



KDIGO 2017 CLINICAL PRACTICE GUIDELINE UPDATE

DIAGNOSIS, EVALUATION,  
PREVENTION, AND TREATMENT  
OF CKD-MBD

SPEAKER'S GUIDE

# SUMMARY OF KDIGO CKD-MBD GUIDELINE RECOMMENDATIONS

This Speaker's Guide combines the new recommendation statements (noted in green) from the KDIGO 2017 Clinical Practice Guideline Update for the Diagnosis, Evaluation, Prevention, and Treatment of Chronic Kidney Disease - Mineral and Bone Disorder (CKD-MBD) with those that remained unchanged from the 2009 KDIGO Clinical Practice Guideline for the Diagnosis, Evaluation, Prevention, and Treatment of CKD-MBD.

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# CHAPTER 1

## INTRODUCTION

# INTRODUCTION (2009 GUIDELINE)

- Definition: mineral, bone, and calcific cardiovascular abnormalities that develop as a complication of CKD.
- Guideline development process
  - Formation of international Work Group
  - Definition of end points
  - Evidence review and grading
  - Writing recommendation statements and rationale
  - Public review
  - Revision of draft and recommendations for research
  - Publication of final Guideline

# CHAPTER 2

# METHODOLOGICAL APPROACH

# OVERVIEW OF METHODOLOGY (WORK GROUP & EVIDENCE REVIEW TEAM)

- Develop topics, define populations, interventions/predictors, and outcomes.
- Create standardized quality assessment and literature extraction forms.
- Run literature searches, screen articles, extract data, and perform critical appraisal.
- Grade quality of outcomes for each study.
- Prepare summary tables.
- Grade quality of evidence and prepare evidence profiles.
- Develop guideline document (see previous slide).



# CHAPTER 3.1

## DIAGNOSIS OF CKD-MBD: BIOCHEMICAL ABNORMALITIES

# ASSESSMENT

**3.1.1:** We recommend monitoring serum levels of calcium, phosphate, PTH, and alkaline phosphatase activity beginning in CKD G3a (1C). In children, we suggest such monitoring beginning in CKD G2 (2D).

**3.1.2:** In patients with CKD G3a–G5D, it is reasonable to base the frequency of monitoring serum calcium, phosphate, and PTH on the presence and magnitude of abnormalities, and the rate of progression of CKD (Not Graded).

# ASSESSMENT

## **3.1.2 (cont'd):** Reasonable monitoring intervals would be:

- In CKD G3a–G3b: for serum calcium and phosphate, every 6–12 months; and for PTH, based on baseline level and CKD progression.
- In CKD G4: for serum calcium and phosphate, every 3–6 months; and for PTH, every 6–12 months.
- In CKD G5, including G5D: for serum calcium and phosphate, every 1–3 months; and for PTH, every 3–6 months.
- In CKD G4–G5D: for alkaline phosphatase activity, every 12 months, or more frequently in the presence of elevated PTH (see Chapter 3.2).

In CKD patients receiving treatments for CKD-MBD, or in whom biochemical abnormalities are identified, it is reasonable to increase the frequency of measurements to monitor for trends and treatment efficacy and side effects (Not Graded).

# ASSESSMENT

**3.1.3:** In patients with CKD G3a–G5D, we suggest that 25(OH)D (calcidiol) levels might be measured, and repeated testing determined by baseline values and therapeutic interventions (2C).

We suggest that vitamin D deficiency and insufficiency be corrected using treatment strategies recommended for the general population (2C).

**3.1.4:** In patients with CKD G3a–G5D, we recommend that therapeutic decisions be based on trends rather than on a single laboratory value, taking into account all available CKD-MBD assessments (1C).

# ASSESSMENT

**3.1.5:** In patients with CKD G3a–G5D, we suggest that individual values of serum calcium and phosphate, evaluated together, be used to guide clinical practice rather than the mathematical construct of calcium-phosphate product ( $\text{Ca} \times \text{P}$ ) (2D).

**3.1.6:** In reports of laboratory tests for patients with CKD G3a–G5D, we recommend that clinical laboratories inform clinicians of the actual assay method in use and report any change in methods, sample source (plasma or serum), or handling specifications to facilitate the appropriate interpretation of biochemistry data (1B).



# CHAPTER 3.2

## DIAGNOSIS OF CKD-MBD: BONE

# TESTING FOR CKD-MBD

**New 3.2.1:** In patients with CKD G3a-G5D with evidence of CKD-MBD and/or risk factors for osteoporosis, we suggest bone mineral density (BMD) testing to assess fracture risk if results will impact treatment decisions (2B).

**Old 3.2.2:** In patients with CKD G3a–G5D with evidence of CKD-MBD, we suggest that BMD testing not be performed routinely, because BMD does not predict fracture risk as it does in the general population, and BMD does not predict the type of renal osteodystrophy (2B).

# RATIONALE FOR UPDATE

- Multiple new prospective studies have documented that lower dual-energy X-ray absorptiometry (DXA) BMD predicts incident fractures in patients with CKD G3a–G5D.
- The order of these first two recommendations was changed, since a DXA BMD result might impact the decision to do a bone biopsy.

# TESTING FOR CKD-MBD

**New 3.2.2:** In patients with CKD G3a–G5D, it is reasonable to perform a bone biopsy if knowledge of the type of renal osteodystrophy will impact treatment decisions (Not Graded).

**Old 3.2.1:** In patients with CKD G3a–G5D, it is reasonable to perform a bone biopsy in various settings including, but not limited to: unexplained fractures, persistent bone pain, unexplained hypercalcemia, unexplained hypophosphatemia, possible aluminum toxicity, and prior to therapy with bisphosphonates in patients with CKD-MBD (Not Graded).

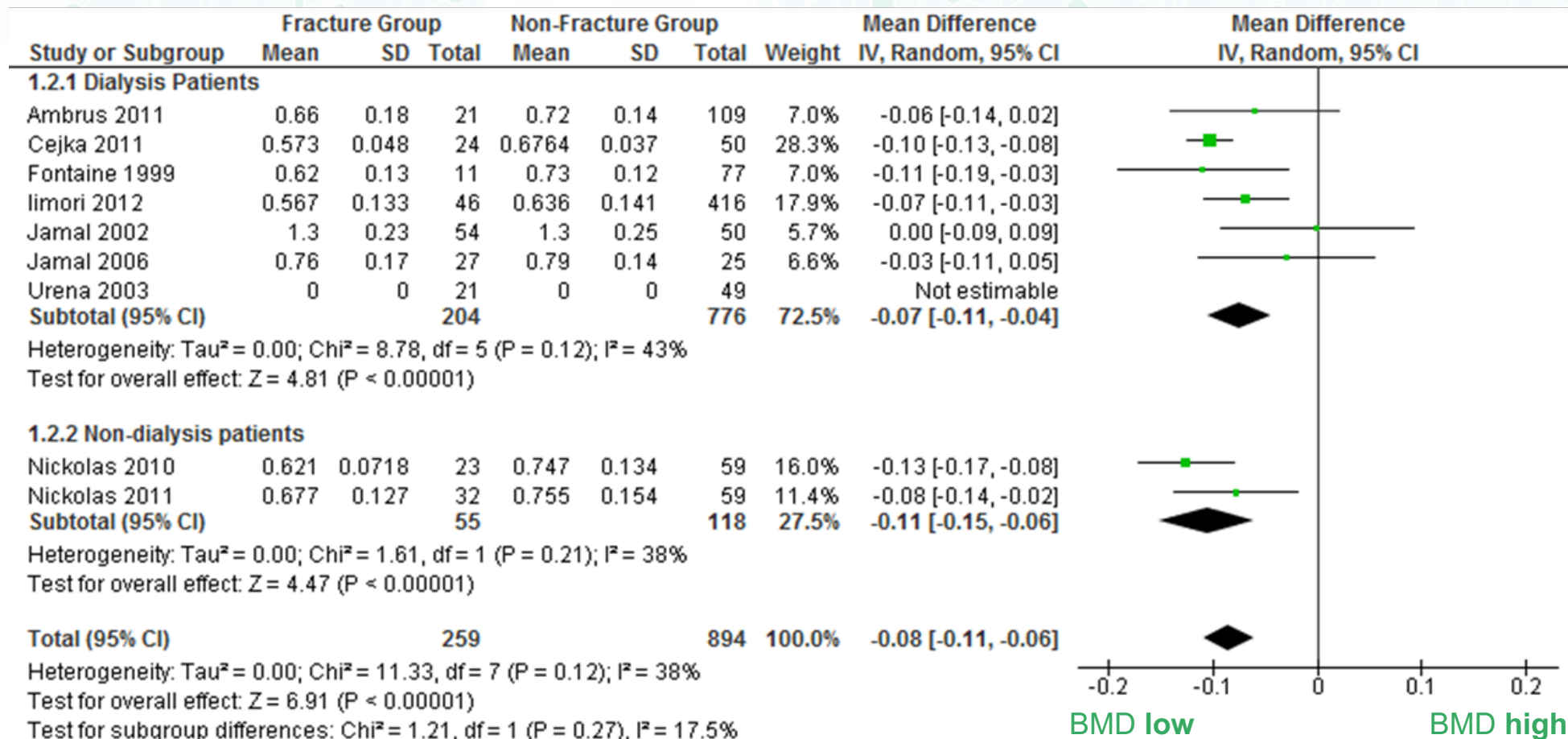
# RATIONALE FOR UPDATE

- The primary motivation for this revision was the growing experience with osteoporosis medications in patients with CKD, low BMD, and a high risk of fracture.
- The lack of ability to perform a bone biopsy may not justify withholding antiresorptive therapy to patients at high risk of fracture.
- The order of these first two recommendations was changed, since a DXA BMD result might impact the decision to do a bone biopsy.



# META-ANALYSIS

## DEXA-determined femoral BMD



# ASSESSMENT

**3.2.3:** In patients with CKD G3a–G5D, we suggest that measurements of serum PTH or bone-specific alkaline phosphatase can be used to evaluate bone disease because markedly high or low values predict underlying bone turnover (2B).

**3.2.4:** In patients with CKD G3a–G5D, we suggest not routinely measuring bone-derived turnover markers of collagen synthesis (such as procollagen type I C-terminal propeptide) and breakdown (such as type I collagen cross-linked telopeptide, cross-laps, pyridinoline, or deoxypyridinoline) (2C).

**3.2.5:** We recommend that infants with CKD G2–G5D have their length measured at least quarterly, while children with CKD G2–G5D should be assessed for linear growth at least annually (1B).

# CASE STUDY: “SAM”

- 55-y.o. male, 9 months following successful kidney transplantation.
- Routine DEXA demonstrated a T-score of  $-2.6$  at the femoral neck.
- He is on low-dose prednisone, tacrolimus, and MMF. In addition, he uses vitamin D supplements.
- Lab values:
  - PTH: 140 pg/mL (15 pmol/L)
  - Calcium: 8.8 mg/dL (2.2 mmol/L)
  - Phosphate: 3.0 mg/dL (1.0 mmol/L)

# CASE STUDY: “SAM”

- **What would you do next?**
  - A. Initiate bisphosphonate therapy
  - B. Refer for subtotal parathyroidectomy
  - C. Wait and see as appropriate
  - D. Lower the dose of prednisone

# CHAPTER 3.3

## DIAGNOSIS OF CKD–MBD: VASCULAR CALCIFICATION



# ASSESSMENT

**3.3.1:** In patients with CKD G3a–G5D, we suggest that a lateral abdominal radiograph can be used to detect the presence or absence of vascular calcification, and an echocardiogram can be used to detect the presence or absence of valvular calcification, as reasonable alternatives to computed tomography-based imaging (2C).

**3.3.2:** We suggest that patients with CKD G3a–G5D with known vascular or valvular calcification be considered at highest cardiovascular risk (2A).

It is reasonable to use this information to guide the management of CKD-MBD (Not Graded).

# CHAPTER 4.1

## TREATMENT OF CKD–MBD: TARGETED AT LOWERING HIGH SERUM PHOSPHATE AND MAINTAINING SERUM CALCIUM

# PHOSPHATE AND CALCIUM

- **New 4.1.1:** In patients with CKD G3a–G5D, treatments of CKD-MBD should be based on serial assessments of phosphate, calcium and PTH levels, considered together (*Not Graded*).

# RATIONALE FOR UPDATE

- This new recommendation was provided in order to emphasize the complexity and interaction of CKD-MBD laboratory parameters.

# PHOSPHATE AND CALCIUM

**New 4.1.2:** In patients with CKD G3a–G5D, we suggest lowering elevated phosphate levels toward the normal range (2C).

**Old 4.1.1:** In patients with CKD G3a–G5, we suggest maintaining serum phosphate in the normal range (2C). In patients with CKD G5D, we suggest lowering elevated phosphate levels toward the normal range (2C).



# RATIONALE FOR UPDATE

- There is an absence of data that efforts to maintain phosphate in the normal range are of benefit to CKD G3a–G4 patients, including some safety concerns.
- Treatment should aim at overt hyperphosphatemia.

# PHOSPHATE AND CALCIUM

**New 4.1.3:** In adult patients with CKD G3a–G5D, we suggest avoiding hypercalcemia (2C).  
In children with CKD G3a–G5D, we suggest maintaining serum calcium in the age-appropriate normal range (2C).

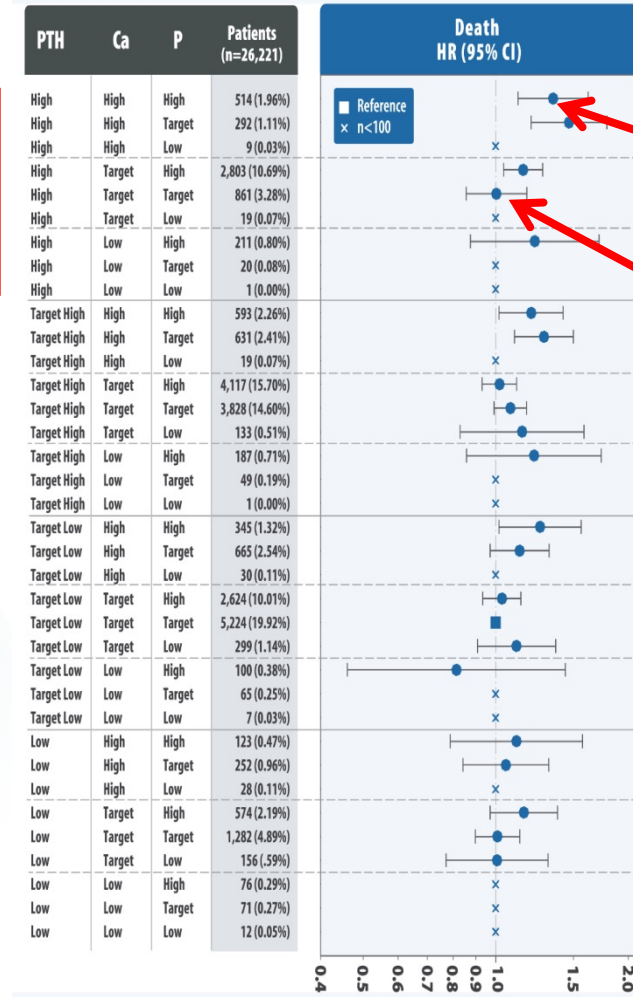
**Old 4.1.2:** In patients with CKD G3a–G5D, we suggest maintaining serum calcium in the normal range (2D).

# RATIONALE FOR UPDATE

- Mild and asymptomatic hypocalcemia (e.g., in the context of calcimimetic treatment) can be tolerated in order to avoid inappropriate calcium loading in adults.

# CKD-MBD PHENOTYPE AND ADJUSTED RISK OF DEATH OR CV HOSPITALIZATION

PTH high



Ca, P high

Ca, P target

Block GA et al. Clin J Am Soc Nephrol. 2013;8:2132-2140.

# PEDIATRIC PERSPECTIVE

- Childhood and adolescence are critical periods for bone mass accrual. A prospective pediatric cohort study showed lower serum calcium levels were independently associated with lower cortical volumetric BMD Z-scores, which predicted future fractures.
- The Work Group recognizes the higher calcium requirements of the growing skeleton and suggests that serum calcium levels are maintained in the age-appropriate normal range.



# PHOSPHATE AND CALCIUM

**New 4.1.4:** In patients with CKD G5D, we suggest using a dialysate calcium concentration between 1.25 and 1.50 mmol/l (2.5 and 3.0 mEq/l) (2C).

**Old 4.1.3:** In patients with CKD G5D, we suggest using a dialysate calcium concentration between 1.25 and 1.50 mmol/l (2.5 and 3.0 mEq/l) (2D).

# RATIONALE FOR UPDATE

- Additional studies of better quality are available; however, they do not allow discrimination of benefits and harm between calcium dialysate concentrations of 1.25 and 1.50 mmol/l (2.5 and 3.0 mEq/l).
- Hence, the wording is unchanged but evidence grade is upgraded from 2D to 2C.

# PHOSPHATE AND CALCIUM

**New 4.1.5:** In patients with CKD G3a–G5D, decisions about phosphate-lowering treatment should be based on progressively or persistently elevated serum phosphate (Not Graded).

**Old 4.1.4:** In patients with CKD G3a–G5 (2D) and G5D (2B), we suggest using phosphate-binding agents in the treatment of hyperphosphatemia.

It is reasonable that the choice of phosphate binder takes into account CKD stage, presence of other components of CKD-MBD, concomitant therapies, and side effect profile (Not Graded).

# RATIONALE FOR UPDATE

- The update emphasizes the perception that early “preventive” treatment of hyperphosphatemia is currently not supported by data (see Rec. 4.1.2).

# PHOSPHATE AND CALCIUM

**New 4.1.6:** In adult patients with CKD G3a–5D receiving phosphate-lowering treatment, we suggest restricting the dose of calcium-based phosphate binders (2B).

In children with CKD G3a–G5D, it is reasonable to base the choice of phosphate-lowering treatment on serum calcium levels (Not Graded).

**Old 4.1.5:** In patients with CKD G3a–G5D and hyperphosphatemia, we recommend restricting the dose of calcium-based phosphate binders and/or the dose of calcitriol or vitamin D analog in the presence of persistent or recurrent hypercalcemia (1B).

In patients with CKD G3a–G5D and hyperphosphatemia, we suggest restricting the dose of calcium-based phosphate binders in the presence of arterial calcification (2C) and/or adynamic bone disease (2C) and/or if serum PTH levels are persistently low (2C).



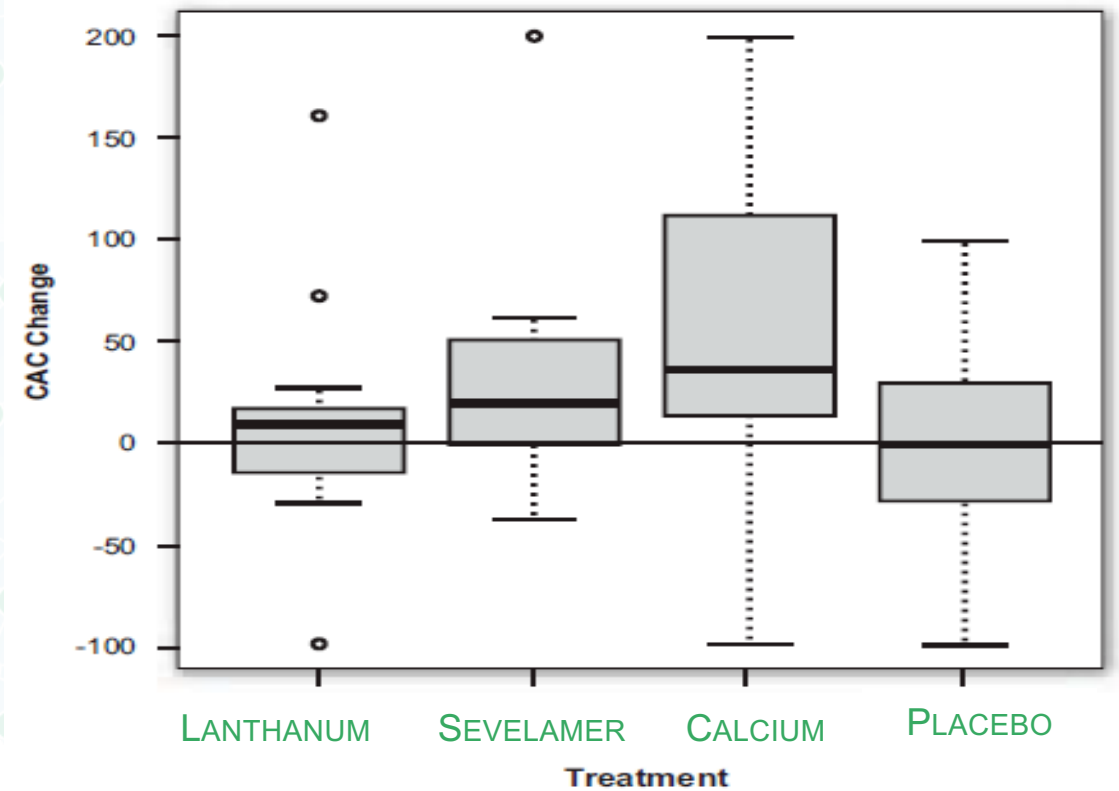
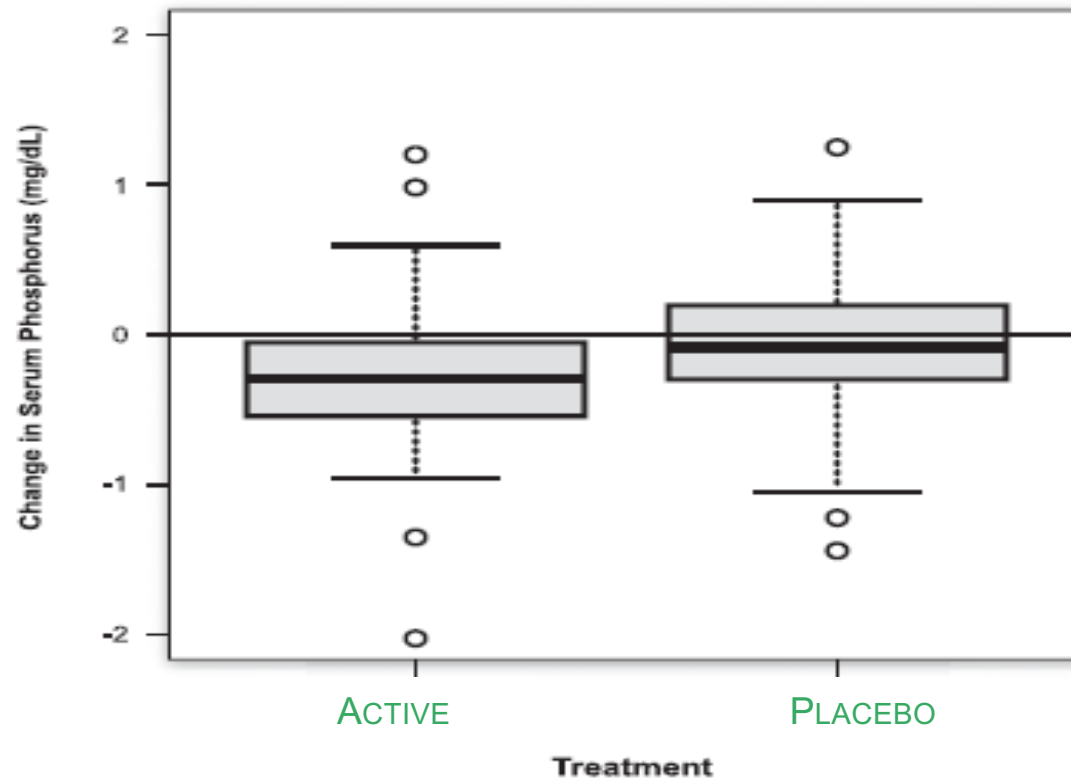
# RATIONALE FOR UPDATE

- New evidence from three randomized control trials (RCTs) supports a more general recommendation to restrict calcium-based phosphate binders in hyperphosphatemic patients of all severities of CKD.

# PHOSPHATE AND CALCIUM

**4.1.7:** In patients with CKD G3a–G5D, we recommend avoiding the long-term use of aluminum-containing phosphate binders, and in patients with CKD G5D, avoiding dialysate aluminum contamination to prevent aluminum intoxication (1C).

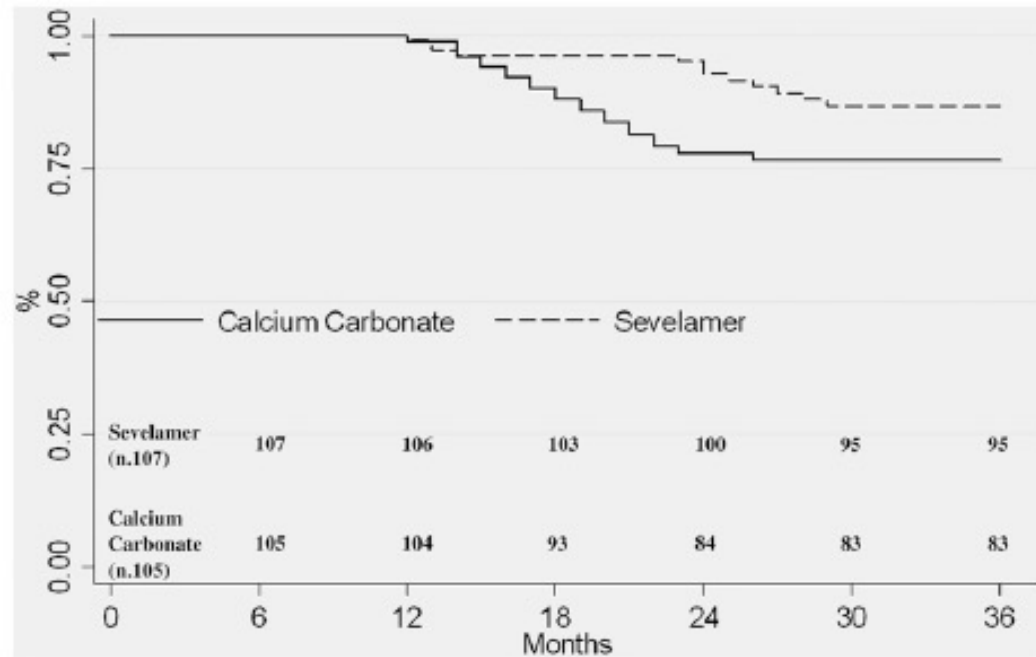
# PHOSPHATE BINDERS IN MODERATE CKD



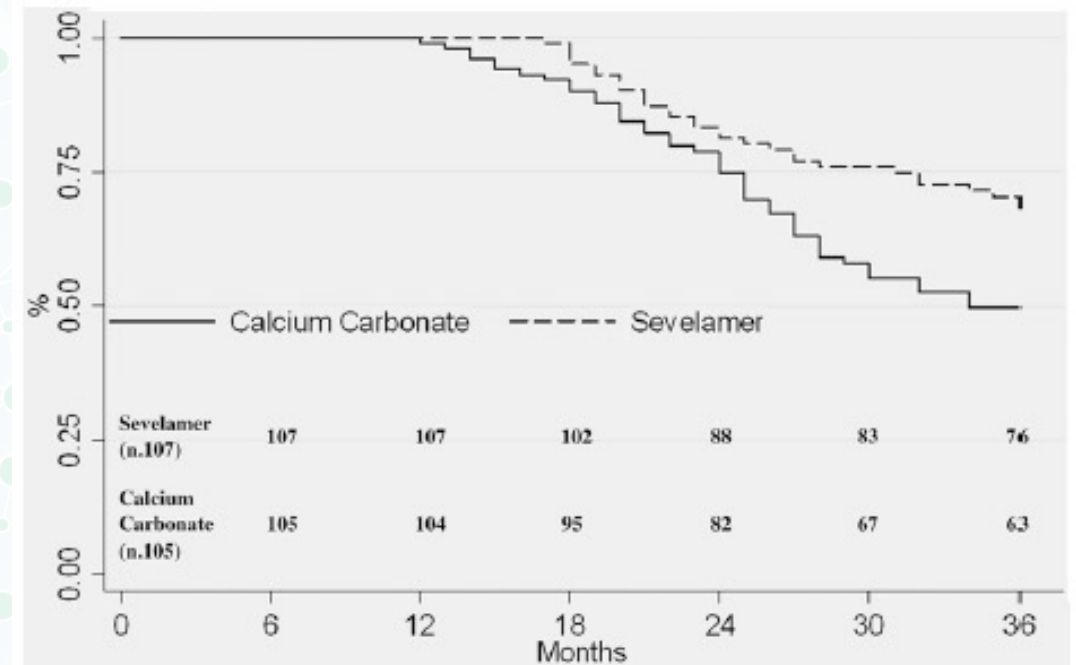
Block G et al. J Am Soc Nephrol. 2012;23:1407-1415.

# PHOSPHATE BINDERS AND MORTALITY

All-Cause Mortality



Dialysis Inception

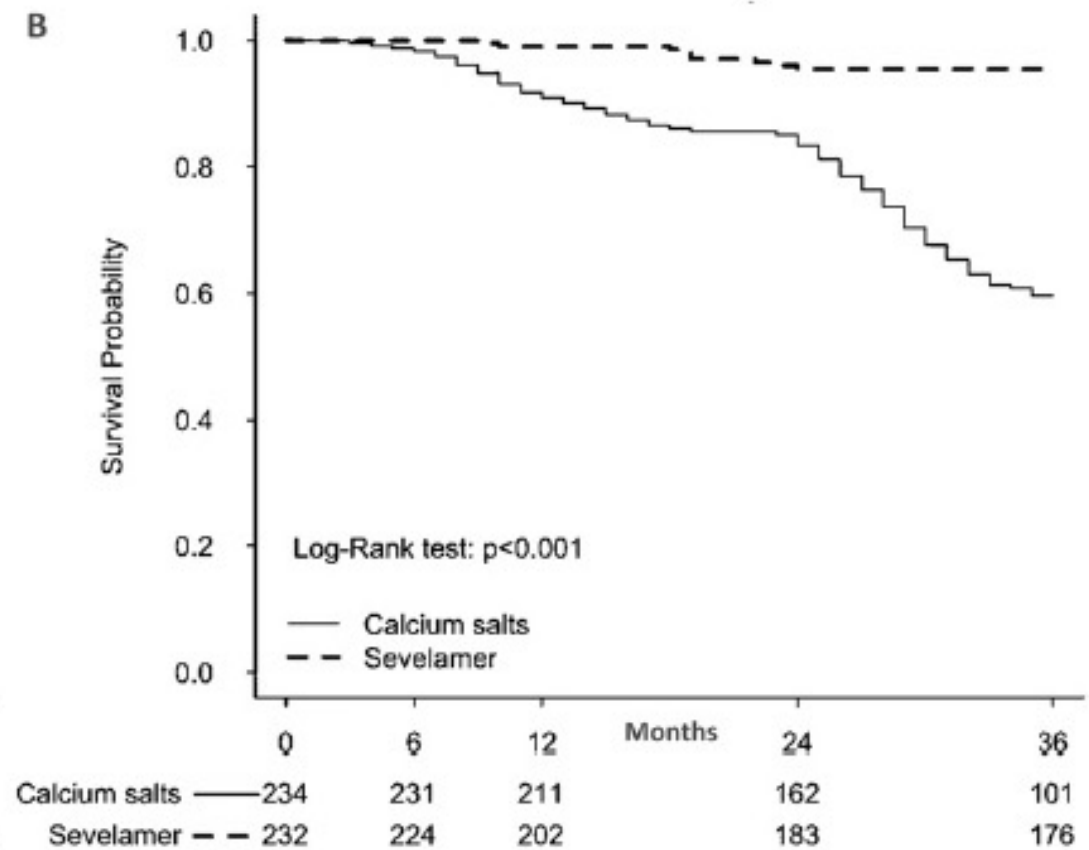
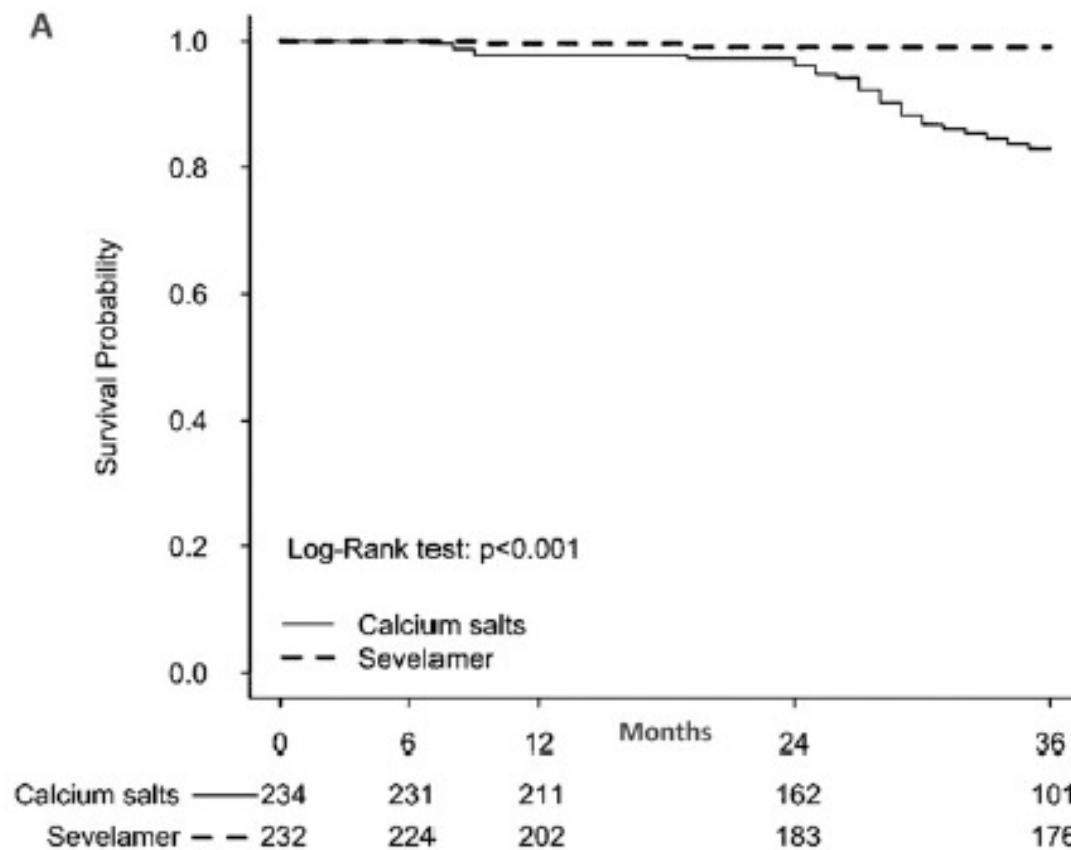


Di Iorio B et al. Clin J Am Soc Nephrol 2012;7:487-493

# SEVELAMER VS. CALCIUM

Arrhythmias

Cardiovascular Mortality





# PEDIATRIC PERSPECTIVE

- Concerns regarding the adverse effects of exogenous calcium may not be generalizable to children.
- Studies of calcium- and non-calcium-containing binders and other therapies that impact calcium balance should consider the needs of the developing skeleton.
- The observation that serum calcium levels were positively associated with increases in BMD in children with CKD, and this association was significantly more pronounced with greater linear growth velocity, illustrates the unique needs of the growing skeleton.

# PHOSPHATE

**New 4.1.8:** In patients with CKD G3a–G5D, we suggest limiting dietary phosphate intake in the treatment of hyperphosphatemia alone or in combination with other treatments (2D). It is reasonable to consider phosphate source (e.g., animal, vegetable, additives) in making dietary recommendations (Not Graded).

**Old 4.1.7:** In patients with CKD G3a–G5D, we suggest limiting dietary phosphate intake in the treatment of hyperphosphatemia alone or in combination with other treatments (2D).

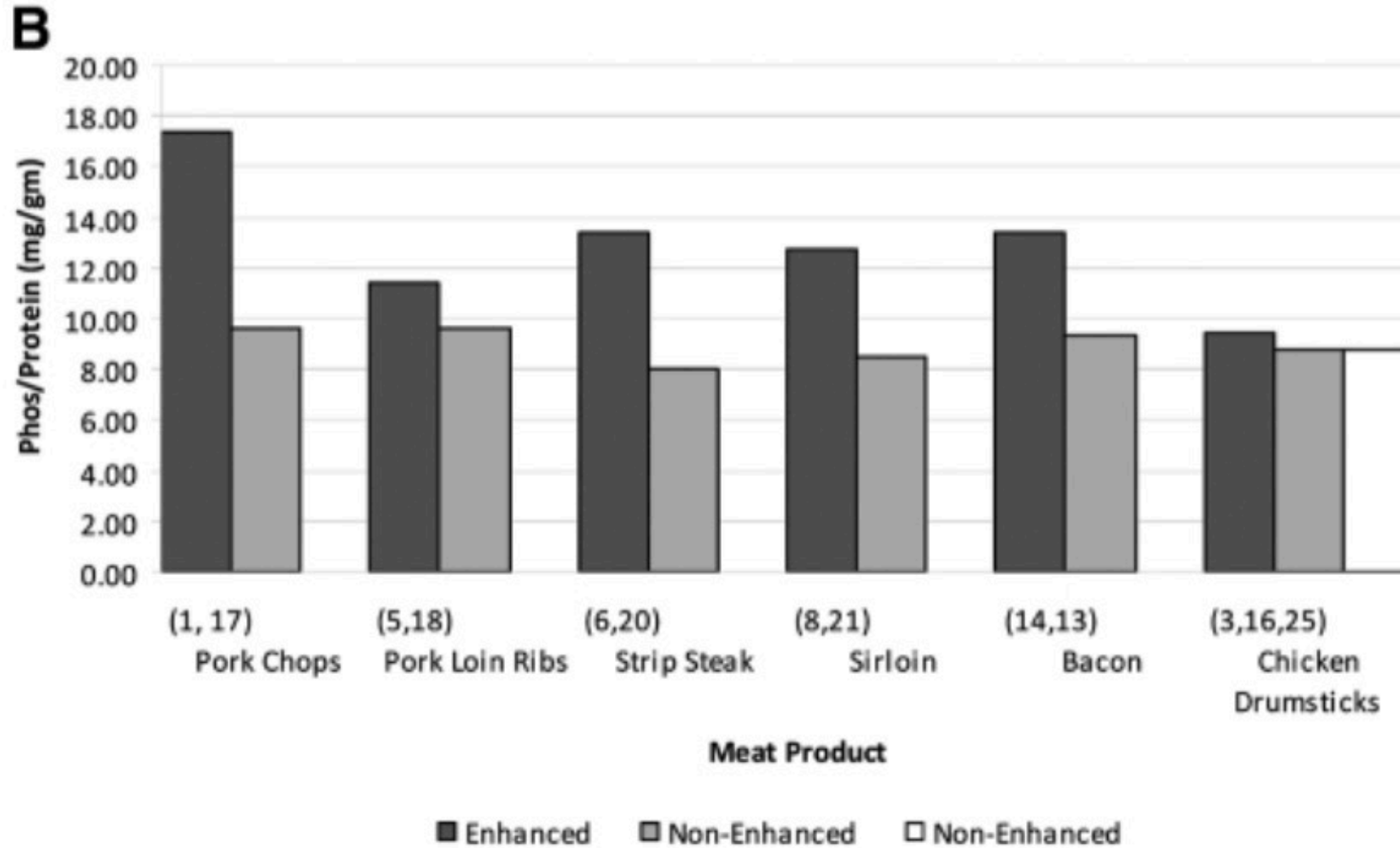
# RATIONALE FOR UPDATE

- New data on phosphate sources were included as an additional qualifier for the previous recommendation.
- These sources included: natural phosphorus (as cellular and protein constituents) contained in raw or unprocessed foods; phosphorus added to foods during processing; and phosphorus in dietary supplements or medications.

# PHOSPHATE

**4.1.9:** In patients with CKD G5D, we suggest increasing dialytic phosphate removal in the treatment of persistent hyperphosphatemia (2C).

# “HIDDEN” PHOSPHATE



Sherman RA et al. Clin J Am Soc Nephrol. 2009;4:1370-1373



# CASE STUDY: “NICKY”

- 67-y.o. female on HD for 2 years.
- Admitted for back pain, due to impression fracture of the tenth thoracic vertebra.
- On daily cholecalciferol (1,000 U), low-dose alfacalcidol, and sevelamer carbonate.
- Lab results:
  - Calcium: 9.0 mg/dL (2.3 mmol/L)
  - Phosphate: 5.7 mg/dL (1.8 mmol/L)
  - PTH: 450 pg/mL (48 pmol/L)
  - Alkaline phosphatase: 140 U/L

# CASE STUDY: “NICKY”

- **What would you do next?**
  - A. Perform DEXA to estimate additional fracture risk.
  - B. Increase the dose of sevelamer carbonate.
  - C. Start denosumab.
  - D. Initiate cinacalcet.
  - E. Add calcium-containing phosphate binder.

# CHAPTER 4.2

## TREATMENT OF ABNORMAL PTH LEVELS IN CKD-MBD

# ASSESSMENT OF PTH

**New 4.2.1:** In patients with CKD G3a–G5 not on dialysis, the optimal PTH level is not known. However, we suggest that patients with levels of intact PTH progressively rising or persistently above the upper normal limit for the assay be evaluated for modifiable factors, including hyperphosphatemia, hypocalcemia, high phosphate intake, and vitamin D deficiency (2C).

**Old 4.2.1:** In patients with CKD G3a–G5 not on dialysis, the optimal PTH level is not known. However, we suggest that patients with levels of intact PTH above the upper normal limit of the assay are first evaluated for hyperphosphatemia, hypocalcemia, and vitamin D deficiency (2C).

It is reasonable to correct these abnormalities with any or all of the following: reducing dietary phosphate intake and administering phosphate binders, calcium supplements, and/or native vitamin D (Not Graded).

# RATIONALE FOR UPDATE

- The Work Group felt that modest increases in PTH may represent an appropriate adaptive response to declining kidney function and have revised this statement to include “persistently” above the upper normal PTH level as well as “progressively rising” PTH levels, rather than “above the upper normal limit”. That is, treatment should not be based on a single elevated value.
- Although the optimal PTH is not known, the Work Group felt that rising PTH levels in CKD G3a-G5 warrant examination of modifiable factors:
  - Vitamin D insufficiency/deficiency
  - Hypocalcemia
  - Hyperphosphatemia
  - High phosphate intake



# CALCITRIOL AND VITAMIN D

**New 4.2.2:** In adult patients with CKD G3a–G5 not on dialysis, we suggest calcitriol and vitamin D analogs not be routinely used (2C). It is reasonable to reserve the use of calcitriol and vitamin D analogs for patients with CKD G4–G5 with severe and progressive hyperparathyroidism (Not Graded).

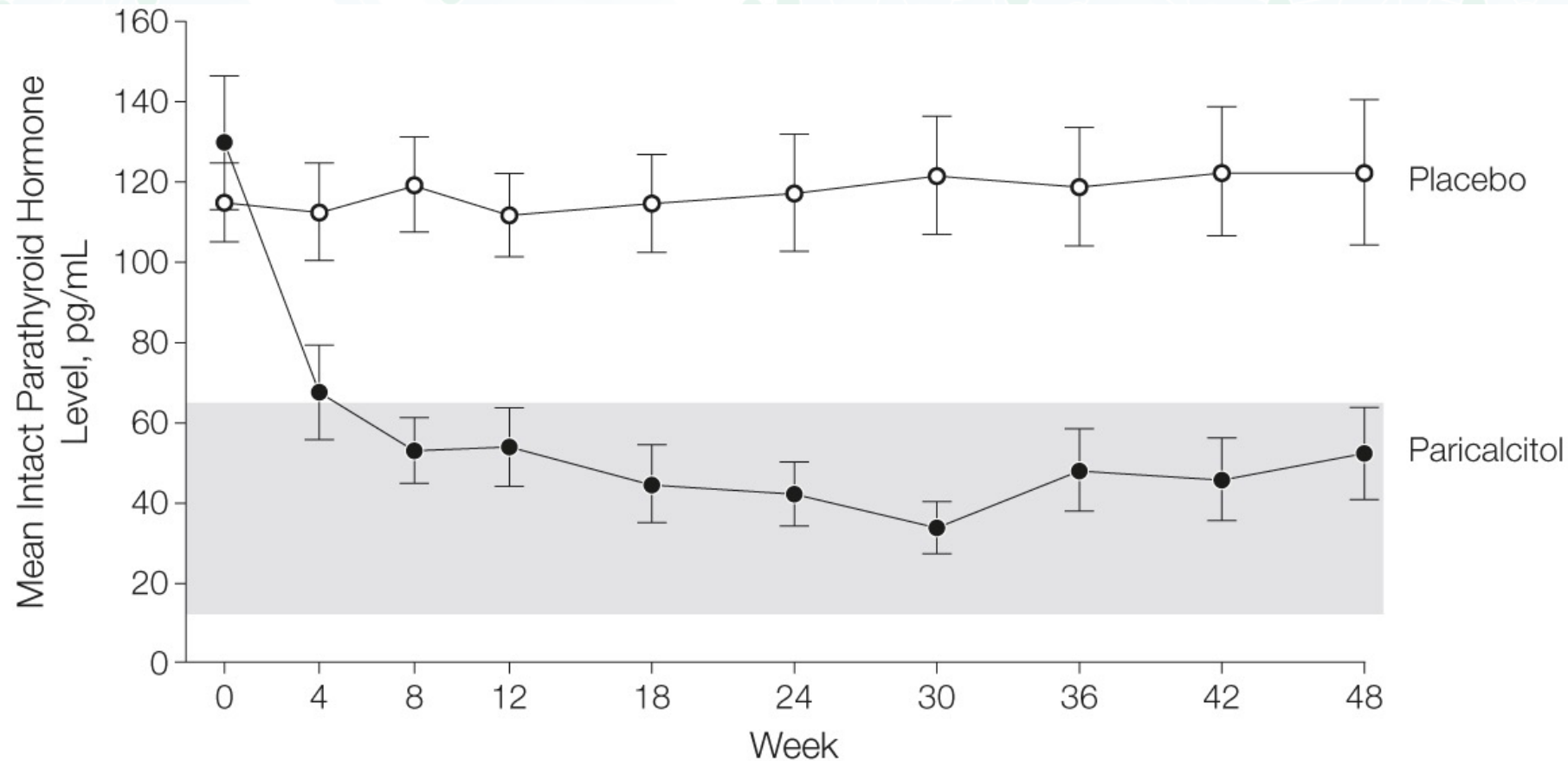
In children, calcitriol and vitamin D analogs may be considered to maintain serum calcium levels in the age-appropriate normal range (Not Graded).

**Old 4.2.2:** In patients with CKD G3a–G5 not on dialysis, in whom serum PTH is progressively rising and remains persistently above the upper limit of normal for the assay despite correction of modifiable factors, we suggest treatment with calcitriol or vitamin D analogs (2C).

# RATIONALE FOR UPDATE

- Suppression of PTH via calcitriol and other vitamin D analogs have been the therapeutic mainstay for the treatment of secondary hyperparathyroidism (SHPT). Multiple RCTs cited in the 2009 Guideline reported benefits of these agents on improving biochemical endpoints, and adverse effects of hypercalcemia were also noted.
- Two trials, PRIMO and OPERA, demonstrated significantly increased risk of hypercalcemia in patients treated with paricalcitol, compared with placebo, in the absence of beneficial effects on surrogate cardiac endpoints.

# THE PRIMO TRIAL

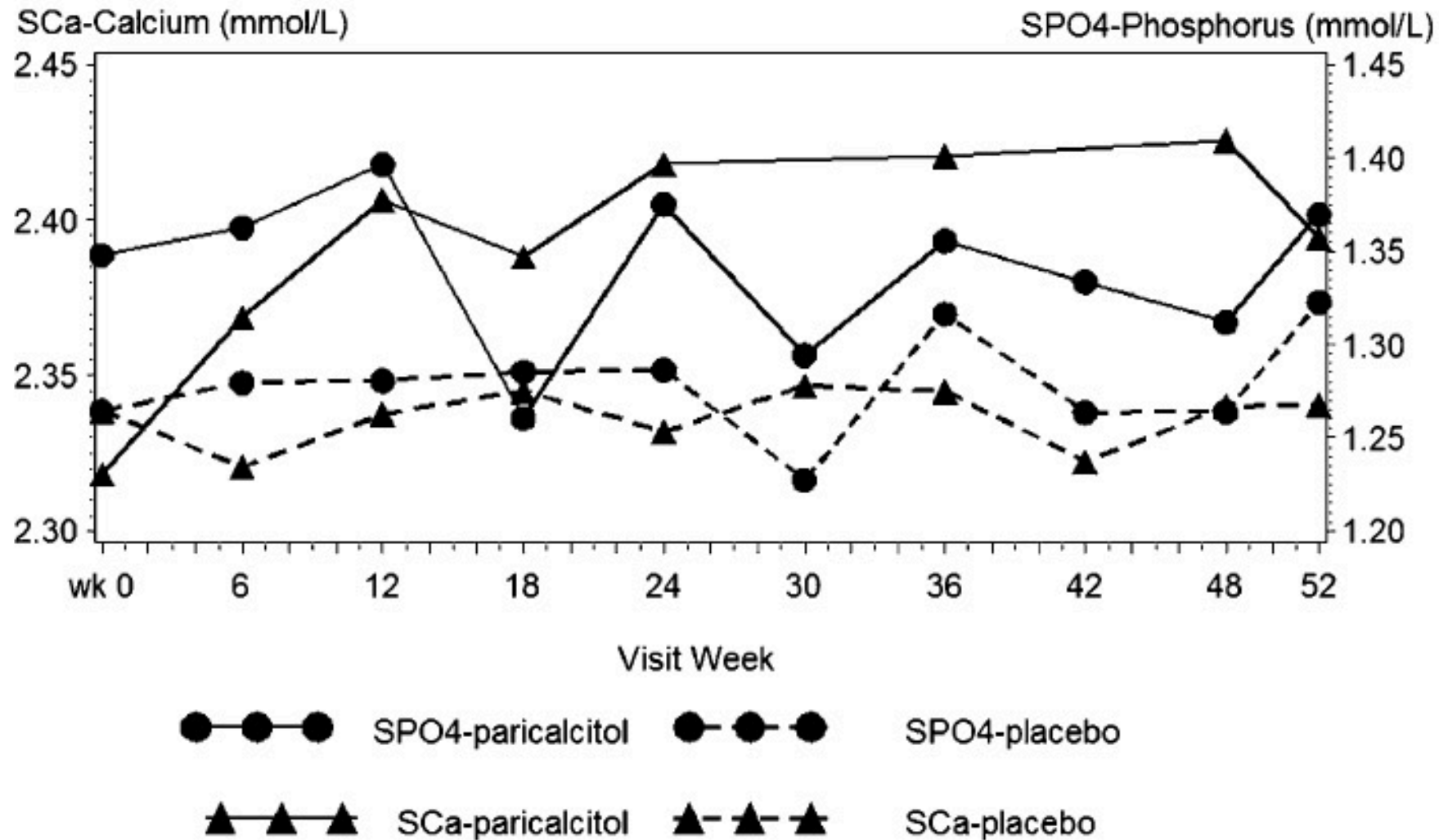


No. of patients

Placebo	112	105	106	104	100	93	94	91	92	85
Paricalcitol	115	111	112	108	104	101	96	92	88	84

Thadani R et al. JAMA. 2012;307:674-684

# THE OPERA TRIAL



# MAINTAINING/LOWERING PTH

**4.2.3:** In patients with CKD G5D, we suggest maintaining intact PTH levels in the range of approximately 2 to 9 times the upper normal limit for the assay (2C).

We suggest that marked changes in PTH levels in either direction within this range prompt an initiation or change in therapy to avoid progression to levels outside of this range (2C).



# MAINTAINING/LOWERING PTH

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

**Old 4.2.4:** In patients with CKD G5D and elevated or rising PTH, we suggest calcitriol, or vitamin D analogs, or calcimimetics, or a combination of calcimimetics and calcitriol or vitamin D analogs be used to lower PTH (2B).

- It is reasonable that the initial drug selection for the treatment of elevated PTH be based on serum calcium and phosphorus levels and other aspects of CKD-MBD (Not Graded).
- It is reasonable that calcium or non-calcium-based phosphate binder dosage be adjusted so that treatments to control PTH do not compromise levels of phosphorus and calcium (Not Graded).

# MAINTAINING/LOWERING PTH

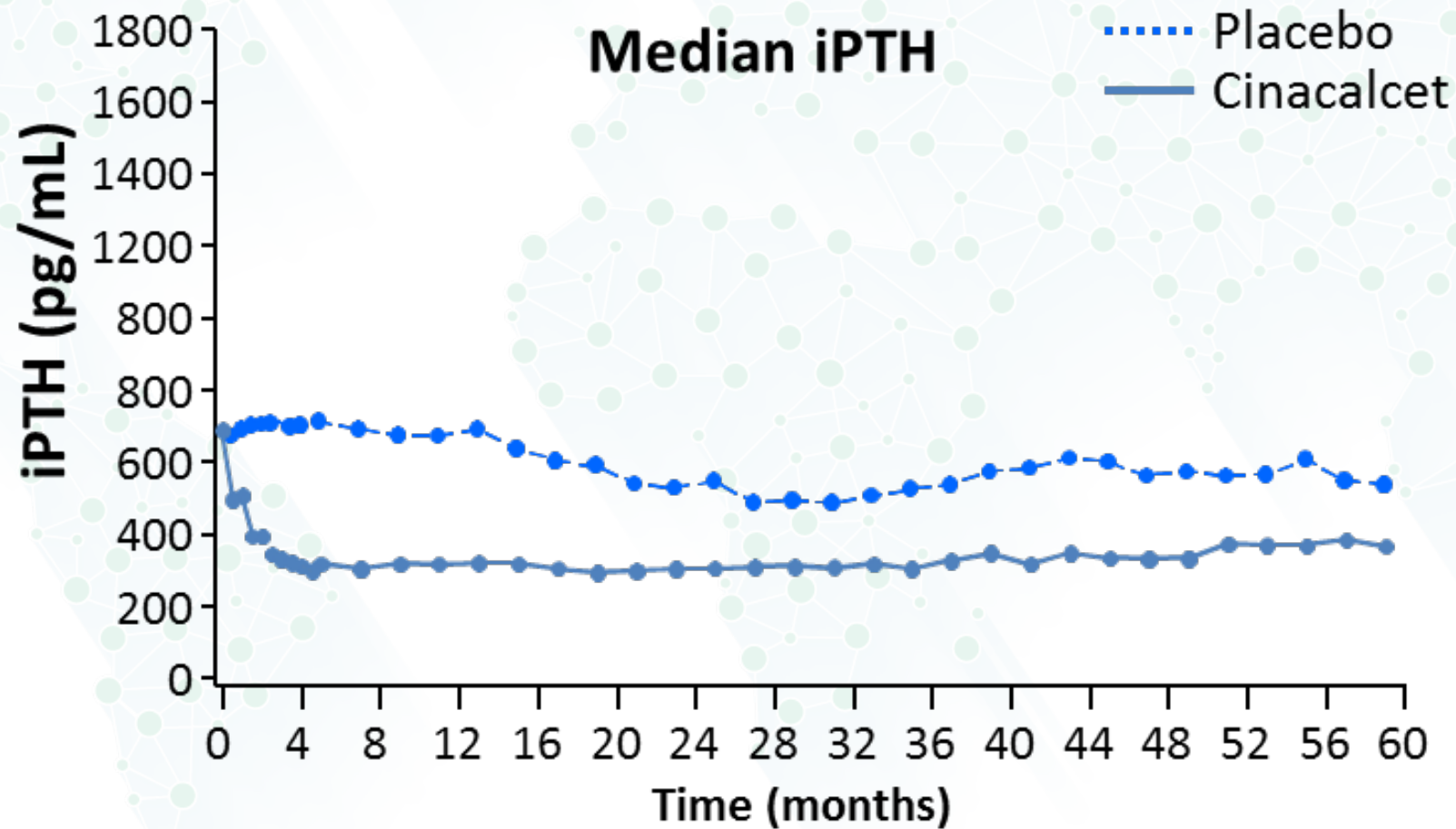
## Old 4.2.4 (cont'd):

- We recommend that, in patients with hypercalcemia, calcitriol or another vitamin D sterol be reduced or stopped (1B).
- We suggest that, in patients with hyperphosphatemia, calcitriol or another vitamin D sterol be reduced or stopped (2D).
- We suggest that, in patients with hypocalcemia, calcimimetics be reduced or stopped depending on severity, concomitant medications, and clinical signs and symptoms (2D).
- We suggest that, if the intact PTH levels fall below two times the upper limit of normal for the assay, calcitriol, vitamin D analogs, and/or calcimimetics be reduced or stopped (2C).

# RATIONALE FOR UPDATE

- Recommendation 4.2.4 originally had not been identified for an update. However, due to a subsequent series of secondary and *post-hoc* publications of the EVOLVE trial, the Work Group decided to re-evaluate it.
- Although EVOLVE did not meet its primary endpoint, the majority of the Work Group were reluctant to exclude potential benefits of calcimimetics for CKD G5D patients, based on subsequent prespecified analyses.
- No PTH-lowering treatment was prioritized at this time, since calcimimetics, calcitriol, and vitamin D analogs are all acceptable first-line options in CKD G5D patients.

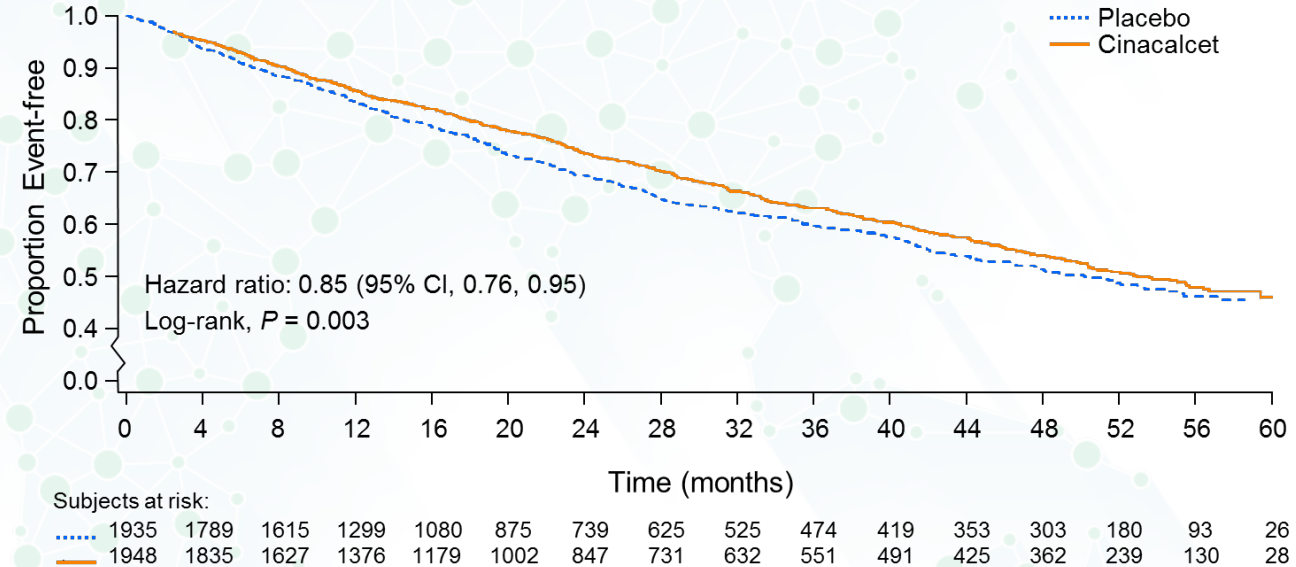
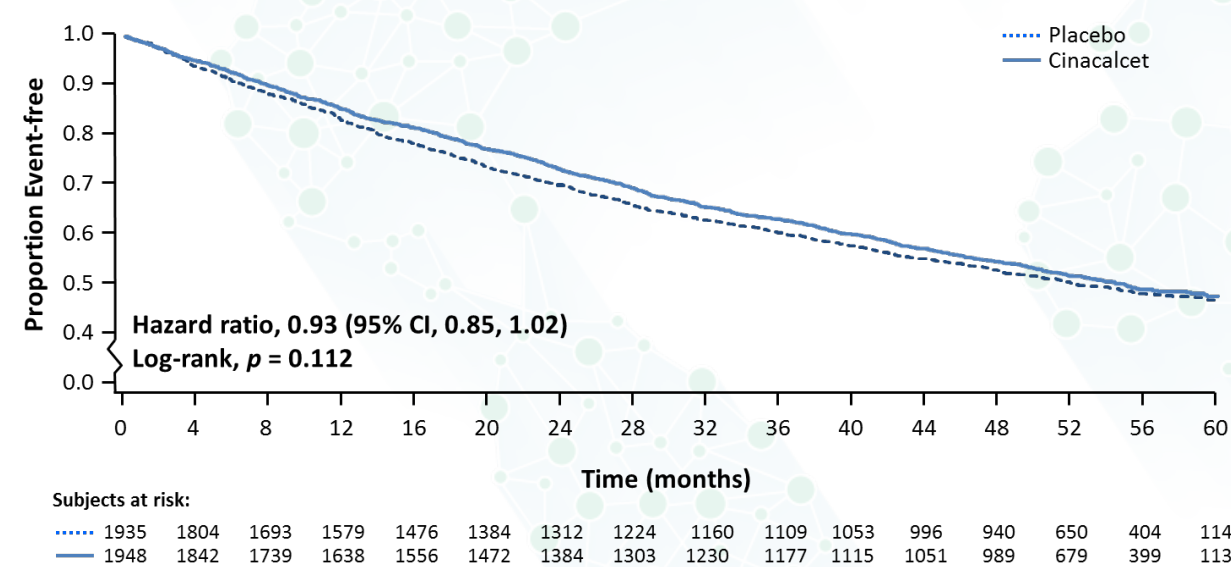
# EVOLVE: LOWERING PTH



Chertow GM, et al. N Engl J Med. 2012;367:2482-2494

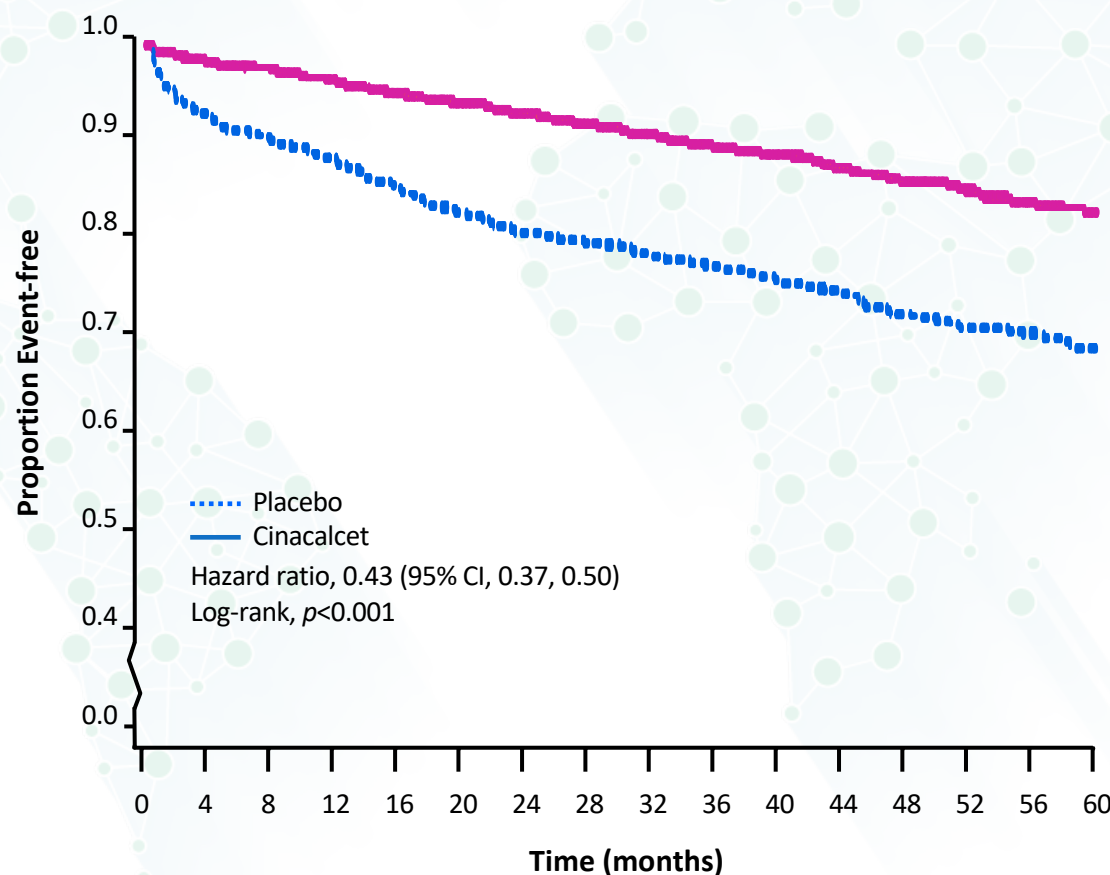


# EVOLVE STUDY: CINACALCET





# TIME TO FIRST EPISODE OF SEVERE UNREMITTING HPT (INTENT-TO-TREAT ANALYSIS)



## Severe, unremitting HPT

- Prespecified and defined as
  - PTH > 1000 pg/ml (106.0 pmol/l) with serum calcium > 10.5 mg/dl (2.6 mmol/l) on 2 consecutive occasions OR
  - PTH > 1000 pg/ml with serum calcium > 10.5 mg/dl on a single occasion and subsequent commercial cinacalcet use within 2 months of the laboratory assessment OR
  - parathyroidectomy

# PEDIATRIC PERSPECTIVE

- Studies of cinacalcet in children are limited to case reports, case series, a single-center experience (with 4 to 28 patients), and an open label study of a single dose in 12 children on dialysis.
- In recognition of the unique calcium demands of the growing skeleton, PTH-lowering therapies should be used with caution in children to avoid hypocalcemia. Future studies are needed in children before issuing pediatric-specific recommendations.

# SEVERE HYPERPARATHYROIDISM

**4.2.5:** In patients with CKD G3a–G5D with severe hyperparathyroidism (HPT) who fail to respond to medical or pharmacological therapy, we suggest parathyroidectomy (2B).

# CASE STUDY: “TOBY”

- 67-y.o. lean male on with eGFR of 25 ml/min/1.73 m<sup>2</sup>, hypertension, ACR (albumin-creatinine ratio) 120 mg/g (1.2 mg/mmol).
- Seen on scheduled outpatient visit.
- Well-controlled blood pressure on lisinopril and metoprolol, besides sodium restriction.
- Lab results:
  - Calcium: 9.6 mg/dL (2.4 mmol/L) [corrected for albumin]
  - PTH: 160 pg/mL (17 pmol/L)
  - Phosphate: 4.2 mg/dL (1.4 mmol/L)

# CASE STUDY: “TOBY”

- **What is the best next step?**
  - A. Advise the patient to start a phosphate-restricted diet.
  - B. Measure concentration of 25(OH) vitamin D.
  - C. Initiate active vitamin D.
  - D. Measure FGF23 to estimate phosphate burden.



# CHAPTER 4.3

## TREATMENT OF BONE WITH BISPHOSPHONATES, OTHER OSTEOPOROSIS MEDICATIONS, AND GROWTH HORMONE

# TREATMENT OPTIONS

**4.3.1:** In patients with CKD G1–G2 with osteoporosis and/or high risk of fracture, as identified by World Health Organization 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 and osteoporosis and/or high risk of fracture, as identified by World Health Organization criteria, we suggest treatment as for the general population (2B).

# TREATMENT OPTIONS

**New 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).

**Old 4.3.3:** In patients with CKD G3a–G3b 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).

# TREATMENT OPTIONS

**New 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).

**Old 4.3.4:** In patients with CKD G4–G5D having biochemical abnormalities of CKD-MBD, and low BMD and/or fragility fractures, we suggest additional investigation with bone biopsy prior to therapy with antiresorptive agents (2C).

# RATIONALE FOR UPDATE

- Rec. 3.2.2 now addresses the indications for a bone biopsy prior to antiresorptive and other osteoporosis therapies. Therefore, the old Rec. 4.3.4 was removed, and Rec. 4.3.3 was broadened from CKD G3a-G3b to CKD G3a-G5D.



# TREATMENT OPTIONS

**4.3.4:** In children and adolescents with CKD G2–G5D and related height deficits, we recommend treatment with recombinant human growth hormone when additional growth is desired, after first addressing malnutrition and biochemical abnormalities of CKD-MBD (1A).

# CHAPTER 5

## EVALUATION AND TREATMENT OF KIDNEY TRANSPLANT BONE DISEASE

# ASSESSMENT

**5.1:** In patients in the immediate post–kidney transplant period, we recommend measuring serum calcium and phosphate at least weekly, until stable (1B).

**5.2:** In patients after the immediate post–kidney transplant period, it is reasonable to base the frequency of monitoring serum calcium, phosphate, and PTH on the presence and magnitude of abnormalities, and the rate of progression of CKD (Not Graded).

# ASSESSMENT

## 5.2 (cont'd): Reasonable monitoring intervals would be:

- In CKD G1T–G3bT, for serum calcium and phosphate, every 6–12 months; and for PTH, once, with subsequent intervals depending on baseline level and CKD progression.
- In CKD G4T, for serum calcium and phosphate, every 3–6 months; and for PTH, every 6–12 months.
- In CKD G5T, for serum calcium and phosphate, every 1–3 months; and for PTH, every 3–6 months.
- In CKD G3aT–G5T, measurement of alkaline phosphatases annually, or more frequently in the presence of elevated PTH (see Chapter 3.2).

In CKD patients receiving treatments for CKD-MBD, or in whom biochemical abnormalities are identified, it is reasonable to increase the frequency of measurements to monitor for efficacy and side effects (Not Graded).

It is reasonable to manage these abnormalities as for patients with CKD G3a–G5 (see Chapters 4.1 and 4.2) (Not Graded).

# ASSESSMENT/TREATMENT

**5.3:** In patients with CKD G1T–G5T, we suggest that 25(OH)D (calcidiol) levels might be measured, and repeated testing determined by baseline values and interventions (2C).

**5.4:** In patients with CKD G1T–G5T, we suggest that vitamin D deficiency and insufficiency be corrected using treatment strategies recommended for the general population (2C).



# ASSESSMENT

**New 5.5:** In patients with CKD G1T–G5T with risk factors for osteoporosis, we suggest that BMD testing be used to assess fracture risk if results will alter therapy (2C).

**Old 5.5:** In patients with an estimated glomerular filtration rate greater than approximately 30 ml/min per 1.73 m<sup>2</sup>, we suggest measuring BMD in the first 3 months after kidney transplant if they receive corticosteroids, or have risk factors for osteoporosis as in the general population (2D).

# ASSESSMENT

**New 5.5:** In patients with CKD G1T–G5T with risk factors for osteoporosis, we suggest that BMD testing be used to assess fracture risk if results will alter therapy (2C).

**Old 5.7:** In patients with CKD G4T–5T, we suggest that BMD testing not be performed routinely, because BMD does not predict fracture risk as it does in the general population and BMD does not predict the type of kidney transplant bone disease (2B).

# RATIONALE FOR UPDATE

- 2009 Rec. 5.5 (addressing CKD transplant patients with  $\text{eGFR} > 30 \text{ ml/min/1.73 m}^2$ ) and Rec. 5.7 (addressing CKD G4T-G5T) were combined to yield 2017 Rec. 5.5.
- There is growing evidence that DXA BMD predicts fractures in patients with CKD across the spectrum of CKD data.

# TREATMENT

**New 5.6:** In patients in the first 12 months after kidney transplant with an estimated glomerular filtration rate greater than approximately 30 ml/min per 1.73 m<sup>2</sup> and low BMD, we suggest that treatment with vitamin D, calcitriol/alfacalcidol, and/or antiresorptive agents be considered (2D).

- We suggest that treatment choices be influenced by the presence of CKD-MBD, as indicated by abnormal levels of calcium, phosphate, PTH, alkaline phosphatases, and 25(OH)D (2C).
- It is reasonable to consider a bone biopsy to guide treatment (Not Graded).

There are insufficient data to guide treatment after the first 12 months.

# TREATMENT

**Old 5.6:** In patients in the first 12 months after kidney transplant with an estimated glomerular filtration rate greater than approximately 30 ml/min per 1.73 m<sup>2</sup> and low BMD, we suggest that treatment with vitamin D, calcitriol/alfacalcidol, or bisphosphonates be considered (2D).

- We suggest that treatment choices be influenced by the presence of CKD–MBD, as indicated by abnormal levels of calcium, phosphorus, PTH, alkaline phosphatases, and 25(OH)D (2C).
- It is reasonable to consider a bone biopsy to guide treatment, specifically before the use of bisphosphonates due to the high incidence of adynamic bone disease (Not Graded).

There are insufficient data to guide treatment after the first 12 months.



# RATIONALE FOR UPDATE

- The second bullet is revised, consistent with the new bone biopsy recommendation (i.e., 2017 Rec. 3.2.2).

# TREATMENT

**5.7:** In patients with CKD G4T–G5T with known low BMD, we suggest management as for patients with CKD G4–G5 not on dialysis, as detailed in Chapters 4.1 and 4.2 (2C).

# KEY MESSAGES

- Prospective studies evaluating BMD testing in adults with CKD represent a substantial advance since the original guideline from 2009, making a reasonable case for BMD testing if the results will impact future treatment.
- It is important to emphasize the interdependency of serum calcium, phosphate, and PTH for clinical therapeutic decision-making.
- Phosphate-lowering therapies may only be indicated in the case of “progressive or persistent hyperphosphatemia”.
- New evidence suggests that excess exposure to exogenous calcium in adults may be harmful in all severities of CKD, regardless of other risk markers.

# KEY MESSAGES

- It is reasonable to limit dietary phosphate intake, when considering all sources of dietary phosphate (including “hidden” sources).
- The PRIMO and OPERA studies failed to demonstrate improvements in clinically relevant outcomes but did demonstrate increased risk of hypercalcemia. Accordingly, routine use of calcitriol or its analogs in CKD G3a-G5 is no longer recommended.
- No consensus was reached to recommend cinacalcet as first-line therapy for lowering PTH in all patients with SHPT and CKD G5D.

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