

# Management of osteoporosis in CKD

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# Introduction

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Falls are the **leading cause** of both fatal & nonfatal injuries in people aged  $\geq 65$

# Introduction

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Although **OP & ABD** share some common clinical characteristics, their pathogenesis, histopathology & treatment are different.

# Epidemiology

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- Fxs were more frequent in dialysis patients:
  - **Non-vertebral fxs** were always much more frequent than the vertebral fxs.
  - Occur at a younger age (**≠ 10 ys younger**)
  - Are associated with a significant increase in morbidity & mortality (**4 × higher**)

# KDIGO 2017 Update for CKD-MBD



- 3.2.1: In patients with CKD **G3a to G5D** with evidence of CKD–MBD &/or risk factors for op, we **suggest BMD** testing to assess fx risk if results will impact treatment decisions.

(Grade 2B)

# KDIGO 2017 Update for CKD-MBD



- 3.2.2: In patients with CKD **G3a to G5D**, it is reasonable to perform a bone biopsy if knowledge of the type of ROD will impact treatment decisions. (Not graded)
- Due to limited clinical experience with performance of bone biopsy & evaluation of the results, as well as growing evidence that antiresorptive therapies are effective in patients with CKD stage G3a to G4, **bone biopsy is no longer a prerequisite for initiation of these therapies.**

# Management

# LIFESTYLE MEASURES

- Including:
  1. Adequate ca & vit D intake
  2. Exercise
  3. Cessation of smoking
  4. Avoiding excessive alcohol intake
  5. Fall prevention



# Adequate ca & vit D intake

- For patients with an eGFR  $<30$  ml/min We suggest ca & vit D supplementation (Grade 2C).
- The target ca intake:
  - Total 1200 mg/d , with  $\leq 500$  mg/d provided by ca supplementation.
- Vit D 800 IU/d

# Hormone Replacement Therapy

- **Premenopausal women** with CKD & low bone mass &/or fragility fx, we suggest OCP (if not contraindicated) (Grade 2B)
- **Men** with CKD, OP, & symptomatic hypogonadism, we recommend testosterone therapy (if not contraindicated) (Grade 1B)

# Comparisons of Interventions for Preventing Falls in Older Adults




## A Systematic Review and Meta-analysis

Andrea C. Tricco, PhD; Sonia M. Thomas, MSc; Areti Angeliki Veroniki, PhD; Jemila S. Hamid, PhD; Elise Cogo, ND; Lisa Striffler, MSc; Paul A. Khan, PhD; Reid Robson, MSc; Kathryn M. Sibley, PhD; Heather MacDonald, MSc; John J. Riva, DC; Kednapa Thavorn, PhD; Charlotte Wilson, MSc; Jayna Holroyd-Leduc, MD; Gillian D. Kerr, MD; Fabio Feldman, PhD; Sumit R. Majumdar, MD; Susan B. Jaglal, PhD; Wing Hui, MSc; Sharon E. Straus, MD, MSc

**IMPORTANCE** Falls result in substantial burden for patients and health care systems, and given the aging of the population worldwide, the incidence of falls continues to rise.

**OBJECTIVE** To assess the potential effectiveness of interventions for preventing falls.

**DATA SOURCES** MEDLINE, Embase, Cochrane Central Register of Controlled Trials, and Ageline databases from inception until April 2017. Reference lists of included studies were scanned.

-  [Editorial page 1659](#)
-  [Supplemental content](#)
-  [CME Quiz at   
jamanetwork.com/learning  
and CME Questions page 1706](#)

# What type of fall-prevention programs may be effective for reducing injurious falls in older people?

- In a network met-analysis including 54 studies & 41 596 participants:
  - Exercise (OR, 0.51)
  - Combined exercise, vision assessment & treatment, & environmental assessment & modification (OR, 0.30)
  - Combined exercise, & vision assessment & treatment (OR, 0.17)
  - Combined clinic-level quality-improvement strategies, multifactorial assessment and treatment, Ca & vit D supplementation (OR, 0.12)were significantly associated with reductions in injurious falls.
- Combinations of interventions likely to be more effective than usual care for preventing injurious falls.

# What type of fall-prevention programs may be effective for reducing injurious falls in older people?

- 1. Be physically active.**
- 2. Check your vision.**
- 3. Wear proper shoes or slippers.**
- 4. Check your medications—especially sleeping pills.**
- 5. Be safe in the bathroom.**
- 6. Get the right equipment.**
- 7. Avoid too much alcohol.**
- 8. Eliminate household hazards.**
- 9. Consider vit D.**
- 10. Talk to your health care team about your risk.**

# KDIGO 2017 Update for CKD-MBD



- 4.2.2: In adult patients with CKD **G3a to G5** not on dialysis, we suggest that calcitriol & vit D analogues **not be routinely** used. (Grade 2C). It is reasonable to reserve the use of them for patients with CKD G4 to G5 with severe & progressive HPTH. (Not graded)

# KDIGO 2017 Update for CKD-MBD



- 4.2.4: In patients with CKD **G5D** requiring PTH-lowering therapy, we suggest calcimimetics, calcitriol, or vit D analogues, or a **combination** of calcimimetics with calcitriol or vit D analogues. (Grade 2B)

# KDIGO 2017 Update for CKD-MBD



- 4.3.1: In patients with CKD **G1–G2** with op &/or high risk of fx, as identified by WHO criteria, we recommend management as for the **general population** (1A).
- 4.3.2: In patients with CKD **G3a–G3b** with PTH in the normal range & op &/or high risk of fx, as identified by WHO criteria, we suggest treatment as for the **general population** (2B).



# KDIGO 2017 Update for CKD-MBD



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

# KDIGO 2017 Update for CKD-MBD



- **Bisphosphonate & Denosumab** are the **most** widely used antiresorptive agents for osteoporosis.
- The amount of bisphosphonate retained in the skeleton is likely a function of:
  - **The baseline remodeling space**
  - **The chronic rate of bone turnover**
  - **The GFR.**

# KDIGO 2017 Update for CKD-MBD



- Approximately **50%** of the absorbed dose of oral & IV bisphosphonates is excreted by the kidney.
- Oral bisphosphonates have **never** been shown to have renal toxicity, while IV bisphosphonates, especially Zolindronic acid, may acutely reduce GFR via a tubular lesions that mimics **ATN**.

# Inhibition of Metaphysial Bone Resorption In vivo by Bisphosphonate

Chemical Modification	Examples	Anti-resorptive potency
First generation: short alkyl	<b>Etidronate</b>	<b>1</b>
	<b>Clodronate</b>	<b>10</b>
Second generation: NH <sub>2</sub> -terminal group	<b>Tiludronate</b>	<b>10</b>
	<b>Pamidronate</b>	<b>100</b>
	<b>Alendronate</b>	<b>100-1000</b>
Third generation: cyclic side chain	<b>Risedronate</b>	<b>1000-10000</b>
	<b>Ibandronate</b>	<b>1000-10000</b>
	<b>Zolendronate</b>	<b>100000</b>

# Bisphosphonates

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- They have a high affinity for bone mineral, & therefore, they are typically retained in the skeleton for **several years**.
- Over the past decade, data suggest that these agents are safe in patients with an eGFR of **15-59** ml/min/1.73m<sup>2</sup>.

# Bisphosphonates

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- Should not be used **routinely** in patients with an eGFR < 30 ml/min & should only be considered in such patients by clinicians with expertise in MBD & after excluding ROD.

# Bisphosphonates

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- For fracturing patients with **eGFR < 15 ml/min** who are candidates for pharmacologic therapy, we suggest an oral bisphosphonate (Grade 2C).
- We typically prescribe **risedronate 35 mg every other week** (ie, one-half the usual dose) & for not more than 3 ys.
- Denosumab is an alternative, although in hemodialysis patients has been associated with clinically significant hypoca.

# Denosumab

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- Is a **monoclonal antibody** that is directed against RANK ligand & inhibits osteoclast proliferation & development.
- 60 mg/6 ms SQ.
- Is effective at reducing the fx risk & the efficacy is not influenced by the kidney function.
- This agent is liable to cause **hypocalcemia** in patients with an impaired renal function.



# Denosumab

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- Hypocalcemia induced by denosumab should be avoided by practicing appropriate precaution & preemptively administering **active vit D** to eligible CKD patients before starting denosumab.
- The serum Ca levels usually reach their nadir around **7 days** after administration, with a less-extensive Ca decrease with the second denosumab administration.

# Teriparatide (rhPTH)

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- 20  $\mu\text{g}/\text{day}$  SQ for 18-24 ms.
- 20  $\mu\text{g}/\text{week}$  in dialysis patients.
- Potential for serum **Ca elevation**.

# Abaloparatide

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- Is an analog of **PTHrp**.
- Is more purely anabolic with approximately **50%** lower risk of hypercalcemia.

# FDA Recommendations for Use of Bisphosphonates in CKD



<b>Bisphosphonate</b>	<b>Acceptable to use in</b>
Alendronate	GFR $\geq$ 35 mL/min/1.73 m <sup>2</sup>
Ibandronate, risedronate, teriparatide	GFR $>$ 30 mL/min/1.73 m <sup>2</sup>
Abaloparatide	Any GFR (but has not been studied in ESRD <sup>1</sup> )
Denosumab	Any GFR <ul style="list-style-type: none"><li>• Studied in women with postmenopausal osteoporosis and normal PTH levels<sup>2</sup></li><li>• Risk for hypocalcemia when used by patients with advanced CKD<sup>2</sup></li></ul>
Romosozumab	N/A (has not been studied in patients with CKD)

# Selective Estrogen Receptor Modulators

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- Raloxifen 60 mg/day
- Estrogen agonist on bone & antagonist effects on breast & uterus

# Selective Estrogen Receptor Modulators

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- SERMs must be administered with caution, since prolongation of the plasma elimination half-life has been reported in patients with CKD.
- SERMS are contraindicated in the patients who have or once had **venous thrombosis** as CKD patients, especially nephrotic patients who may suffer from coexisting venous thrombosis.

GFR  $\leq$  60 ml/min/1.73 m<sup>2</sup>

+

CKD MBD\*  $\pm$  clinical risk factors for fractures\*\*

Lifestyle interventions<sup>Δ</sup>

+

CKD MBD management

+

DXA scan every 1–2 years

T-score  $\leq$  -2.5

$\pm$  Fracture

T-score  $>$  -2.5

+ Fracture

- Fracture



