An individualized approach to osteoporosis treatment in a patient with CKD

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There is a sense of hopelessness ("therapeutic nihilism") among doctors in bone clinics.
In other words, the patients are seen as too difficult or complex for the available medications to help.

Management of Osteoporosis in CKD Patients

- Is it really effective?
- When to start?
- For whom?
- Agent selection?

How to treat osteoporosis without harming the kidneys or worsening mineral disorders?

Bone quality ≠ bone quantity, Fracture risk ≠ DXA T-score alone

Dialysis Patient

64-year-old man on hemodialysis for 3 years presented to you with L1 vertebral fracture after minor fall.

Labs: Ca 8.2, P 6.1, ALP 110, iPTH 80

Meds: Sevelamer, Calcitriol

Who needs to be Tested?

KDIGO 2017:

Consider BMD if results would directly influence treatment

BMD Testing in CKD Patients

- **CKD Stages 1-3 (GFR ≥30 mL/min):**

BMD testing is **recommended** as per general population guidelines (e.g., postmenopausal women, older men with risk factors like prior fractures or glucocorticoid use).

- **CKD Stages 4-5 (GFR <30 mL/min) and Dialysis-Dependent (CKD G5D):**

Routine BMD is not recommended due to altered bone metabolism (e.g., adynamic bone disease, osteomalacia) and poor correlation with fracture risk.

BMD Testing in CKD Patients

Stages 4-5 (GFR <30 mL/min) and Dialysis-Dependent (CKD G5D):

Consider BMD if results would directly influence treatment:

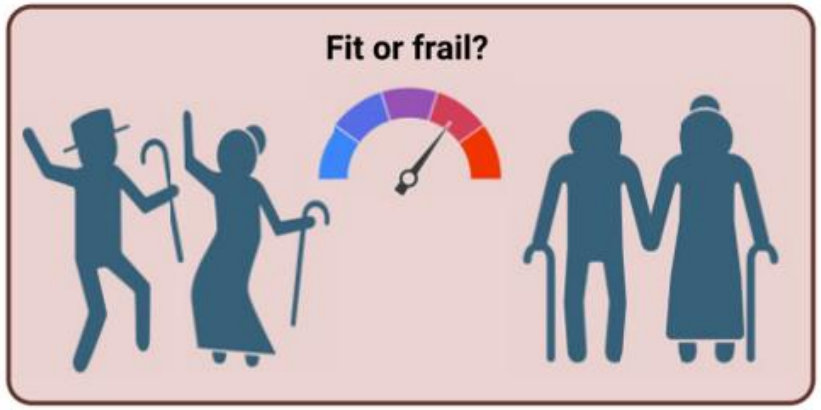
High-Risk Patients(postmenopausal status, prior fragility fractures, steroid use)

Without CKD-MBD

Biopsy-confirmed adynamic bone disease

Transplant candidates/recipients often require BMD due to steroid-induced osteoporosis risk.

Treatment



Nonpharmacologic interventions

Pharmacologic Therapy

Antiresorptive

Anabolic

Mixed

Antiresorptive: Bisphosphonates

Bone effects: Increases BMD but accumulate in bones and induce "Frozen Bone" by decreasing bone turnover which leads to fracture.

Renal effect: Nephrotoxicity (Zoledronic acid is contraindicated in GFR<30, Risedronate is the safest one)

If bisphosphonates are administered, the dosing interval and duration should be modified (typically risedronate 35 mg every other week [ie, half the usual dose] and for not more than three years).

Antiresorptive: Denosumab

Hypocalcemia, a hungry bone response

Cardiovascular side effects?

On January 19, 2024 FDA Adds Boxed Warning on Denosumab for Patients With Advanced CKD

- Frequent monitoring of calcium in the blood, especially for **the first 2 to 10 weeks** after each denosumab injection, is recommended.
- More **severe kidney failure**, lower **baseline serum calcium** and **parathyroid hormone** levels, and **younger age** were risk factors for hypocalcemia.

Annals of Internal Medicine®

Original Research | 7 January 2025

Cardiovascular Safety and Fracture Prevention Effectiveness of Denosumab Versus Oral Bisphosphonates in Patients Receiving Dialysis: A Target Trial Emulation

Authors: Soichiro Masuda, MD, PhD, Toshiki Fukasawa, PhD, Shuichi Matsuda, MD, PhD, and Koji Kawakami, MD, PhD

AUTHOR, ARTICLE, & DISCLOSURE INFORMATION

Publication: Annals of Internal Medicine • Volume 178, Number 2 • https://doi.org/10.7326/ANNALS-24-03237

Cardiovascular Safety and Fracture Prevention Effectiveness of Denosumab Versus Oral Bisphosphonates in Patients Receiving Dialysis

The weighted 3-year risk difference for MACE was 8.2%, The weighted 3-year risk difference for composite fractures was -5.3%.

EDITORIAL

Treating Osteoporosis with Denosumab in Patients on Hemodialysis

The Good, the Bad, and the Ugly

Nickolas, Thomas L.

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Treating Osteoporosis with Denosumab in Patients on Hemodialysis: The Good, the Bad, and the Ugly

The Good: 3D imaging analyses imply that denosumab is an important agent to **heal cortical bone defects** in kidney failure

The Bad: How do we safely manage risk of **hypocalcemia**?

The Ugly: How do we manage **denosumab cessation** because the main agent used to mitigate risk of rebound is a bisphosphonate, which might expose our patients to other risks?

Anabolic agents: Teriparatide, Abaloparatide

teriparatide may be beneficial in adynamic bone disease (Once-weekly)

There is not enough data regarding Abaloparatide efficacy in patients with CKD-MBD.

Mixed agent: Romosozumab

Not enough data

May increase the risk of cardiovascular events

CKD patients are already at elevated cardiovascular risk

KDIGO 2017 Clinical Practice Guideline Update for the Diagnosis, Evaluation, Prevention, and Treatment of CKD-MBD

Chapter 4.3: Treatment of bone with bisphosphonates, other osteoporosis medications, and growth hormone

4.3.3: In patients with CKD G3a–G5D with biochemical abnormalities of CKD-MBD and low BMD and/or fragility fractures, we suggest that treatment choices take into account the magnitude and reversibility of the biochemical abnormalities and the progression of CKD, with consideration of a bone biopsy *(2D)*.

Rationale

Recommendation 3.2.2 now addresses the indications for a bone biopsy prior to antiresorptive and other osteoporosis therapies. Therefore, the original Recommendation 4.3.4 from the 2009 KDIGO CKD-MBD Guideline has been removed, and Recommendation 4.3.3 has broadened from CKD G3a to G3b to CKD G3a to G5D. Nevertheless, when such treatment choices are considered, their specific side effects must also be taken into account (e.g., antiresorptives will exacerbate low bone turnover, denosumab may induce significant hypocalcemia), and the risk of their administration must be weighed against the accuracy of the diagnosis of the underlying bone phenotype.

Chronic kidney disease–mineral and bone disorder: conclusions from a Kidney Disease: Improving Global Outcomes (KDIGO) Controversies Conference

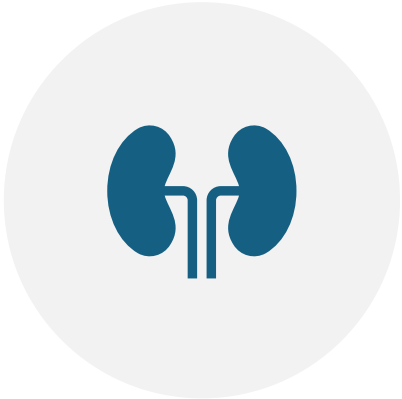
OPEN

Markus Ketteler[1], Pieter Evenepoel[2,3], Rachel M. Holden[4], Tamara Isakova[5], Hanne Skou Jørgensen[6,7], Hirotaka Komaba[8], Thomas L. Nickolas[9], Smeeta Sinha[10,11], Marc G. Vervloet[12], Michael Cheung[13], Jennifer M. King[13], Morgan E. Grams[14], Michel Jadoul[15] and Rosa M.A. Moysés[16]; for Conference Participants[17]

UpToDate 2025

Our approach is largely consistent with the 2017 KDIGO

Decision about treatment is made by tow parameters:



EGFR (≥30 ML/MIN VS <30 ML/MIN)

PRESENCE OF ABSENCE OF CKD-MBD

eGFR ≥30 mL/min & no CKD-MBD

→ Treat as patients without CKD

eGFR ≥30 mL/min & CKD-MBD

→ Treat only if there is a history of fragility fracture

(High turn over: Antiresorptive, Low turn over: Anabolic)

eGFR <30 mL/min (High-Risk Patients Only) Without CKD-MBD

eGFR 15–30

- *Option 1:* Oral bisphosphonate (e.g., reduced-dose risedronate)
- *Option 2:* Denosumab (hypocalcemia risk; monitor closely).

eGFR <15

- Oral bisphosphonate (e.g., risedronate 35 mg biweekly) **only if biopsy excludes osteodystrophy**.

Some experts do not administer bisphosphonates to patients with eGFR <30

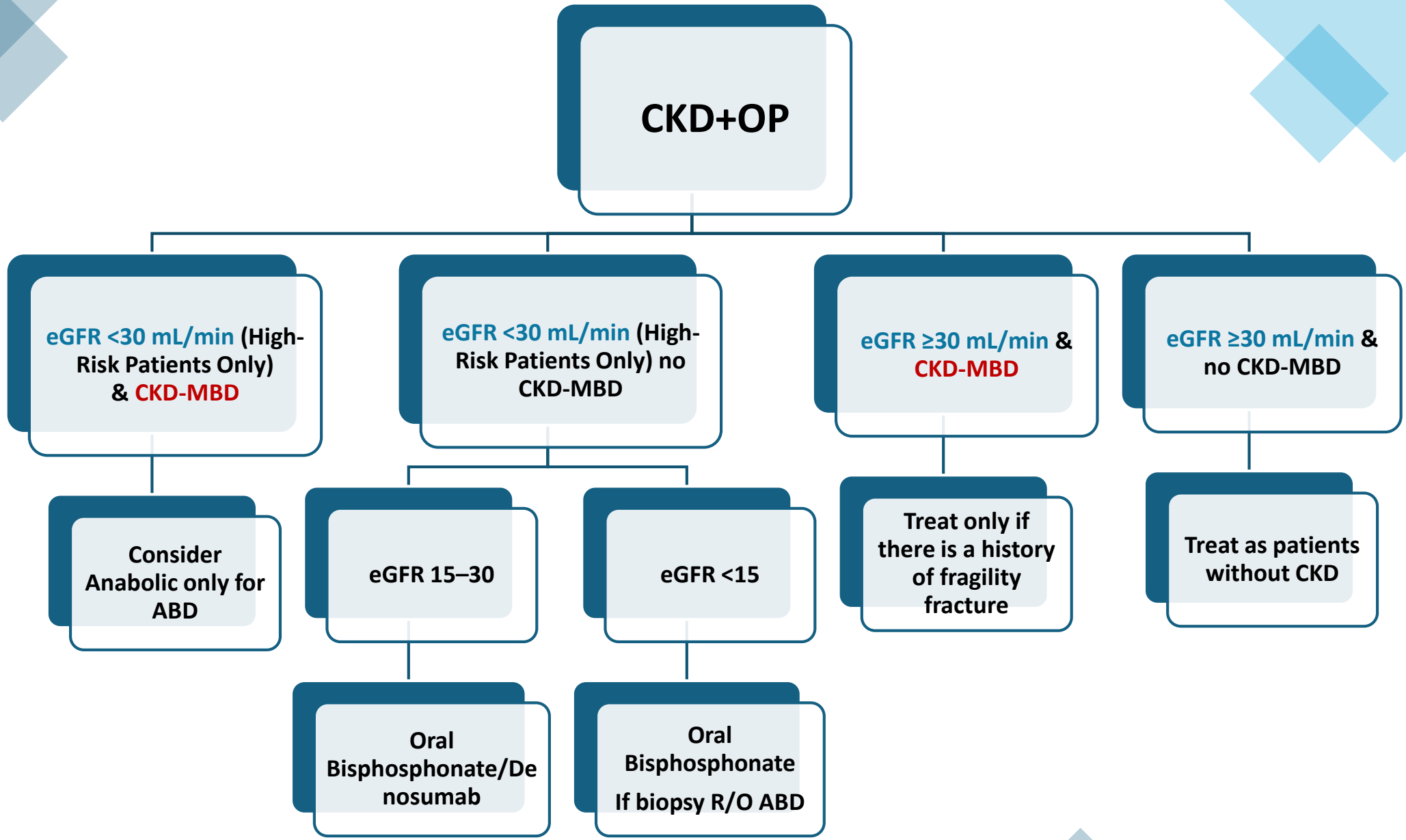
eGFR <30 mL/min (High-Risk Patients Only) With CKD-MBD

→ **Avoid antiresorptive**

Focus on CKD-MBD management

→ Consider anabolic

only for biopsy-confirmed adynamic bone disease


CKD+OP
eGFR <30 mL/min (High-Risk Patients Only) & CKD-MBD
Consider Anabolic only for ABD
eGFR <30 mL/min (High-Risk Patients Only) no CKD-MBD
eGFR 15–30
Oral Bisphosphonate/Denosumab
eGFR <15
Oral Bisphosphonate
If biopsy R/O ABD
eGFR ≥30 mL/min & CKD-MBD
Treat only if there is a history of fragility fracture
eGFR ≥30 mL/min & no CKD-MBD
Treat as patients without CKD

MONITORING THERAPY

There is no consensus

MONITORING THERAPY

➢ **eGFR ≥30 mL/min/1.73 m²**

like patients without CKD (serial BMD)

➢ **eGFR <30 mL/min/1.73 m²**

Ca, P, PTH, Vit.D (10 days after Denosumab, 2 weeks after Teriparatide)

Biochemical markers of bone turnover should not be used to monitor response to therapy in patients with eGFR <30

BMD: two years after osteoporosis therapy

Take Home Messages

Take Home Messages

CKD fundamentally changes osteoporosis diagnosis & treatment.

CKD-MBD optimization is the foundation.

In the presence of CKD-MBD in advanced CKD & dialysis patients, treatment of osteoporosis is nearly impossible!

Individualization is non-negotiable: CKD stage, MBD status, fracture risk, comorbidities, patient factors.

More **severe kidney failure**, lower **baseline serum calcium** and **parathyroid hormone** levels, and **younger age are** risk factors for denosumab induced hypocalcemia.

Take Home Messages

Treatment depends on CKD stages & presence or absence of CKD-MBD.

There is no consensus on monitoring therapy.

Check Ca, P, PTH, Vit.D (10 days after Denosumab, 2 weeks after Teriparatide)

Biochemical markers of bone turnover should not be used to monitor response.

BMD two years after osteoporosis therapy

Close multidisciplinary collaboration (Nephrology/Endocrinology/Rheumatology) is crucial.

"In CKD-MBD, osteoporosis management isn’t just about bones — it’s about balancing renal safety, fracture risk, and metabolic complexities."

There is no one-size-fits-all approach