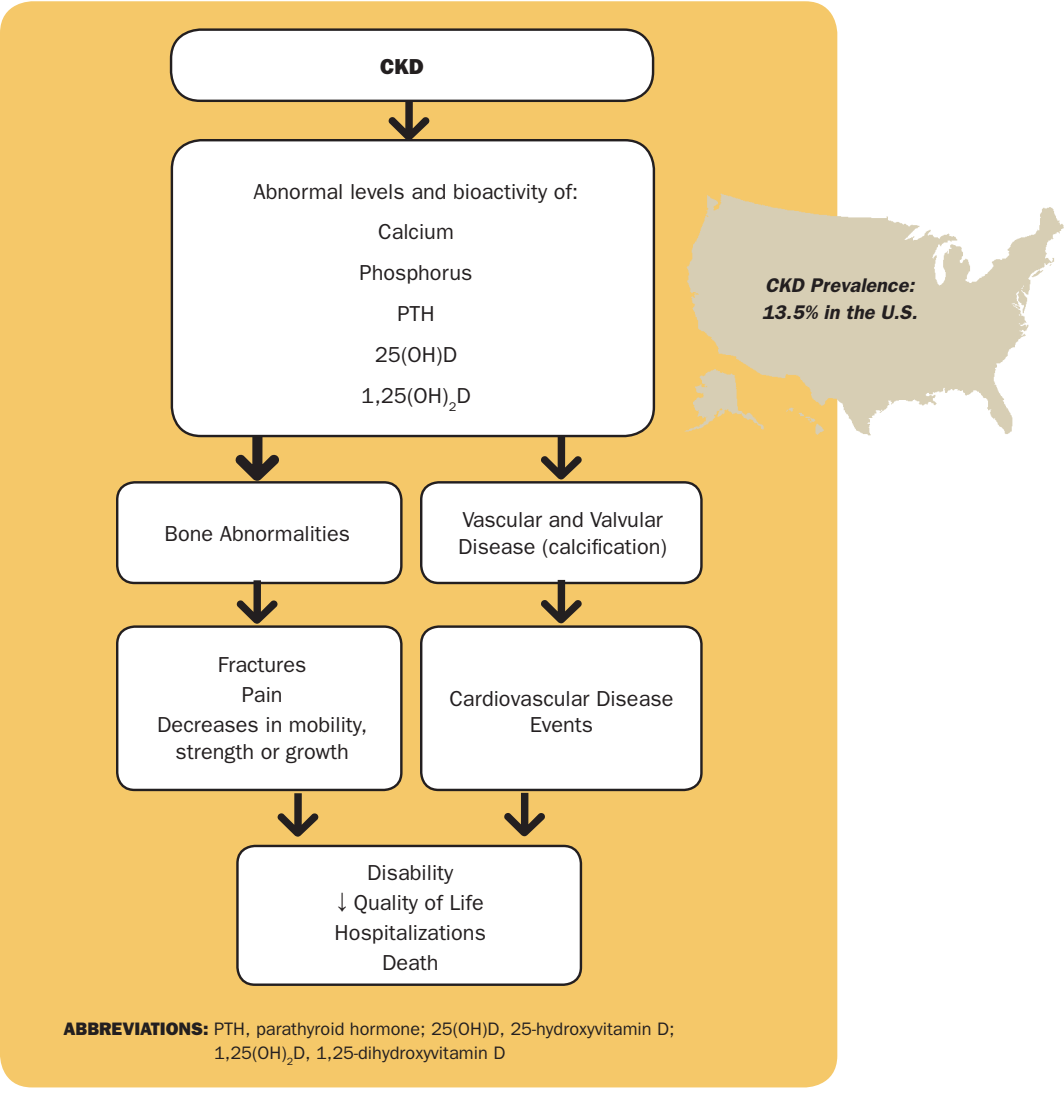
National Kidney Foundation®

KDOQI

Evaluation and Treatment of Chronic Kidney Disease-Mineral and Bone Disorder (CKD-MBD)



Based on selected guidelines from the KDOQI U.S. Commentary on the 2009 KDIGO Clinical Practice Guideline for the Diagnosis, Evaluation, Prevention and Treatment of CKD-MBD[1].

Summary of KDIGO Recommendations[2] on Evaluation

CKD Stages 3-5 and Dialysis (D)

	BIOCHEMICAL COMPONENTS				BONE			BLOOD VESSELS
CKD STAGE (GFR IN mL/ min/1.73 m²)	**Ca,P**	**PTH**	**ALP**	**25(OH)D**	**BONE-SPECIFIC ALP**	**BONE BIOPSY**	**BMD**	**CALCIFICATION**
Stage 3 (30–59)	Once (1C);§ then every 6 – 12 months (NG)*	Once (1C);§ then based on level and CKD progression (NG)	Once (1C) §	Once (2C); then based on level and treat-ments (2C)	Can be used to evaluate bone disease (2B)	In various settings and before treatment with bisphospho-nates (NG)	No routine testing in presence of CKD-MBD (2B)	Routine screening not recommended
Stage 4 (15–29)	Every 3 – 6 months (NG)	Every 6 – 12 months (NG)	Every 12 months†† (NG)					
Stage 5 (<15 or dialysis)	Every 1 – 3 months (NG)	Every 3 – 6 months (NG)						

ABBREVIATIONS: 25(OH)D, 25-hydroxyvitamin D (calcidiol); ALP, alkaline phosphatase; BMD, bone mineral density; Ca, calcium; GFR, glomerular filtration rate; P, phosphorus; PTH, parathyroid hormone.

§ In children, monitoring of Ca, P, ALP is suggested beginning in CKD stage 2 (2D).

†† More frequently in presence of elevated PTH

Base the frequency of laboratory measurements on presence and magnitude of abnormalities and rate of CKD progression. Increase frequency intervals as needed to monitor for trends, treatment efficacy and side effects. ***G 3.1.2 (NG)***

Base therapeutic decisions on trends rather than a single laboratory value, taking into account all available CKD-MBD assessments. ***G 3.1.4 (1C)***

Highlights from the **KDOQI** Commentary

- The practitioner needs to review patterns and temporal trends to make clinical decisions. No data support a specific testing frequency.
- This statement provides the necessary flexibility for more frequent measurement when levels are changing rapidly and to monitor the effects of treatments, including potential adverse effects.
- Clinicians need to standardize within their outpatient clinical practices and dialysis units the method of sample collection, processing and assays used.

***ON ALL PAGES OF THIS TOOL,** the number and letters in parentheses refer to strength of recommendation (see table on back cover); NG - statement NG

CKD Stages 1-5 Transplant (T)

	BIOCHEMICAL COMPONENTS†				BONE	
CKD STAGE (GFR IN mL/ min/1.73 m²)	**Ca, P**	**PTH**	**ALP**	**25(OH)D**	**BONE BIOPSY**	**BMD**
Stage 1T (>90)	Every 6 – 12 months (NG)	Once and then based on level and CKD progression (NG)	Every 12 months§ (NG)	Once and then based on level and treatments (2C)	Consider to guide treatment, specifically before treatment with bisphosphonates (NG)	In first 3 mo post-transplant if patient receives corticosteroids or has risk factors for osteoporosis (2D)
Stage 2T (60-89)						
Stage 3T (30–59)						
Stage 4T (15–29)	Every 3 – 6 months (NG)	Every 6 – 12 months (NG)				No routine testing (2B)
Stage 5T (<15)	Every 1 – 3 months (NG)	Every 3 – 6 months (NG)				

ABBREVIATIONS: 25(OH)D, 25-hydroxyvitamin D (calcidiol); ALP, alkaline phosphatase; BMD, bone mineral density; Ca, calcium; GFR, glomerular filtration rate; P, phosphorus; PTH, parathyroid hormone; T, transplant.

§ More frequently in presence of elevated PTH

It is suggested that in patients with CKD stages 3-5D, individual values of serum calcium and phosphorus, elevated together, be used to guide clinical practice rather that the mathematical construct of the calcium-phosphorus product (Ca x P). ***G 3.1.5 (2D)***

Highlights from the **KDOQI** Commentary

- Assessment of CKD-MBD should begin in stage 3. In CKD stage 3, some patients have already developed abnormalities of CKD-MBD, in particular, secondary hyperparathyroidism (SHPT). However, the rate of change and severity of abnormalities are highly variable among patients.
- For dialysis provider performance measures that typically focus on laboratory values at a single point in time, the recommendation to consider trends over time has significant implications.

Biochemical Abnormalities in Kidney Transplant Recipients[†]

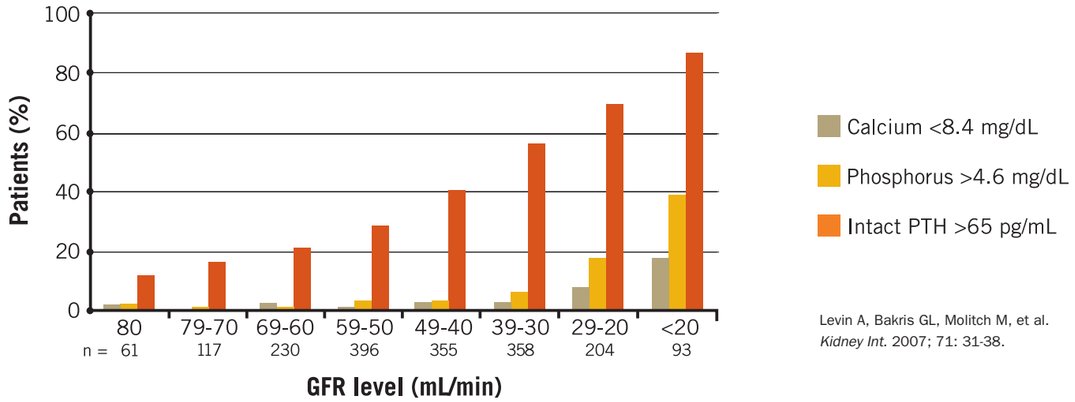
DURING IMMEDIATE POST-TRANSPLANT PERIOD (GENERALLY LESS THAN 12 MONTHS)	AFTER IMMEDIATE POST-TRANSPLANT PERIOD (GENERALLY GREATER THAN 12 MONTHS)
Glomerular filtration rate (GFR) rapidly changing.	More stable graft function achieved.
Hypophosphatemia occurs in a large proportion of patients.	Serum phosphorus returns to normal for most patients.
Serum calcium tends to normalize after transplant. Serum calcium stabilizes at the higher end of the normal range within 2 months.	
PTH levels decrease significantly during the first 3 months.	PTH typically stabilizes at elevated values.
	Low levels of $1,25(OH)_2D$ typically do not reach normal values until almost 18 months.

ABBREVIATION: $1,25(OH)_2D$, 1,25-Dihydroxyvitamin D.

+Scope and magnitude of the biochemical abnormalities fluctuate dramatically in early post-transplant compared with late post-transplant period.

Recommendation: Clinical laboratories should inform clinicians of the actual assay method in use and report any change in methods, sample source (plasma or serum), and handling specifications to facilitate appropriate interpretation of biochemistry data. ***G 3.1.6 (1B)***

Prevalence of Abnormal Serum Calcium, Phosphorus, and Intact PTH by GFR



Levin A, Bakris GL, Molitch M, et al. *Kidney Int.* 2007; 71: 31-38.

Sources and Magnitude of the Variation in the Measurement of Serum Calcium, Phosphorus, PTH, and Vitamin D Sterols

VARIABLE	CALCIUM	PHOSPHORUS	PTH	VITAMIN D STEROLS
COEFFICIENT OF VARIATION	+	+	++	++
DIURNAL VARIATION	+	++	++	–
SEASONAL VARIATION				++
VARIATION WITH MEALS	+	+	+	–
VARIATION WITH DIALYSIS TIME	+	+		
ASSAY VALIDITY	+++	+++	+	+

PTH, parathyroid hormone; +, minimal or low; ++ , moderate; +++, high or good; –, no variability; blank space, not tested.

Highlights from the **KDOQI** Commentary

- Ultimately, the practitioner in the U.S. needs to individualize the decision for whether, when and how often to measure vitamin D and below what threshold and to what target range to treat.
- The serum vitamin D level that represents “sufficiency” is the subject of an ongoing debate and is complicated by variability in measurements of vitamin D compounds.
- Most immunoassays have reasonably good precision. Using liquid chromatography-mass spectroscopy to measure 25-hydroxyvitamin D has excellent precision.
- Analytic problems with PTH measurement include: (1) poor standardization among different PTH assays, (2) high biological variation within individuals, and (3) uncertainty about the role of unmeasured PTH fragments.

Evaluation of CKD–MBD:
Bone

No single diagnostic procedure or test can accurately evaluate the broad spectrum of bone disorders that can occur in CKD.

Suggestions: The gold standard diagnosis for the bone component of CKD-MBD is bone biopsy-based histological analysis in patients with CKD stages 3-5D.

- Routine bone mineral density (BMD) testing is not suggested, because it does not predict fracture risk as it does in the general population or predict the type of renal osteodystrophy. ***G 3.2.2 (2B)***
- Serum PTH or bone-specific alkaline phosphatase can be used to evaluate bone disease because markedly high or low values predict underlying bone turnover. ***G 3.2.3 (2B)***
- Routine measurement of bone-derived turnover markers of collagen synthesis and breakdown is not suggested. ***G 3.2.4 (2C)***

It is reasonable to perform a bone biopsy in various settings including but not limited to: ***G 3.2.1 (NG)***

- Unexplained fractures
- Persistent bone pain
- Unexplained hypercalcemia
- Unexplained hypophosphatemia
- Possible aluminum toxicity
- Prior to therapy with bisphosphonates in patients with CKD-MBD.

Highlights from the **KDOQI** Commentary

- The value of alkaline phosphatase in clinical decision-making remains to be proved.
- Bone specific alkaline phosphatase derives more specifically from bone, but the test is not readily available.
- In the U.S., wide implementation of the bone biopsy statement would require a great pool of individuals with proficiency in the interpretation of bone biopsy.
- Because bone biopsy is not feasible in most patients, serum markers may be useful, especially when values are very abnormal.
- Although there is a large number of elderly with CKD stage 3 and low BMD, the statement that bone biopsy is reasonable prior to therapy with bisphosphonates applies only to those who have CKD-MBD, which in practical terms means increased PTH or phosphate level.
- Bone biopsy should be considered in patients for whom the cause of clinical symptoms and biochemical abnormalities is not certain and for whom the effect of treatment needs to be assessed.

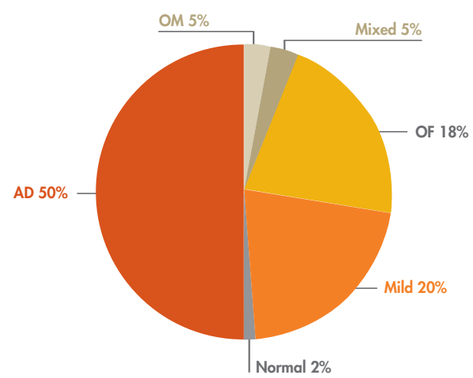
FRACTURES

Compared to age-matched controls, patients with CKD stages 3-5D and 1T-5T have an increased risk of fractures that can result in significant disability and mortality.

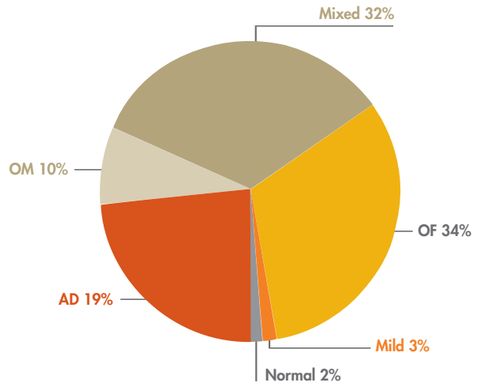
Bone formation (turnover) is high in those with osteitis fibrosa and mild disease, and low in those with osteomalacia and adynamic bone disease. Mineralization is abnormal in those with osteomalacia and mixed disease.

Bone fragility is due to varying combinations of low bone mineral content and abnormal bone quality.

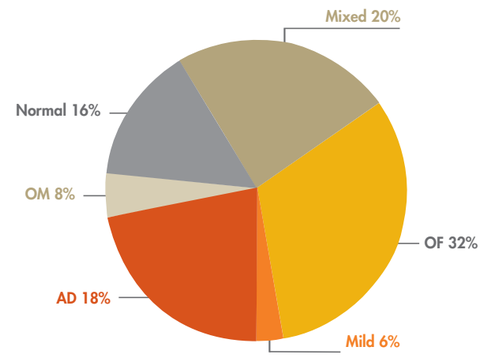
Peritoneal Dialysis



Hemodialysis



CKD STAGES 3-5



PREVALENCE OF TYPES OF BONE DISEASE AS DETERMINED BY BONE BIOPSY IN PATIENTS WITH CKD-MBD.

AD, adynamic bone disease; OF, osteitis fibrosa; OM, osteomalacia.

Bone Abnormalities in Kidney Transplant Recipients (KTRs)

BACKGROUND

- In non-kidney-transplant recipients, a low BMD or loss of BMD predicts fracture, but data are lacking for kidney transplant recipients.
- The risk of fractures after kidney transplant is high.

Most transplant patients have preexisting bone disease of CKD (CKD-MBD), but new insults to bone can also occur after transplant. → Fractures and morbidity

Bone mineral density (BMD) rapidly decreases in the first 6-12 months and continues to decrease at a lower rate for many years.

Influencing Factors:
- Deleterious effects of immunosuppressive agents
- Impaired kidney function
- Hypogonadism
- Diabetes
- Smoking
- Lack of physical activity
- Time on dialysis and transplantation

→ Post-transplant bone disease

Highlights from the KDOQI Commentary

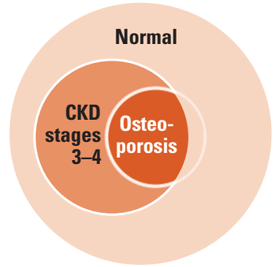
- The uncertainty surrounding the value of BMD for predicting underlying bone disease, fracture or other clinical outcomes in KTRs increases with more advanced stages of CKD.
- CKD-MBD in KTRs is an even more heterogeneous disease than in nontransplant patients. It is the consequence of many different factors, including pretransplant CKD-MBD, effects of immunosuppressive drugs, level of kidney function recovery and risk factors for osteoporosis.
- Although routine testing for BMD in patients with CKD stages 4-5T is discouraged, some patients may still undergo testing that shows low BMD. This discretionary recommendation suggests that these individuals be referred to as having low BMD rather than osteoporosis.

Definition of Renal Osteodystrophy

Renal osteodystrophy (ROD) is an alteration of bone morphology in patients with CKD.

It is one measure of the skeletal component of the systemic disorder of CKD-MBD that is quantifiable by histomorphometry of bone biopsy.*

Overlap Between Osteoporosis and CKD Stages 3–4
Most of this overlap is seen because both CKD and bone loss increase considerably with age.



OSTEOPOROSIS OR ROD?

- The pathogenesis of bone disease in patients with CKD-MBD is different from that in postmenopausal osteoporosis. Therefore, extrapolating results of studies from osteoporosis to patients with CKD stages 3-5D may not be valid, especially with concerns of long term safety.
- Osteoporosis is traditionally diagnosed as low bone mineral density (BMD).
  - » Most patients with postmenopausal or age-related osteoporosis have early stages of CKD.
  - » Patients with more advanced stages of CKD, in whom the biochemical abnormalities of mineral metabolism that define CKD-MBD are present, have ROD.
  - » Both ROD and idiopathic osteoporosis can lead to increased bone fragility and fractures, but have different pathophysiological backgrounds.
- Given the pathophysiologic and diagnostic differences between ROD and idiopathic osteoporosis, the definition of "osteoporosis" in adults is most appropriate only for those in CKD stages 1-3. In later CKD stages, those with low BMD should be designated as having CKD-MBD with low BMD.

*** CHRONIC KIDNEY DISEASE-MINERAL AND BONE DISORDER**

A systematic disorder of mineral and bone metabolism due to CKD manifested by either one or a combination of the following:

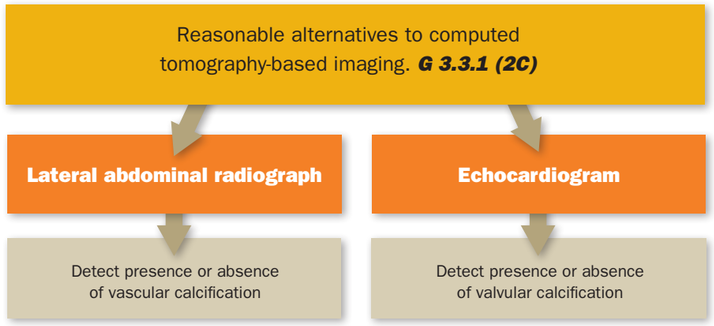
- Abnormalities of calcium, phosphorus, PTH, or vitamin D metabolism
- Abnormalities in bone turnover, mineralization, volume, linear growth or strength
- Vascular or other soft tissue calcification

Evaluation of CKD–MBD:
Vascular Calcification

Suggestion: Patients with CKD stages 3-5D with known vascular/valvular calcification be considered at the highest cardiovascular risk. ***G 3.3.2 (2A)***

- The prevalence and severity of calcification of the arteries and cardiac valves increase as kidney function decreases.
- Calcification is more severe and follows an accelerated course in people with CKD compared with healthy people.
- The presence and severity of cardiovascular calcification predict cardiovascular morbidity and mortality.
- The approach to all patients with calcification should be to minimize CVD risk factors and control biochemical parameters of CKD-MBD.

Screening for Calcification



Highlights from the **KDOQI** Commentary

- The approach to atherosclerosis-related cardiovascular calcification is extrapolated from the general population, but this approach may or may not apply to everyone in the CKD population, especially in CKD stage 5D.
- In the U.S., screening of asymptomatic patients for calcification is not suggested.
- If the clinician wants to perform untargeted testing for calcification, "using lateral abdominal radiography and echocardiography provides as much or as little useful information as the more costly tests using CT-based imaging."
- It is reasonable to use this information to guide the management of CKD-MBD. However, it has not been shown that modification of treatment strategies based on calcification tests can achieve better patient outcomes.

Treatment of Abnormal PTH Levels

Severe hyperparathyroidism (HPT) is associated with morbidity and mortality in patients with CKD stages 3–5. Observational studies consistently report an increased relative risk of death in CKD stage 5D patients who have PTH values at the extremes (less than two or greater than nine times the upper normal limit of the assay).

Once developed, severe HPT may be resistant to medical/pharmacological therapy and may persist following transplantation.

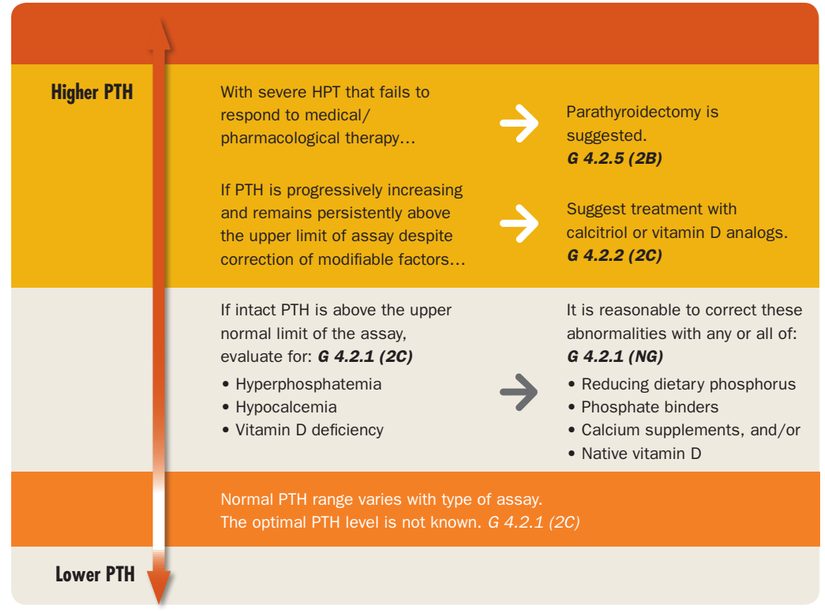
PROGRESSIVE INCREASES OF PTH SHOULD BE AVOIDED.

- Marked changes in PTH levels should trigger a response to avoid a future level outside the range.
- Decreased vitamin D production, hypocalcemia and phosphorus retention lead to secondary HPT.
- Accurate measurement of PTH is valuable for diagnosis and treatment.

Establishing narrow target ranges for serum intact PTH is difficult because:

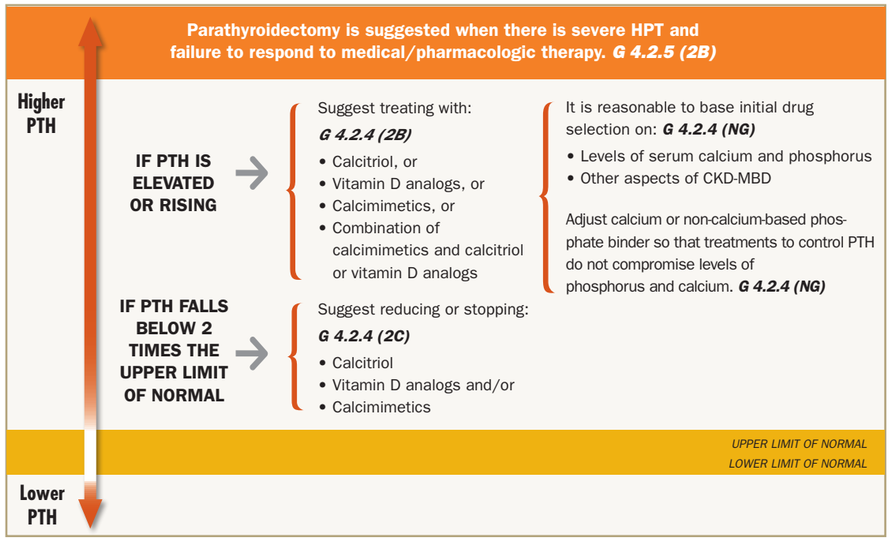
- Studies demonstrate that the median intact PTH increases and the range widens with progressive CKD.
- There are methodologic problems with the measurement of PTH, because assays differ in their measurement of accumulating PTH fragments and there is interassay and biological variability.
- The predictive value of PTH for underlying bone histology is poor when PTH values are between approximately two and nine times the upper normal laboratory range according to the assay used.

CKD Stages 3-5 ND



CKD Stage 5D

Suggestion: Maintain PTH at approximately 2 to 9 times upper normal limit for assay. If PTH changes markedly in either direction within this range, initiate or change therapy to avoid progression to levels outside this range. ***G 4.2.3 (2C)***



Highlights from the **KDOQI** Commentary

- The suggested PTH level range for patients with CKD stage 5D is not supported by high-quality evidence.
  - To date, no randomized controlled trial has examined whether treatment to achieve a specific PTH target improves clinical outcomes.
  - For stage 5D, the suggested action of maintaining intact PTH levels in the range of approximately 2-9 times the upper reference range limit is discretionary.
  - The PTH level suggested by KDIGO corresponds to 120-660 pg/mL (depending on the assay).
  - The point at which PTH level is associated with all cause mortality varies between 400-600 pg/mL.
  - This gives flexibility to U.S. practitioners in using and adjusting treatments that are effective in decreasing PTH levels, despite lack of proof of a clinical benefit of a specific range.
  - In stage 5D, caution should be exercised to avoid hypercalcemia and increases in serum phosphorus.
  - The number of parathyroidectomies in the U.S. has decreased in the past 10-15 years given the effectiveness of medical treatment of SHPT and lack of evidence showing clear superiority of parathyroidectomy on meaningful clinical outcomes. However, in patients with acceptable surgical risk in whom medical therapy has failed, parathyroidectomy performed by an expert surgeon effectively decreases PTH, calcium, and phosphorus levels.

Management of Vitamin D Deficiency/Insufficiency

Vitamin D is an important therapeutic consideration in SHPT.

In patients with CKD stages 3-5 not on dialysis therapy in whom serum PTH levels are progressively rising and remain persistently above the upper limit of normal for the assay despite correction of modifiable factors, we suggest treatment with calcitriol or vitamin D analogues. ***G 4.2.2 (2C)***

*In CKD stages 3-5D, [**G 3.1.3 (2C)**] and stages 1-5T [**G 5.4 (2C)**] we suggest vitamin D deficiency and insufficiency be corrected using treatment strategies recommended for the general population.*

Vitamin D Deficiency and Insufficiency

are associated with

- Cardiovascular disease
- Autoimmune disorders
- Malignancies
- Bone disease
- Musculoskeletal weakness
- Insulin resistance

Supplementation with either ergocalciferol or cholecalciferol is recommended, but the optimal treatment regimen is not known.

The primary source of vitamin D is sunlight, and the increased risk of skin cancer in kidney transplant patients mandates the use of appropriate sunscreen protection, further increasing the need for oral intake of vitamin D.

Highlights from the **KDOQI** Commentary

- The U.S. practitioner needs to individualize the decision about the threshold to treat.
- Recommendations for vitamin D repletion in the general population specify a cholecalciferol dose of 1,000-2,000 IU/d. However, a more aggressive dosing regimen may be used in patients with CKD.
- There are no data supporting the clinical superiority of any vitamin D analogues available in the U.S. compared with calcitriol or placebo.

Beyond Biochemical Targets Alone:
An Approach to Risk Based on Multiple Parameters

CKD STAGE (GFR mL/min/1.73 m²)	SERUM PHOSPHORUS	SERUM CALCIUM
STAGE 3 (30–59)	Maintain within normal range ***G 4.1.1 (2C)***	Maintain within normal range ***G 4.1.2 (2D)***
STAGE 4 (15–29)		
STAGE 5 (<15)		
STAGE 5D	Lower toward the normal range ***G 4.1.1 (2C)***	
KIDNEY TRANSPLANT RECIPIENT	Manage as in patients with CKD stages 3-5 (nondialysis) ***G 5.2 (NG)***	

Hypercalcemia after kidney transplantation is usually due to hyperparathyroidism (HPT) that persists from the preceding CKD period. Increased serum calcium concentration can persist for years after transplantation.

Parathyroid gland hyperplasia, especially autonomous parathyroid growth, does not easily resolve after recovery of kidney function, except in mild cases or when secondary to vitamin D deficiency.

In patients with nonsuppressible nodular parathyroid hyperplasia, persistently elevated PTH levels after restoration of normal renal function with a transplant may have a primary role in maintaining a high bone turnover.

Abnormal PTH secretion persists in 30% to 50% of recipients.

Managing Hyperphosphatemia

	DIET	PHOSPHATE BINDERS AND OTHER MEDICATIONS	DIALYTIC PHOSPHATE REMOVAL
CKD stages 3-5 and kidney transplant recipients (KTRs) with hyperphosphatemia	Suggest limiting dietary phosphate intake alone or in combination with other treatments ***G 4.1.7 (2D)***	Suggest using phosphate binders ***G 4.1.4 (2D)***, taking into account (NG): • CKD stage • Presence of other components of CKD-MBD • Concomitant therapies • Side effect profile	N.A.
CKD stages 3-5 and KTRs with hyperphosphatemia and persistent or recurrent hypercalcemia		Recommend restricting dose of: ***G 4.1.5 (1B)*** • Calcium-based phosphate binders and/or • Calcitriol or vitamin D analogue	
CKD stages 3-5 and KTRs with hyperphosphatemia and arterial calcification and/or adynamic bone disease and/or persistently low PTH levels		Suggest restricting the dose of calcium-based phosphate binders ***G 4.1.5 (2C)***	
CKD stage 5D		Suggest using phosphate binding agents. ***G 4.1.4 (2B)*** Suggest the choice of agent should take into account: ***G 4.1.4 (NG)***: • CKD stage • Presence of other components of CKD-MBD • Concomitant therapies • Side effect profile	Suggest increasing dialytic phosphate removal in the treatment of hyperphosphatemia ***G 4.1.8 (2C)***.

Highlights from the **KDOQI** Commentary

Diet Recommendations

- Dietary phosphate restriction could not be strongly endorsed as a primary intervention for the management of CKD-MBD due to insufficient data.
- While dialysis unit dietitians can counsel patients regarding phosphorus and protein intake, dietary counseling is more difficult to obtain in other settings for patients not on dialysis.
- Dietary phosphorus restriction can:
  - Keep phosphorus normal in CKD 3-5
  - Serve as an adjunct to other methods in dialysis patients.
- Adequate protein intake should be maintained.
- In the U.S., processed and fast foods account for a significant portion of dietary phosphorus.

Phosphate Binder Recommendations

- The suggested course of action allows individualization of therapy.
- It also provides flexibility to choose a binder based on its profile of effects and side effects and allows combining binders to minimize side effects from high doses of one agent.
- There is no proven superiority of any one drug or class for clinical outcomes.
- It has not been examined in placebo-controlled randomized trials whether lowering hyperphosphatemia decreases mortality and morbidity.
- Clinicians should discuss the potential benefits and harms of drug therapy with their patients.
- Individualize decision-making based on patient and clinical differences.
- Treatment to achieve a serum phosphorus level within the reference range may not be possible because:
  - The number of pills is too large, or
  - Dietary restriction may affect quality of life.
- Note that mobilization of phosphorus from the skeleton is not affected by binder treatment.

Dialytic Phosphate Recommendations

- In the U.S., the most common prescription is thrice-weekly hemodialysis, typically for 3.5 to 4 hours per session. Any deviation from this delivery model encounters logistic, administrative and financial challenges.
- Studies of clinical outcomes comparing conventional to more extended or more frequent dialysis is needed to support changes in the status quo.
- No evidence supports clinically meaningful differences in phosphorous removal among different dialysis membranes or dialyzers in current routine use.

Managing Serum Calcium

In patients with CKD stages 3-5D, we suggest maintaining serum calcium levels in the reference range. ***G 4.1.2 (2D)***

Highlights from the KDOQI Commentary

- The threshold for high calcium levels associated with an increased relative risk for all-cause mortality is 9.5 to 11.4 mg/dL (varies among studies).
- A calcium level outside the reference range requires evaluation for treatment effects or other causes.
- Not known:
  - * At what level of low serum calcium does risk increase?
  - * Does treatment-related hypocalcemia confer a risk similar to that of identical calcium levels not related to treatment?

In patients with CKD stage 5D, we suggest using a dialysate calcium concentration between 1.25 and 1.50 mmol/L (2.5 and 3.0 mEq/L). ***G 4.1.3 (2D)***

Highlights from the KDOQI Commentary

- In stage 5D, the U.S. practitioner needs to use judgment for PD and HD patients about lowering dialysate calcium concentration.
- Selecting the dialysate concentration requires consideration of:
  - * Patient's calcium levels and other components of CKD-MBD
  - * Concomitant therapies with phosphate binders, calcitriol, vitamin D analogues or calcimimetics and treatment goals
  - * In the absence of robust data, the practitioner should weigh safety concerns in determining the optimal dialysate concentration.

Managing Bone Abnormalities

CKD STAGES 1 and 2	With osteoporosis and/or high risk of fracture, as identified by World Health Organization (WHO) criteria…	Manage as per general population. ***G 4.3.1 (1A)***
CKD STAGE 3	With PTH in the normal range and osteoporosis and/or high risk of fracture, as identified by WHO criteria…	Treat as per the general population. ***G 4.3.2 (2B)***
	With biochemical abnormalities of CKD-MBD and low BMD and/or fragility fractures…	Suggest treatment choices taking into account the magnitude and reversibility of the biochemical abnormalities and the progression of CKD, with consideration of a bone biopsy. ***G 4.3.3 (2D)***
CKD STAGES 4 -5 D	With biochemical abnormalities of CKD-MBD and low BMD and/or fragility fractures…	Perform additional investition with bone biopsy prior to therapy with antiresorptive agents. ***G 4.3.4 (2C)***

Highlights from the KDOQI Commentary

- Given the high prevalence of early stages of CKD in elderly patients who are likely to have osteoporosis, this recommendation calls attention to the need to evaluate fracture risk in this population and treat accordingly.
- In patients in whom HPT has been corrected, GFR is stable and risk of a fracture outweighs the potential long-term risk of inducing irreversible low bone turnover, therapy with bisphosphonates may be considered.
- If therapy with bisphosphonates is given, lower dose and shorter treatment duration should be considered.
- In individuals with CKD stages 4-5D and biochemical evidence of CKD-MBD, trial data for the efficacy and safety of antiresorptive agents are lacking. A bone biopsy is suggested before therapy with bisphosphonates, teriparatides or raloxifene.

KTRs With Low BMD in Immediate Post-Kidney-Transplant Period

CKD STAGES 1–3T GFR >30 mL/min/1.73 m² with low BMD	Consider treatment with vitamin D, calcitriol/alphacalcidiol, or bisphosphonates in the first 12 months. ***G 5.6 (2D)*** Base treatment choices on presence of CKD-MBD, as indicated by abnormal levels of calcium, phosphorus, PTH, alkaline phosphatases, and 25(OH)D. ***G 5.6 (2C)*** Consider bone biopsy to guide treatment, specifically before the use of bisphosphonates due to the high incidence of adynamic bone disease. ***G 5.6 (NG)*** There are insufficient data to guide treatment after the first 12 months.
CKD STAGES 4–5T GFR <30 mL/min/1.73 m² with low BMD	Suggest management as for patients with CKD stages 4–5 not on dialysis. ***G 5.8 (2C)***

Highlights from the **KDOQI** Commentary

- In patients with CKD stages 4-5T, it seems prudent that treatment with bone-specific therapies other than those aiming at correcting abnormalities of calcium, phosphorus, PTH and vitamin D levels would be guided by a bone biopsy.
- Treatment data from the general population without CKD, patients with CKD without a kidney transplant, or other solid-organ transplant patients without CKD-MBD cannot be directly extrapolated.

Implementation of the guideline recommendations in outpatient dialysis patients is likely to be affected greatly by the introduction of new payment policies created through the Medicare Improvements for Patients and Providers Act of 2008 (MIPPA).

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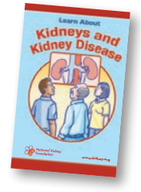

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Grade for Strength of Recommendation	Strength	Wording	Grade for Quality of Evidence	
Level 1	Strong	"We recommend…should"	A	High
			B	Moderate
Level 2	Weak	"We suggest…might"	C	Low
			D	Very Low

NOTE: Ungraded statements (NG) are used in areas where guidance was based on common sense and/or the question was not specific enough to undertake a systematic evidence review.

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