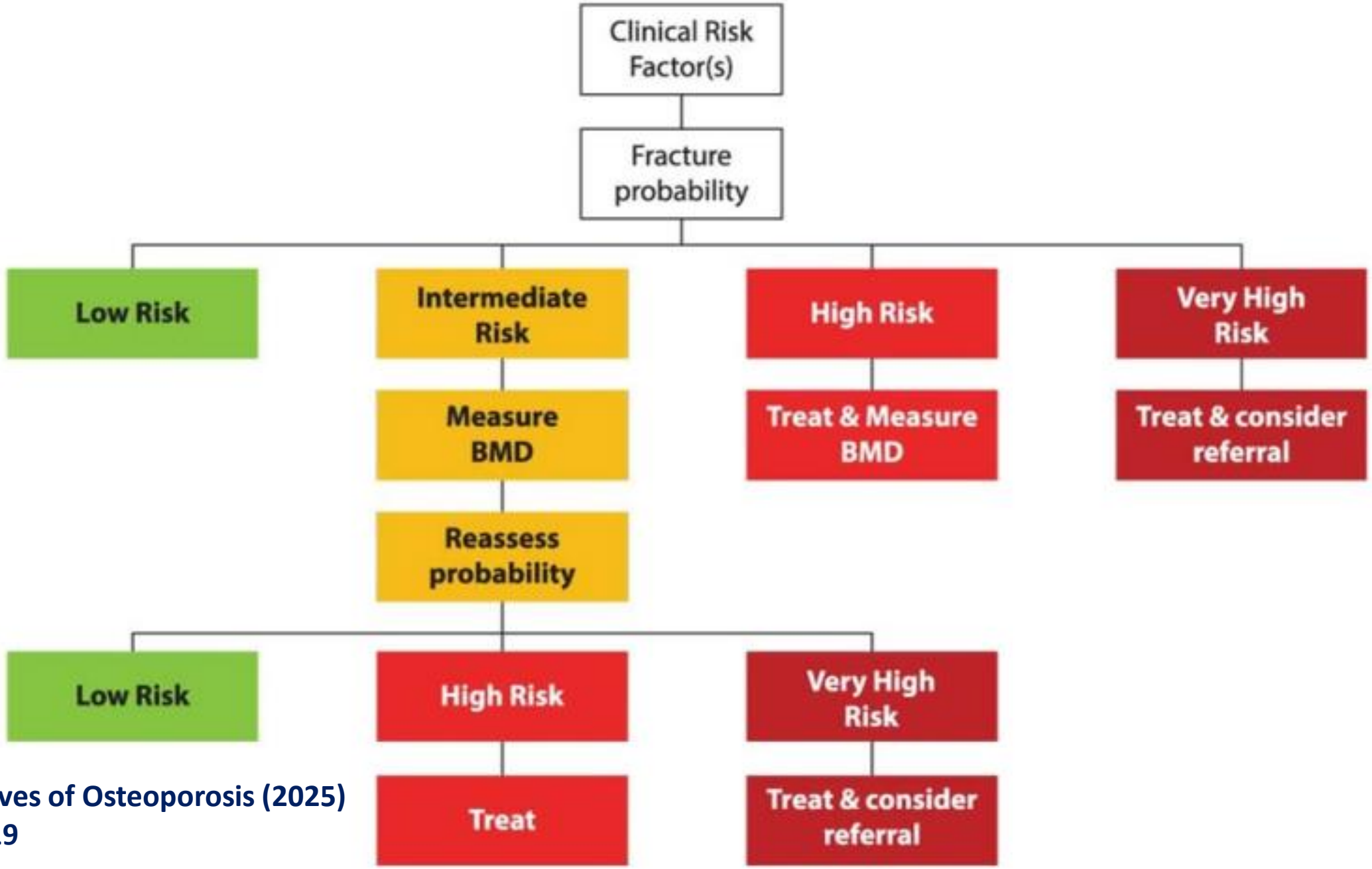
Archives of Osteoporosis (2025) 20:119

# When selecting drug treatments to prevent fractures in postmenopausal women, and men age≥50 years

**Indications of very high risk include the presence of important risk factors, including :**

- **A recent vertebral fracture (within the last 2 years)**
- **≥2 vertebral fractures (whenever they have occurred)**
- **BMD T-score≤ –3.5**
- **Treatment with high dose glucocorticoids (≥7.5 mg/day of prednisolone or equivalent over 3 months)**
- **The presence of multiple clinical risk factors**
- **Particularly with a recent fragility fracture indicating high imminent risk of re-fracture; or other indicators of very high fracture risk, including as defined by FRAX.**

**Archives of Osteoporosis (2025) 20:119**




Archives of Osteoporosis (2025) 20:119

# Osteoporosis in patients with CKD

- **In one study , 27 percent of patients with osteoporosis had grade 3 CKD and 3% had eGFR lower than 35 mL/min/1.73 $m^2$ .**
- **The management of osteoporosis in these patients is more complex than in patients without CKD .**
- **It  depends upon whether the patient also has coexisting GKD-MBD.**
- **Because bone disorders are related to vascular calcifications, any treatments that modify bone may also impact the vasculature.**

**Uptodate 2025**

# Pharmacological treatment of CKD associated osteoporosis

**For patients with eGFR ≥30 mL/min/1.73 $m^2$, who do not have evidence of CKD-MBD, and who are candidates for pharmacologic therapy:**

- **The choice of pharmacologic therapy is similar as for patients without CKD.**

- **Pharmacologic therapy for osteoporosis can be used without change in dosing in patients with G1 to G3 CKD .**

- **Intravenous zoledronic acid is contraindicated in patients with a GFR below 35 mL/min/1.73 $m^2$.**

**Uptodate 2025**

# Osteoporosis in patients with chronic kidney disease

- **Patients with CKD stages IV and V have not only a bone quantity but also a bone quality problem that increases fracture risk .**
- **Diagnosis of osteoporosis by DXA underestimates fracture risk.**
- **Clear evidence-based guidance on osteoporosis treatment in CKD has been lacking .**
- **It is largely because these patients are excluded from major osteoporosis trials .**

*Osteoporos Int* 33, 2259–2274 (2022)

# Osteoporosis and CKD: Why This Matters

**As kidney function declines:**

- **Bone mineral density decreases**
- **Fracture risk rises progressively**

**Hip fracture risk doubles in pre-dialysis CKD and increases up to eightfold in ESKD.**

- **Most alarming is mortality: in dialysis patients, up to 64% die within one year after a hip fracture.**

**Osteoporosis International October 2025**

# Osteoporosis and CKD: Why This Matters

- **Osteoporosis affects 1 in 3 women and 1 in 5 men over 50, but CKD independently amplifies this risk.**

**This makes fracture prevention in CKD not a quality-of-life issue alone—but a survival issue.**

- **Hip fracture risk doubles in pre-dialysis CKD and increases up to eightfold in ESKD.**
- **Most alarming is mortality: in dialysis patients, up to 64% die within one year after a hip fracture.**

**Osteoporosis International October 2025**

# Fractures are severe, debilitating, and preventable

- **Fractures result in prolonged rehabilitation, long-term pain, and increased health care costs.**

- **Only half of patients with a hip fracture regain mobility and remain at their prefracture level of independence.**

- **Moreover, despite treatments targeting the biochemical abnormalities of CKD-MBD, fracture incidence more than doubled from 1992 to 2009 in patients with CKD stage 5D.**

*Clinical Journal of the American Society of Nephrology* 18(9):p 1116-1118, September 2023

# A Paradigm Shift: From “CKD-MBD” to Two Clinical Syndromes

**KDIGO proposes moving away from the traditional triad of:**

- **biochemical abnormalities**
- **renal osteodystrophy**
- **vascular calcification**

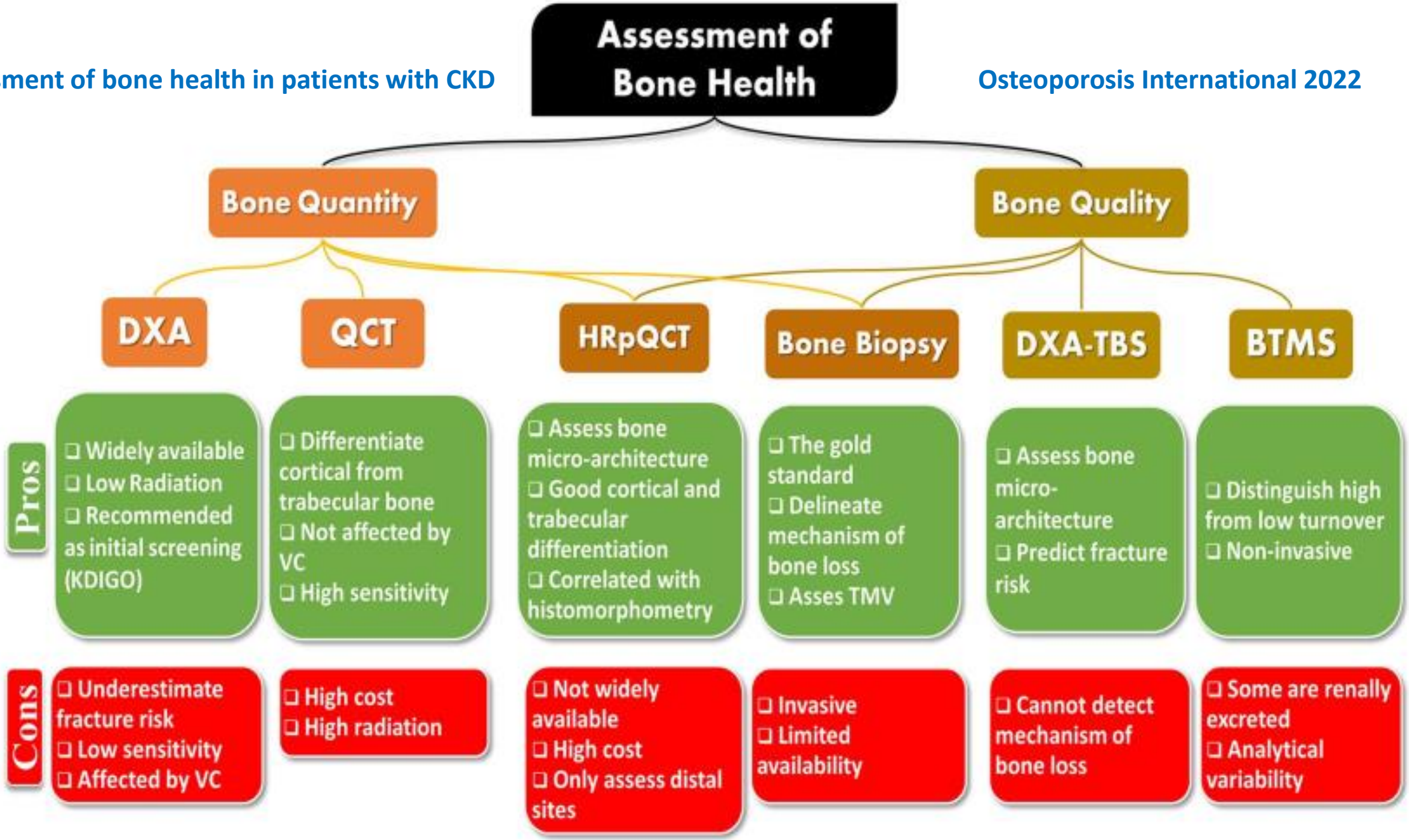
**toward two clinically meaningful syndromes:**

1. **CKD-Associated Osteoporosis**
   - Encompasses renal osteodystrophy (ROD)
   - Focuses on fracture risk and bone strength, not turnover alone
2. **CKD-Associated Cardiovascular Disease**
   - Includes vascular and valvular calcification, LVH, and heart failure
   - Recognizes disturbed mineral metabolism as a modifier, not the sole driver

Kidney International (2025) 107, 405–423

## Assessment of bone health in patients with CKD

## Osteoporosis International 2022



# Non-pharmacological interventions to reduce fracture risk in CKD

- **Ensure sufficient nutrition, paying special attention to the calcium balance.**
- **Promote cessation of smoking and moderation of alcohol intake.**
- **Physical function Encourage exercise, to maintain physical function and reduce the risk of falls.**
- **Resistance training may be particularly beneficial to skeletal health.**

*Clinical Kidney Journal*, 2023, vol. 16, no. 3, 456–472

# Recommended calcium intake in adults and children with chronic kidney disease – a European consensus statement

*Nephrol Dial Transplant*, 2024, 39, 341–366

Focus of study was to establish optimal calcium intake in chronic kidney disease (in adults and children) which is not addressed in current clinical practice guidelines

## Methods

Literature review by expert panel

Delphi survey

Revision based on survey response

## Results


## Key recommendations:

### Adults

Total calcium intake (diet and medications): 800–1000 mg/day

### Children

Total calcium intake: age-appropriate normal range

This consensus statement provides key evidence and clinical practice points on calcium management that may assist in clinical decision-making in children and adults with CKD.

Evenepoel, P. *et al.*
NDT (2023)
@NDTSocial

# Recommended calcium intake in adults and children with chronic kidney disease – a European consensus statement

Focus of study was to establish optimal calcium intake in chronic kidney disease (in adults and children) which is not addressed in current clinical practice guidelines

## Results

*Nephrol Dial Transplant*, 2024, 39, 341–366


**The main clinical practice points include a suggested total calcium intake from diet and medications not exceeding 1500 mg/day to maintain a neutral calcium balance in adults with CKD.**

Revision based on survey response

Total calcium intake (diet and medications): 800–1000 mg/day

Total calcium intake: age-appropriate normal range

Evenepoel, P. *et al.*
NDT (2023)
@NDTSocial

This consensus statement provides key evidence and clinical practice points on calcium management that may assist in clinical decision-making in children and adults with CKD.

# Targeting 25-hydroxyvitamin D levels >75 nmol/L (> 30 ng/mL) and < 150 nmol/L (< 60 ng/mL )

- **Aim to maintain serum 25-hydroxyvitamin D (25[OH]D) levels > 75 nmol/L ( > 30 ng/mL) in adults and children with CKD, on dialysis, and after kidney transplantation.**

## Upper limit to avoid toxicity:

- **Avoid very high 25(OH)D levels > 150–200 nmol/L (60–80 ng/mL) to reduce the risk of toxicity.**

## Avoid mega-doses:

- **Very large single doses (≥ 100 000 IU) are not recommended because of safety concerns.**

A European consensus statement. *Nephrology Dialysis Transplantation, 2025*

# Management of CKD associated osteoporosis

- **Bone-specific medications are usually used after controlling the parameters of CKD-mineral and bone disorders.**
- **Antiresorptive treatments ( bisphosphonates, and denosumab) play a beneficial role in the management of osteoporosis in patients lacking evidence of LBT.**
- **Osteoanabolics are expected to have a promising role in CKD with LBT.**

**Osteoporosis international Oct 2025**

# Renal Osteodystrophy: The Traditional View vs the New Reality

- For decades, we were taught that secondary hyperparathyroidism and high bone turnover dominated CKD.

**However, contemporary bone biopsy studies tell a different story:**

- Low bone turnover (LBT) now predominates
- Adynamic bone disease is highly prevalent
- This shift is seen even in early CKD stages

**Large biopsy series show:**

- ~60% of dialysis patients have LBT
- Up to 80% of patients with CKD stages 2–3 demonstrate LBT

**This paradigm shift has major therapeutic implications.**

Osteoporosis International October 2025

# Why Low Bone Turnover Is Dangerous

**Low bone turnover is not benign.**

**Clinically, it is associated with:**

- **Increased fracture risk**
- **Poor microdamage repair**
- **Hypermineralized, brittle bone**

**Systemically, it is strongly linked to:**

- **Vascular calcification**
- **Coronary artery calcification progression**
- **Cardiovascular mortality**

**Osteoporosis International October 2025**

# Diagnosis of Adynamic bone disease (ABD)

- Serological markers, though unable to solely confirm the diagnosis of ABD, can be helpful in guiding clinicians .
- This especially holds true in the case of an asymptomatic patient.
- **Patients with PTH levels <150 pg/mL have a 97% positive predictive value for ABD.**
- PTH levels >450 pg/mL have a 100% positive predictive value for Osteitis fibrosa cystica (OFC).

Journal of Clinical & Translational Endocrinology. Volume 5, Sep 2016.

RENAL FAILURE
2025, VOL. 47, NO. 1, 2530162
https://doi.org/10.1080/0886022X.2025.2530162

Taylor & Francis
Taylor & Francis Group

STATE OF THE ART REVIEW

OPEN ACCESS Check for updates

# Adynamic bone disorder in chronic kidney disease: meta-analysis and narrative review of potential biomarkers as diagnosis and therapeutic targets

**Biomarkers like bone-specific alkaline phosphatase (BaLP) and intact PTH (iPTH) show promise in distinguishing between low and high bone turnover.**

**Meta-analysis suggests that levels of iPTH below 150 pg/mL or BaLP levels below 20 µg/l indicate low bone turnover.**

# PTH Cut-offs and Adynamic Bone Disease in CKD

- No single PTH cut-off defines ABD
- KDIGO discourages rigid numeric thresholds
- Emphasis on trends and clinical context
- iPTH <150 pg/mL suggests low turnover
- iPTH <50–100 pg/mL strongly supports ABD

Renal Failure 2025, VOL. 47, NO. 1, 2530162

# Interpret ALP with PTH

- ✓**High PTH + high BSAP → high turnover**
- ✓**High PTH + normal/low BSAP → possible PTH resistance**
- ✓**Low PTH + low BSAP → adynamic bone disease**
- ✓**Falling BSAP with stable PTH → overtreatment**

Adynamic bone disorder in chronic kidney disease: meta-analysis and narrative review of potential biomarkers as diagnosis and therapeutic targets

## Anti resorptive drugs may worsen low turnover

- Increase bone brittleness
- Limited fracture benefit in ABD

## Anabolic therapy

- Restore bone formation
- Improve microarchitecture

Renal Failure 2025, VOl. 47, NO. 1, 2530162

Canadian Society of Nephrology/
Société canadienne de néphrologie
CSN/SCN

CANADIAN JOURNAL OF
KIDNEY HEALTH AND DISEASE
Journal canadien de la santé et de la maladie rénale

Original Clinical Research Quantitative

# The Efficacy and Safety of Bisphosphonate Therapy for Osteopenia/Osteoporosis in Patients With Chronic Kidney Disease: A Systematic Review and Individual Patient-Level Meta-Analysis of Placebo-Controlled Randomized Trials

Canadian Journal of Kidney Health and Disease
Volume 11: 1–11

DOI: 10.1177/20543581241283523
journals.sagepub.com/home/cjk

Sage

# The Efficacy and Safety of BP Therapy for Osteopenia/Osteoporosis in Patients With CKD: A Systematic Review

- Of 39 eligible studies, individual patient-level data was available for 7 studies, **all of which were studies of ibandronate.**
- Of 7428 participants (5010 ibandronate, 2418 placebo), 100% were female, 98.6% were white, the mean body mass index was 25.7 kg/m2 (SD 3.9), 18.9% were smokers and there were 740 fracture events.
- The mean eGFR was 69.1 mL/min/1.73 m2 (SD 15.9) including 14.5%, 54.9%, 27.5%, 3.0%, and 0.2% stages G1, G2, G3A, G3B, and G4 CKD.
- **Ibandronate increased hip and lumbar spine BMD and decreased the risk of fracture in the overall population but in patients with stage G3B CKD, it increased the risk of fracture .**

Canadian Journal of Kidney Health and Disease, 2024

# The Efficacy and Safety of BP Therapy for Osteopenia/Osteoporosis in Patients With CKD: A Systematic Review

- Of 39 eligible studies, individual patient-level data was available for 7 studies, **all of which were studies of ibandronate.**

**Ibandronate did not impact eGFR over 12 months but increased the risk of hypocalcemia (HR 1.324, 95% CI 1.056, 1.660) with no evidence of any effect modification by CKD stage (all tests of interaction $p > 0.05$) .**

- **Ibandronate increased hip and lumbar spine BMD and decreased the risk of fracture in the overall population but in patients with stage G3B CKD, it increased the risk of fracture .**

Canadian Journal of Kidney Health and Disease, 2024

# Bisphosphonates

## CKD G1–G3A:

- Treat as general population
- Proven BMD and fracture benefit

## CKD G3B:

- Increased fracture risk despite BMD gain
- Likely low-turnover bone disease

Whitlock RH et al. Can J Kidney Health Dis. 2024

# Advanced CKD and Dialysis

## CKD G4–G5 (non-dialysis):

- Sparse evidence
- Routine bisphosphonates discouraged

## Dialysis:

- High risk of adynamic bone disease
- Bisphosphonates generally contraindicated

Damasiewicz MJ, Nickolas TL. Curr Opin Nephrol Hypertens. 2020

frontiers in Pharmacology

SYSTEMATIC REVIEW
published: 11 February 2022
doi: 10.3389/fphar.2022.822178

Check for updates

# Efficacy of Osteoporosis Medications for Patients With Chronic Kidney Disease: An Updated Systematic Review and Network Meta-Analysis

**Teriparatide and denosumab seem to be the most effective treatments for preventing bone loss and reducing the risk of fracture in our network comparison.**

**However, because of the limitations and potential biases in the reviewed studies, there is still some uncertainty about the best treatment options for osteoporosis in patients with CKD or a history of kidney transplantation.**

Received: 22 November 2022 | Revised: 25 April 2023 | Accepted: 12 May 2023

DOI: 10.1111/hdi.13098

REVIEW ARTICLE

Mineral Bone Disorder

# Effects of denosumab on bone mineral density and bone metabolism in patients with end-stage renal disease: A systematic review and meta-analysis

**They found that denosumab treatment of dialysis dependent patients with ESRD increased the BMDs of the lumbar spine and femoral neck, and decreased ALP and PTH levels.**

**The overall incidence of denosumab associated hypocalcemia was 35%.**

# Long-Term Efficacy and Safety of Denosumab: Insights beyond 10 Years of Use

- **Denosumab's well-documented efficacy up to 10 years includes substantial increases in BMD at the lumbar spine ( 21.7% ) and total hip (9.2%) , and persistently low fracture rates in long-term extension cohorts .**

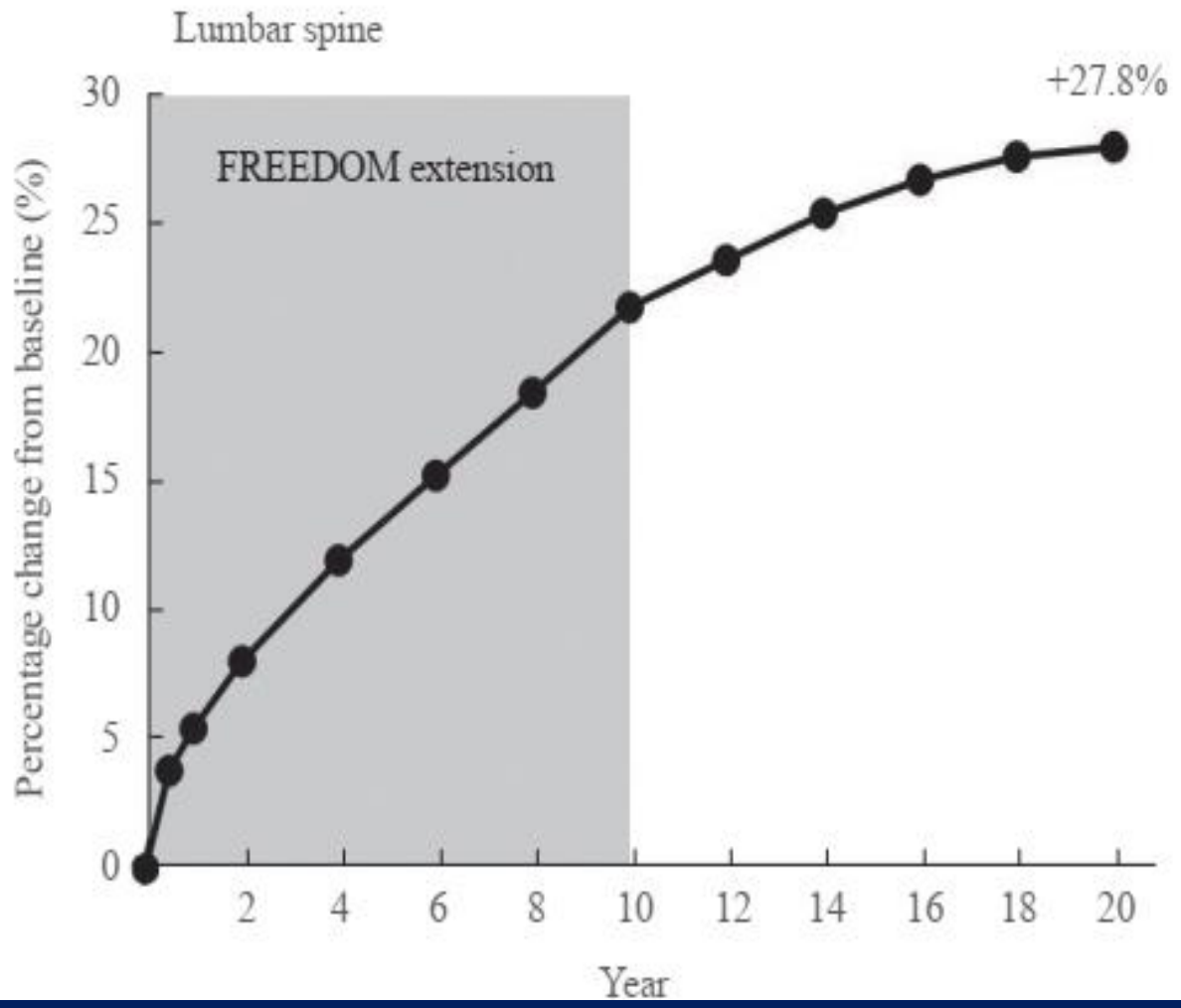
## Modeling and indirect evidence suggest that:

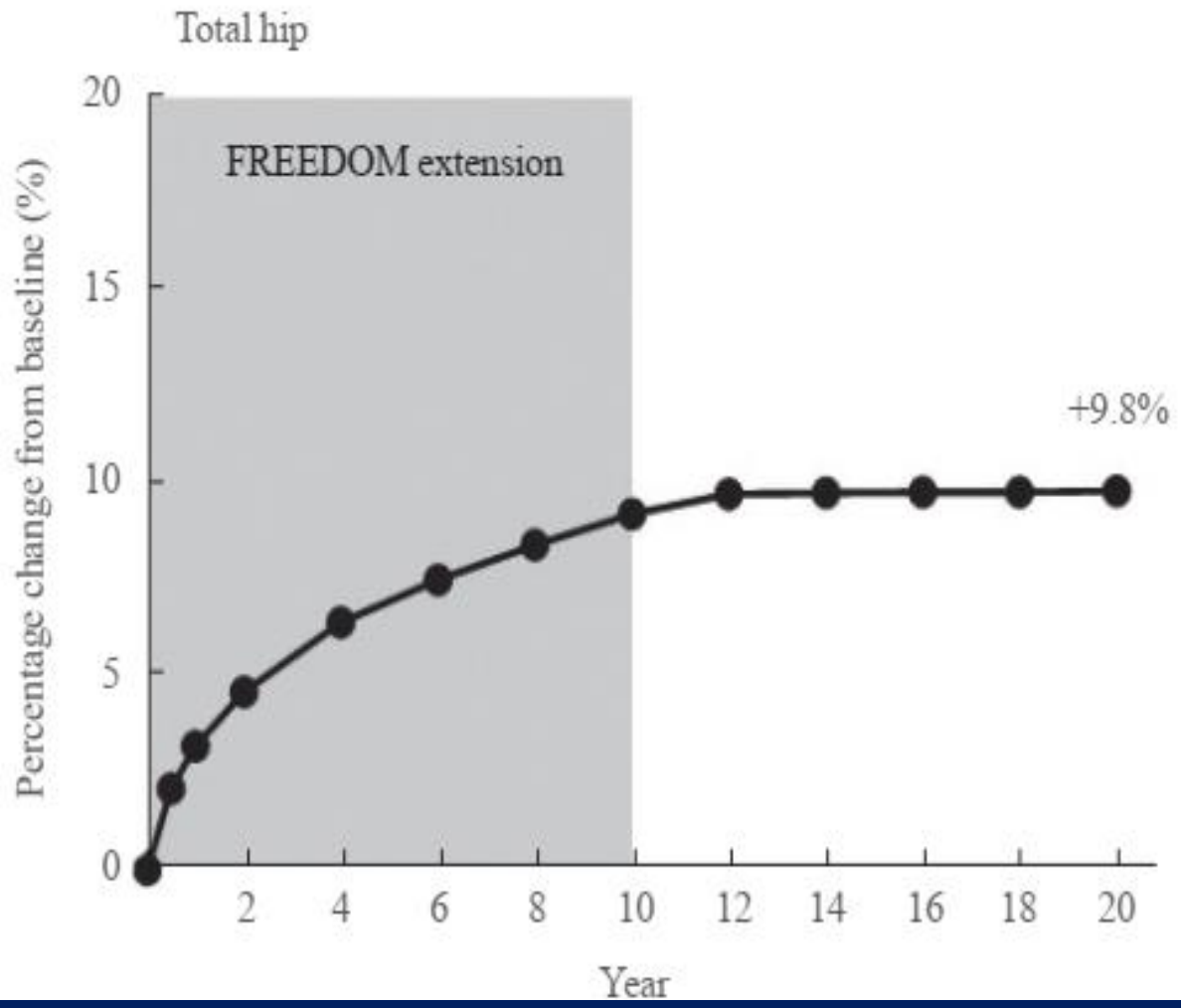
- **Continued administration beyond 10 years may maintain or augment BMD particularly at the spine — with hip BMD plateauing yet remaining stable above baseline .**

- **Predictive models indicate that additional gains in BMD may occur with extended therapy, although real-world data beyond the first decade remain sparse and require further prospective study**

Endocrinol Metab 2025;40:47-56

# Prediction of the duration of Dmab treatment and percentage change from baseline in lumbar spine and total hip bone mineral density




Endocrinol Metab 2025;40:47-56

# Treating Osteoporosis with Dmab in Patients on HD

## The Good, the Bad, and the Ugly

- **A meta-analysis of patients on dialysis treated with denosumab included 12 studies with a total of 348 participants.**

- **Denosumab increased areal BMD at the femoral neck and lumbar spine by 9.10% (95% confidence interval, 4.07% to 14.13%) and 9.00% (95% confidence interval, 5.93% to 12.07%), respectively.**

- **These data should generate excitement regarding the use of denosumab as a bone-protective therapy in patients on hemodialysis.**

*Clinical Journal of the American Society of Nephrology* 18(9):p 1116-1118, September 2023

# Treating Osteoporosis with Dmab in Patients on HD

## The Good, the Bad, and the Ugly

- **In one study, 7.3% of participants sustained severe hypocalcemia; although none were hospitalized and severity was mitigated with measures that increased calcium intake.**
- **A meta-analysis of dialysis patients treated with denosumab reported a pooled rate of hypocalcemia of 35.0%.**
- **Data from studies suggest that hypocalcemia risk can be mitigated by supplementation with calcium, vitamin D, and calcitriol.**
- **With hypocalcemia risk mitigation strategies, should we just start everyone on dialysis with low BMD on denosumab?**

*Clinical Journal of the American Society of Nephrology* 18(9):p 1116-1118, September 2023

# Treating Osteoporosis with Dmab in Patients on HD

## The Good, the Bad, and the Ugly

- There is an ongoing investigation by the FDA on the risk of severe hypocalcemia in patients on dialysis receiving denosumab.
- **When stopping denosumab, there is risk for bone loss and fracture due to rebound resorption.**
- In the general population, risk of bone loss and fracture after cessation is mitigated by initiation of a high potency bisphosphonate .
- Third, not everyone with ROD can receive denosumab.
- It is unclear what happens to bone quality in the setting of preexisting low bone turnover or adynamic disease.

*Clinical Journal of the American Society of Nephrology* 18(9):p 1116-1118, September 2023

# Pharmacologic therapy for CKD associated osteoporosis

- **Patients with an eGFR <30 mL/min/1.73 $m^2$ with a fragility fracture may be candidates for pharmacologic therapy.**

- **Such patients require exclusion of other forms of CKD-MBD as a cause of fracture .**

- **For fracturing patients with eGFR of 15 to 30 mL/min/1.73 $m^2$ who are candidates for pharmacologic therapy, they suggest an oral bisphosphonate .**

- **If an oral BP is not tolerated, an IV bisphosphonate could be considered in lieu of no treatment, particularly in patients at high risk for recurrent fracture and mortality.**

**Uptodate 2025**

## Effects of anti-osteoporotic drugs in patients with CKD : a systemic review and network meta-analysis of BMD , clinical fracture rate and renal function

- **Fracture prevention is achievable in CKD patients**
- **Sclerostin inhibitors appear most effective for reducing clinical fractures**
- **PTH analogs provide the greatest BMD gains**
- **Denosumab and bisphosphonates remain effective options, particularly in earlier CKD stages**
- **Importantly, renal function is not significantly compromised by these therapies**

**Frontiers in Pharmacology 2025**

# Teriparatide and abaloparatide

- **Teriparatide and abaloparatide are PTH and PTH-related peptide analogues, respectively, with anabolic effects on bone.**

- **Patients with proven ABD, irreversible ABD post-parathyroidectomy or relative hypoparathyroidism with PTH resistance are expected to benefit most from these agents .**

- **They may also be suitable for patients with osteoporosis in the absence of high bone turnover disease .**

*Clinical Kidney Journal*, 2025, vol. 18, no. 10, sfaf228

# Teriparatide and renal insufficiency

- **The lumbar spine and femoral neck BMD increased among all renal function subgroups after teriparatide.**
- **Renal insufficiency did not affect these improvements since fracture risk reduction was similar between patients with mild to moderate versus without renal dysfunction .**
- **A recent post-hoc analysis of a study among Japanese women with OP, high fracture risk, and stages 4–5 CKD, concluded that teriparatide increased BMD .**
- **Intermittent teriparatide therapy may have an anabolic action increasing bone turnover, bone volume, and mineralization in patients with ESKD and secondary hyperparathyroidism without impairing renal function and mineral metabolism .**

**Ther Apher Dial. 2024;28:671–689.**

# Teriparatide and renal insufficiency

- **According to pilot studies in dialysis patients, teriparatide increased BMD and may be a good option in patients with CKD G4–G5D with low bone turnover and irreversible adynamic bone disease .**

**The anabolic effect of intermittent PTH on bone is possibly mediated through:**

**(1) activation of PTH-1 receptor in osteoblasts that increases osteoblasts .**

**(2) inhibition of sclerostin binding to osteoblasts .**

**Ther Apher Dial. 2024;28:671–689.**

# Teriparatide and renal insufficiency

## Teriparatide is contraindicated in patients with :

- Hypercalcemia, previous skeletal radiotherapy, bone malignancies, or metastases .

- After discontinuation, continuing with denosumab or bisphosphonate is necessary to maintain/increase BMD .

- Transient hypotension is a possible adverse event that has been reported in 36% of hemodialysis patients with once-weekly administration of teriparatide .

Ther Apher Dial. 2024;28:671–689.

# Teriparatide and abaloparatide

- The optimal dosing regimen of teriparatide is to be determined and the optimal duration of treatment is uncertain .
- It is often limited to 2 years due to the theoretical risk of osteosarcoma.
- Abaloparatide has been trialled in patients with renal impairment up to CKD stage 3 and has been shown to have similar efficacy and safety profiles across early CKD stages .
- Data for both drugs in advanced CKD are lacking.

*Clinical Kidney Journal*, 2025, vol. 18, no. 10, sfaf228

# The Risk of Developing Osteosarcoma After Teriparatide Use: A Systematic Review

- **The currently available literature demonstrates the lack of any substantial evidence pointing towards any increased risk of osteosarcoma formation .**

- **This study demonstrates the highest level of clinical evidence in this matter given that all of the pre-existing literature had been systematically reviewed and analysed.**

- **These findings coupled with the clinical efficacy of TPTD can certainly alter the current treatment guidelines for osteoporosis .**

**Orthopedic Research and Reviews 2023:15**

# The Wnt/β-Catenin Pathway: A Shared Bone–Vessel Axis

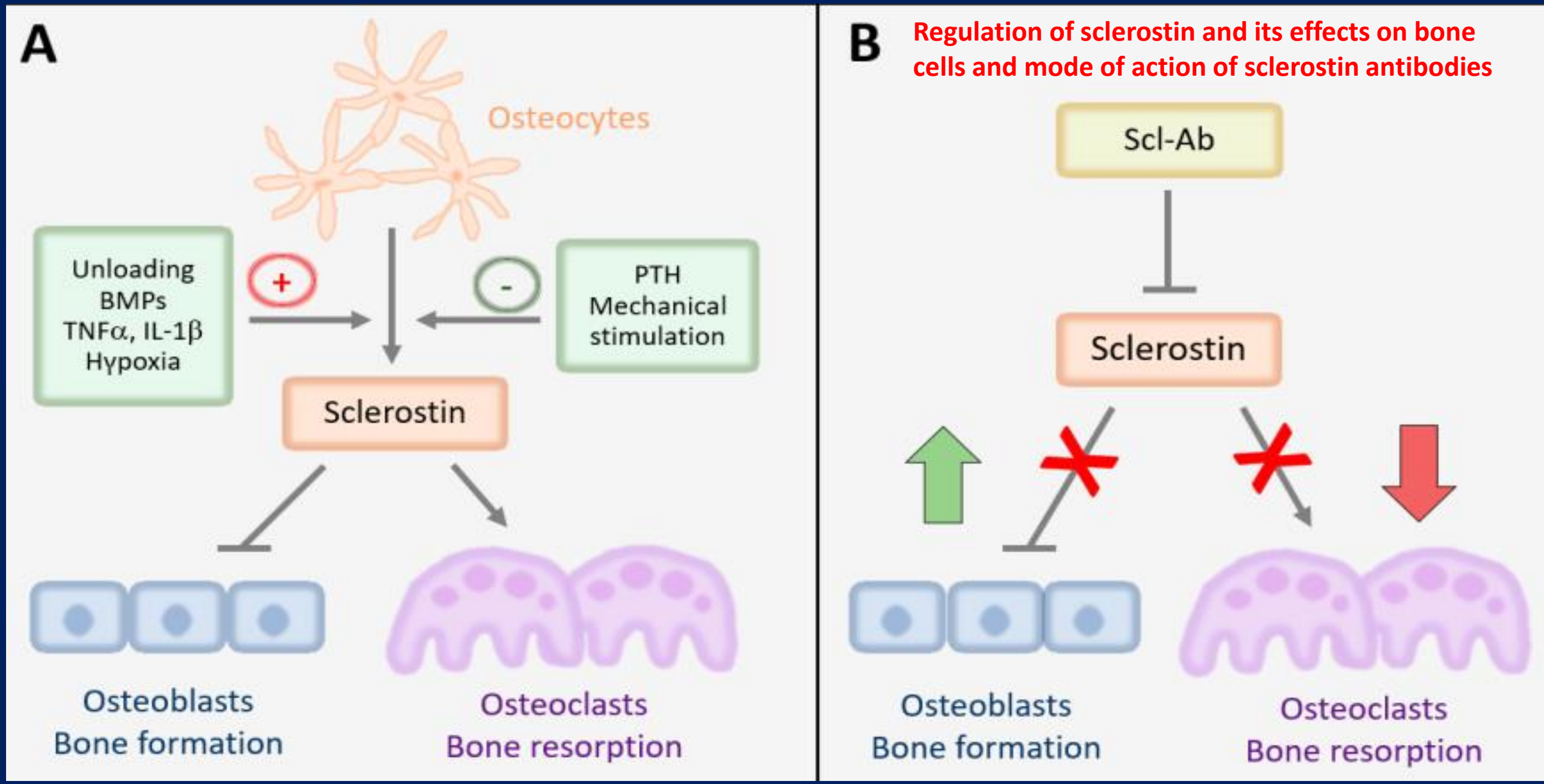
## The Wnt/β-catenin pathway is central to:

- Osteoblast differentiation and survival
- Increased bone formation
- Suppression of bone resorption via osteoprotegerin

## Osteocytes regulate this pathway through sclerostin, a potent Wnt inhibitor.

- Loss of sclerostin causes high bone mass in humans
- Sclerostin levels rise as kidney function declines

Osteoporosis International October 2025




*J. Clin. Med.* 2021, *10*, 787

# Sclerostin Beyond Bone: The Vascular Question

- **Vascular smooth muscle cells can undergo osteogenic transformation in CKD.**
- **Sclerostin is expressed in calcified vessels .**
- **Uremic calcified aorta release sclerostin into circulation**
- **Vascular-derived sclerostin may suppress bone formation**

**This suggests a bone–vascular crosstalk, possibly bidirectional.**

Osteoporosis International October 2025

# Sclerostin Beyond Bone: The Vascular Question

- **Vascular smooth muscle cells can undergo osteogenic transformation in CKD.**

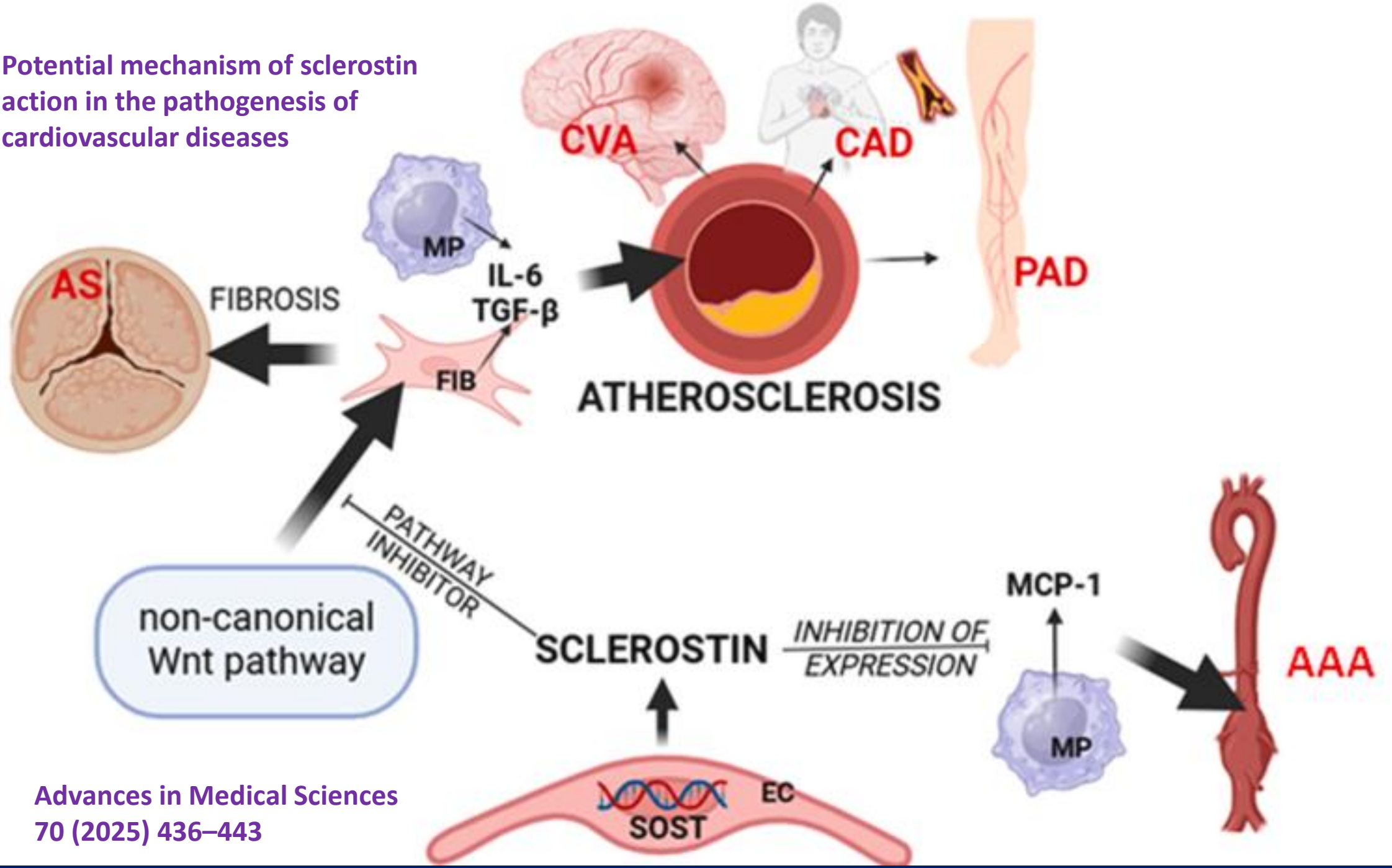
**The critical question is:**

**If sclerostin is protective in vessels, is blocking it dangerous?**
**This uncertainty frames the debate around romosozumab in CKD.**

**This suggests a bone–vascular crosstalk, possibly bidirectional.**

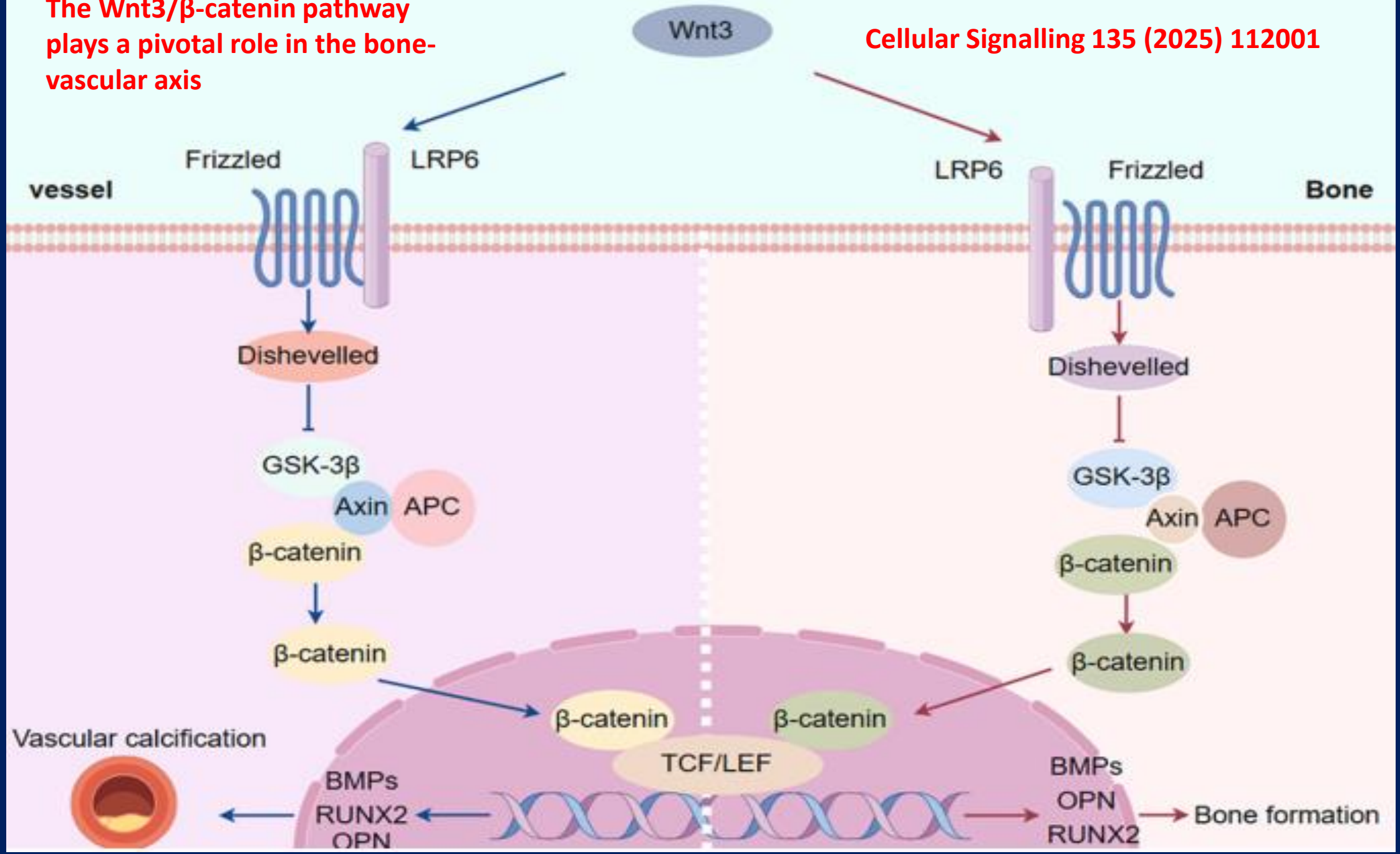
Osteoporosis International October 2025

**Potential mechanism of sclerostin action in the pathogenesis of cardiovascular diseases**




**Advances in Medical Sciences 70 (2025) 436–443**

**The Wnt3/β-catenin pathway plays a pivotal role in the bone-vascular axis**



# Bone - vascular axis and the Wnt - sclerostin pathway

- Sclerostin, secreted by osteocytes, inhibits Wnt signaling.
- In CKD, sclerostin levels rise markedly, suppressing bone formation.
- Vascular smooth muscle cells undergo osteogenic transformation, expressing Wnt-related proteins and sclerostin themselves .

## This creates a bone–vascular crosstalk, where:

- Low bone turnover reduces skeletal calcium buffering
- Excess calcium is redirected toward vascular calcification
- Cardiovascular risk escalates

Thus, CKD bone disease is not merely skeletal—it is systemic and lethal .

Osteoporosis international Oct 2025

# Post-hoc Analysis: Efficacy and Safety of Romosozumab in Postmenopausal Women With Osteoporosis and Mild-to-Moderate CKD

- **This post-hoc analysis pooled data from the FRAME (romosozumab vs placebo) and ARCH (romosozumab vs alendronate) phase III trials to specifically evaluate women with mild-to-moderate CKD .**

## Participants were stratified by baseline kidney function:

- **Normal renal function**
- **CKD stage 2 (eGFR 60–89 mL/min/1.73 $m^2$)**
- **CKD stage 3 (eGFR 30–59 mL/min/1.73 $m^2$)**

**Patients with severe CKD (eGFR <35 in ARCH) or uncontrolled secondary hyperparathyroidism were excluded.**

Miller et al. JBMR 2022

# Post-hoc Analysis: Efficacy and Safety of Romosozumab in Postmenopausal Women With Osteoporosis and Mild-to-Moderate CKD

- **Romosozumab retains efficacy in postmenopausal women with CKD stages 2–3 .**

- **The safety profile is comparable to patients with normal renal function .**

- **Mild-to-moderate CKD should not be considered a contraindication to romosozumab .**

**What it does *not* answer:**

- **Effects in CKD stages 4–5**
- **Impact on vascular calcification**
- **Long-term cardiovascular outcomes in CKD**

Miller et al. JBMR 2022

Calcified Tissue International (2023) 112:34–44
https://doi.org/10.1007/s00223-022-01031-6

ORIGINAL RESEARCH

# One-Year Romosozumab Treatment Followed by One-Year Denosumab Treatment for Osteoporosis in Patients on Hemodialysis: An Observational Study

**This prospective, observational, single-center cohort study included 13 prior osteoporosis treatment-naïve patients on HD with osteoporosis.**

**They first received ROMO once monthly for 12 months (210 mg; subcutaneously once every month).**

**Thereafter, they received denosumab (DENO) for an additional 12 months (60 mg; subcutaneously once every 6 months) .**

# One-Year ROMO Treatment Followed by One-Year Denosumab Treatment for Osteoporosis in Patients on Hemodialysis: An Observational Study

- **No new cases of fractures were noted.**

- **The median one-year percentage changes (from the baseline) in the BMDs at the lumbar spine (LS), total hip (TH), and femoral neck (FN) were+ 9.0%, + 2.5%, and + 4.7%, respectively.**

- **These changes were maintained for 24 months.**

- **The corresponding relative changes from the baseline to 24 months thereafter were +14.9%,+5.4%, and+6.5%, respectively.**

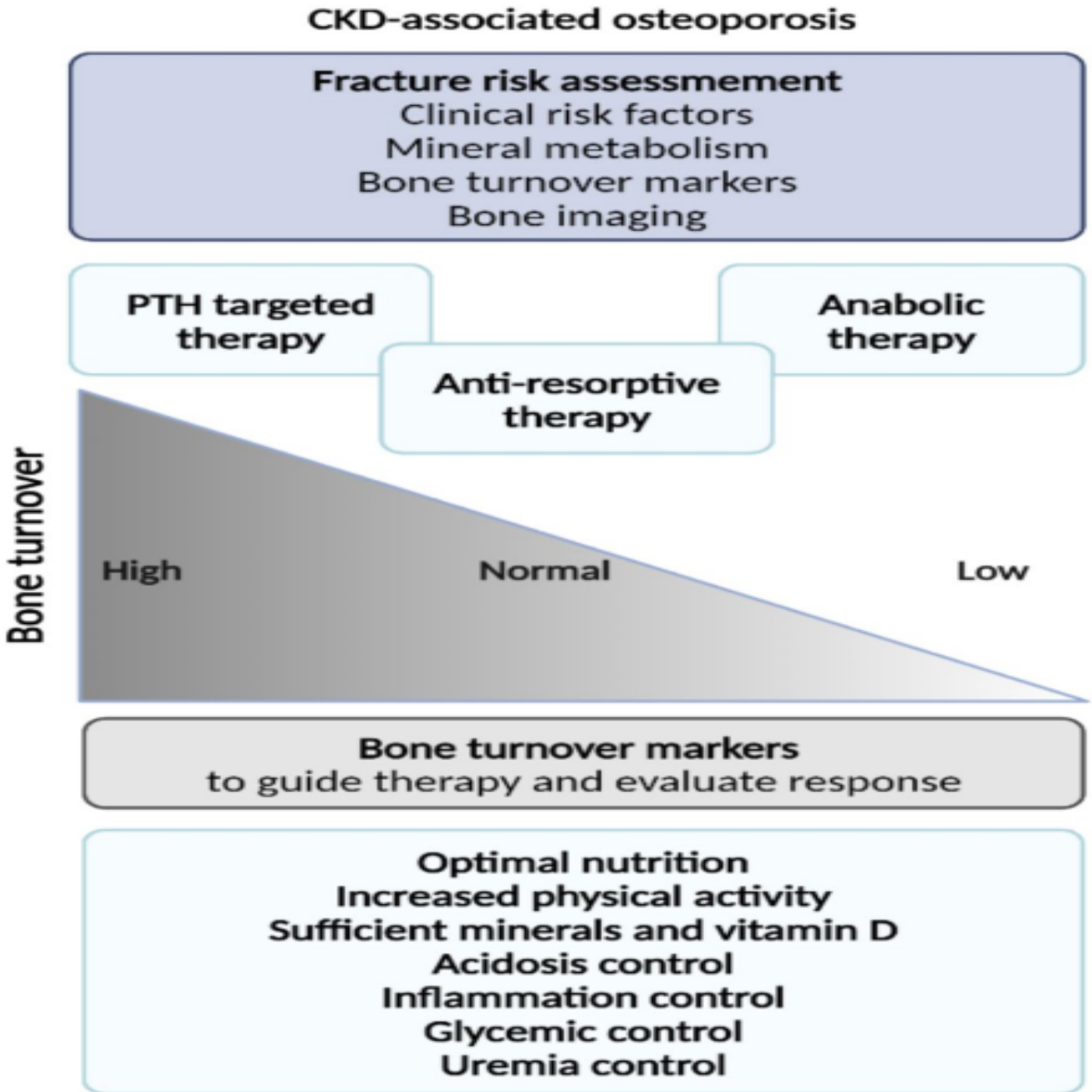
Calcified Tissue International (2023) 112:34–44

# One-Year ROMO Treatment Followed by One-Year Denosumab Treatment for Osteoporosis in Patients on Hemodialysis: An Observational Study

- **Coronary artery and thoracic aorta calcification scores increased slightly from baseline to 12 months thereafter.**
- **However, fatal events (cardiovascular disease-associated and all-cause deaths) did not occur during ROMO treatment.**
- **Effectiveness of ROMO was better in patients who had severe osteoporosis with low TH BMD, low FN BMD, and high tartrate-resistant acid phosphatase 5b level at ROMO initiation.**

Calcified Tissue International (2023) 112:34–44

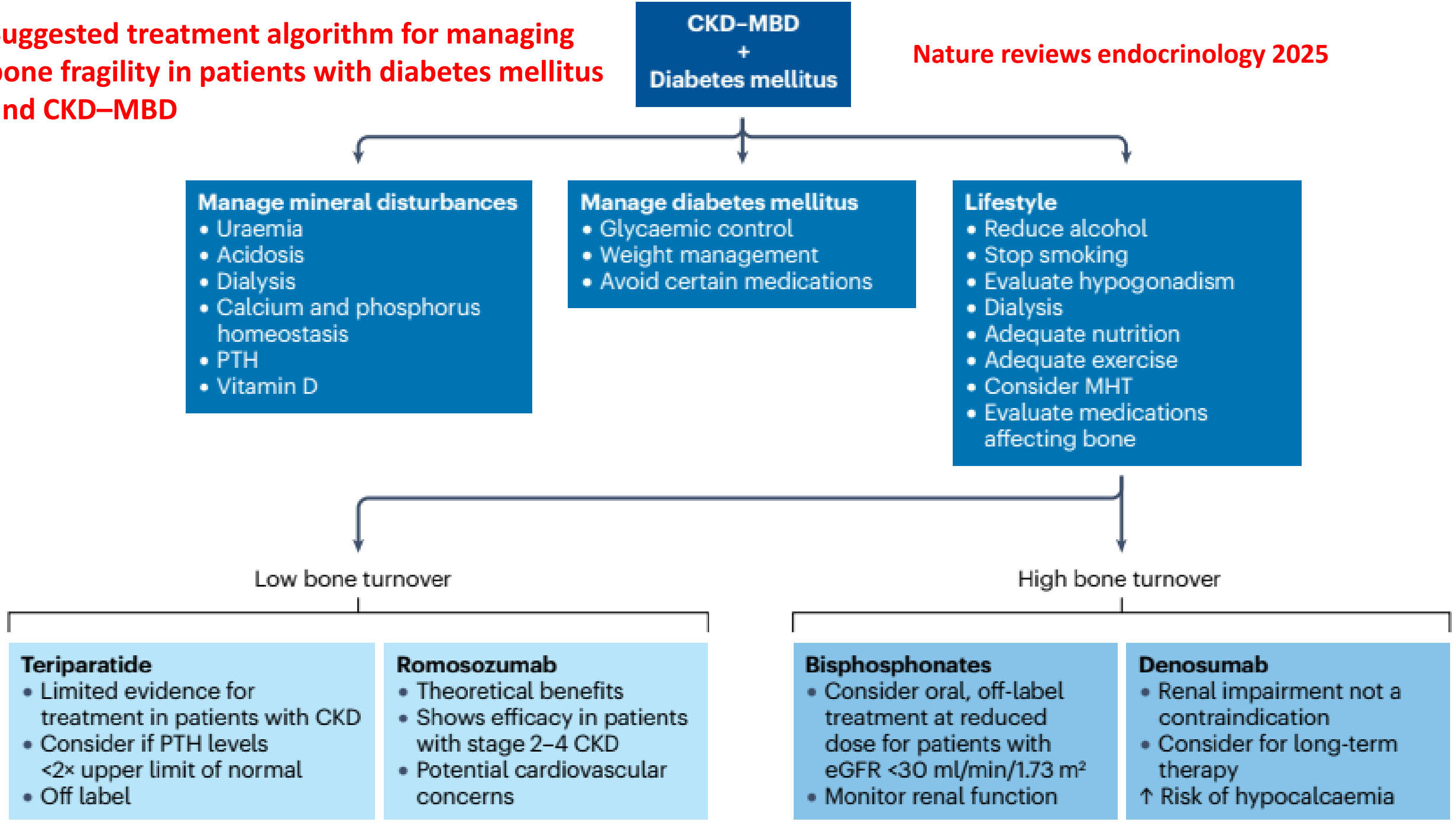
**Bone turnover markers in the management of CKD-associated osteoporosis**



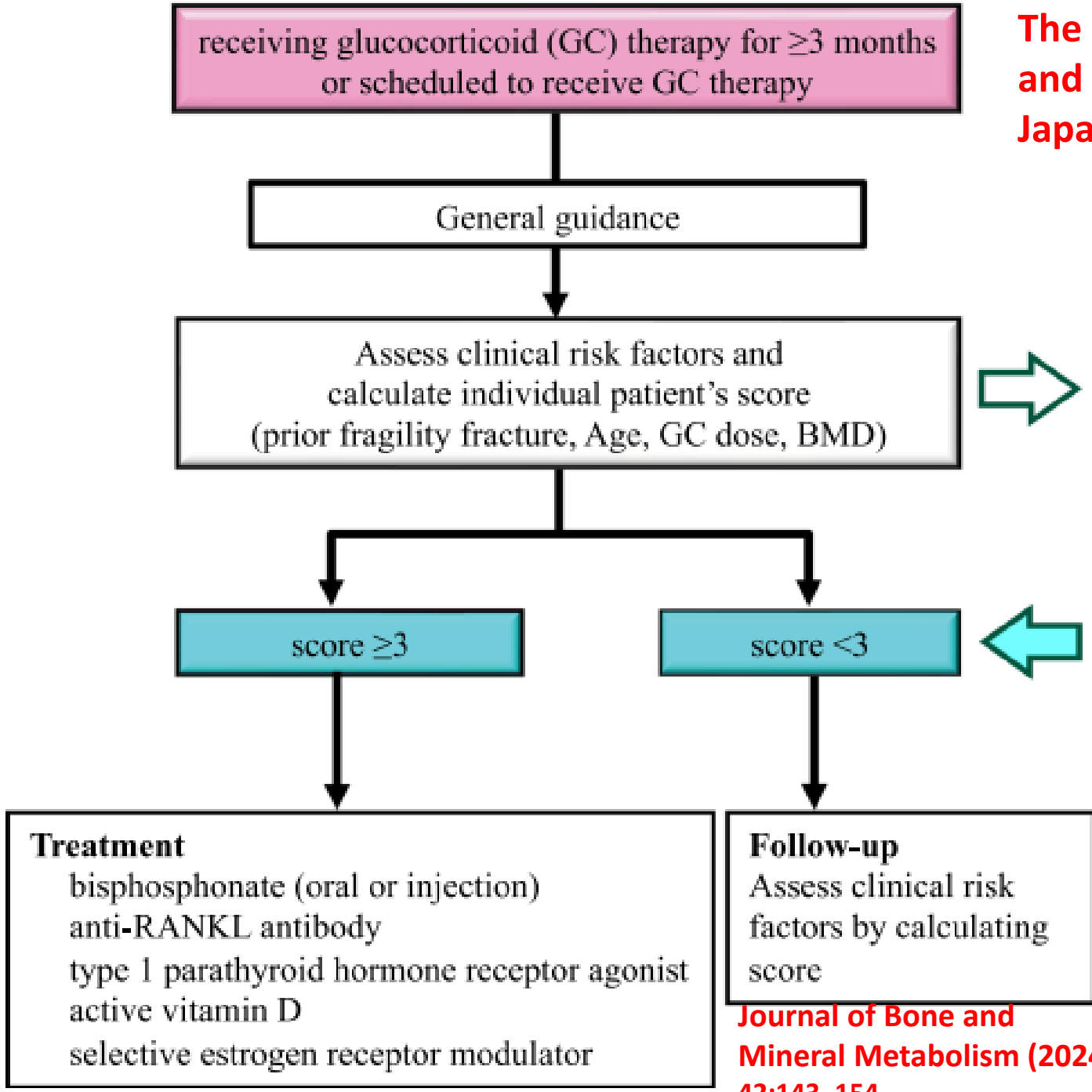

Osteoporosis International (2025) 36:579–608

# Suggested treatment algorithm for managing bone fragility in patients with diabetes mellitus and CKD–MBD

Nature reviews endocrinology 2025



# The 2023 Guidelines for the Management and Treatment of GIOP published by the Japanese Society




| Risk factors | | Score |
|---|---|---|
| Prior fragility fractures | No | 0 |
| | Yes | 7 |
| Age (years) | <50 | 0 |
| | 50≤ <65 | 2 |
| | ≥65 | 4 |
| GC dose (PSL equivalent mg/day) | <5 | 0 |
| | 5≤ <7.5 | 1 |
| | ≥7.5 | 4 |
| BMD (%YAM) | ≥80 | 0 |
| | 70≤ <80 | 2 |
| | <70 | 4 |

Journal of Bone and Mineral Metabolism (2024) 42:143–154

# Conclusion

- CKD fractures ≠ simple osteoporosis
- Bone quality and turnover are critical
- Assess risk → correct CKD-MBD
- High turnover → antiresorptive
- Low turnover → anabolic agent

Nephrol Dial Transplant, 2025, 40, 48–59
https://doi.org/10.1093/ndt/gfae197
Advance access publication date: 24 September 2024

# Multidisciplinary team approach for CKD-associated osteoporosis

**CKD-MBD contributes substantially to the burden of cardiovascular disease and fractures in patients with CKD.**

**A kidney–bone MDT with expertise in CKD-MBD and osteoporosis may improve and expand the approach to diagnosis and treatment of CKD-associated osteoporosis.**

**Thereby improving fracture risk management and contributing to closing the treatment gap in patients with CKD.**

# Thanks for your attention